Fatigue at the Workplace: Measurement and Temporal Development

by

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Authors Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final versions, as accepted by my examiners.

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Abstract

Fatigue at the workplace has been described as a multidimensional construct, affecting the overall state of the whole organism, which may be a consequence of prolonged work and various psychological, socioeconomic, and environmental factors. In the short term, fatigue may lead to discomfort, diminished motor control, reduced proprioception, increased force variability, and reduced strength capability, resulting in reduced performance, lowered productivity, deficits in work quality, and increased incidence of accidents and human errors. Fatigue may also lead to longer-term adverse health outcomes such as chronic fatigue syndrome, myalgia, and burnout syndromes, and may be a precursor to WMSDs – work-related musculoskeletal disorders. If indeed fatigue is a precursor to WMSDs and other long-term health outcomes, it may then be a relevant biomarker for cumulative exposure to repetitive and/or sustained work, and thus a useful risk indicator and/or a design and evaluation tool. However, little is known of the temporal pattern of fatigue development and its relationships with disorder risks and work performance. The objective of this thesis was to identify and evaluate a battery of fatigue measures for both laboratory and field-based research, and provide insight into fatigue development in work-relevant task conditions.

Six studies were designed to address these objectives. In the first study, measures and analysis methods that detect fatigue-related changes were identified by a group of expert fatigue researchers. The second was an exploratory study focused on the responsiveness of a select number of measures during a workday and multiple workdays in realistic physically demanding residential plumbing work. In the third study, a selected number of conventional and novel measures were evaluated for their reliability and sensitivity in a controlled laboratory setting. This study also addressed the responsiveness of measures during a test battery or during the fatiguing activity (i.e., continuously), and the time between cessation of activity and test battery in which measures remain responsive. The fourth study reported on whether circadian effects were detectable by selected measures, providing insight towards the daylong reliability of these measures. In the fifth study, measures were evaluated in four fatiguing conditions, representing changes in type of contraction, intensity, and body segment. Furthermore, the pattern of fatigue development and the temporal responsiveness of measures were described. Finally, measures were assessed over an 8-hour light precision micropipetting task to investigate temporal responsiveness of measures and fatigue development. Errors were quantified and the effects of scheduled work breaks were reported.

In study 1, fifty-seven measures were identified based on outcomes and/or effects of fatigue in the workplace. Based on the perceived validity, reliability, and practicality in laboratory and field investigations, four measures were recommended for both settings: maximum voluntary contractions, questionnaires and fatigue scales, Borg's rating of perceived exercise or discomfort, and visual analog scales. On the other hand, twenty-five measures were not recommended for field studies, including methods traditionally recognized as "gold standard" in measuring cellular and metabolic changes.

In study 2, fatigue was documented in realistic physically demanding work while employing a set of measures to provide a comprehensive picture of fatigue development. Not all measures revealed increasing fatigue over the workday or over the workweek, which may be a result of measures reflecting different fatigue processes. Thus, the study reinforced the need of a complementary set of measures, reflecting multiple domains, to measure and interpret the temporal development of fatigue. Two measures, rating of perceived discomfort and grip strength, indicated significant differences within a work day, notably an increase at the beginning and end of the shift (perceived discomfort) and a decrease between mid-shift and end of shift (grip strength). It was speculated that within-day trends were consistent with central fatigue mechanisms. Over multiple workdays, both central and peripheral components displayed a significant day effect. Fatigue accumulation over the workweek was observed with grip strength, physiological resting tremor, and postural tremor measures, particularly between day 1 (Tuesday) and day 4 (Friday).

In study 3, test-retest reliability ranged between "poor agreement" and "almost perfect agreement". In terms of sensitivity, action tremor, MMG RMS amplitude, postural tremor, and rating of perceived fatigue were highly responsive. Perceived fatigue remained elevated, relative to baseline, until 11 minutes post-exercise. Postural and physiological tremor persisted from baseline until the third minute of recovery. Action tremor, however, quickly recovered within the first minute of recovery. This current study found that for most of the measures, there were no statistical differences between test battery and continuous measurement, but a few measures were approaching statistical significance. Action tremor and mechanomyography collected during a test contraction, and perceived fatigue assessed by a visual analog scale, were found to be most reliable, most responsive, comparable to continuous measures, and sensitive after the fatiguing activity, and should be considered with other measures of interest, as part of a test battery.

In study 4, only two measures revealed a statistically significant time-of-day effect: mechanomyography of a flexor forearm muscle and action tremor at 30% MVC. These two measures exhibited rhythmicity based on cosinor analysis. Therefore a degree of caution might be required when interpreting daylong fatigue with these two measures, whereas the other measures may not be susceptible to, or detect, significant diurnal effects. Although the remaining measures did not reveal statistically significant time effects, most measures were characterized with similar patterns to those found in previous literature.

In study 5, there was no one universal measure that was common, in terms of responsiveness, in all exercise conditions. Although no single measure was found to be most responsive in *all* conditions, there were measures responsive in *most* exercise conditions as either a continuous or test battery measure. This was the case with action tremor. A maximum voluntary contraction, which is dependent on processes in both central and peripheral domains, was similarly responsive. Rating of perceived fatigue, which has been cited as a centrally mediated indicator, was also found to increase with exercise progression in hand conditions. Therefore fatigue measures, reflecting changes to both central and peripheral processes, may be useful in measuring tasks and exercises of varying parameters. In this study, we support earlier investigations on the pattern of fatigue development in isometric and time-varying (e.g., intermittent isometric, concentric) contractions. The temporal responsiveness of central and peripheral measures, on the other hand, may be a better reflection of the intensity of the task. The shoulder intermittent condition was not consistent with the expected pattern for an intermittent isometric contraction. However, the study protocol may have inadvertently generated lower muscle activity, and therefore the extent of fatigue may have been minimal. There remains a need to understand complex combinations of task-dependent factors in both fatigue development and temporal responsiveness.

In study 6, nine measurement parameters revealed significant increases in fatigue over the work period. Traditional field measures (i.e., MVC and EMG) did not lead to extraordinary time effects. Error rates followed similar trends to the 9 significant measurements: an increase from baseline towards mid-morning, a slight decrease prior to the lunch break, a nadir after lunch, and increasing fatigue effects over the course of the afternoon. Error rates, however, might not be a sole consequence of fatigue – cognitive and physical; but might also reflect changes in arousal level. Over the pipetting task, there was interplay between peripheral and central fatigue mechanisms in three body segments: thumb, hand, and shoulder. Fatigue developed at a "local" level (i.e., at the three body segments) and was consistent with expected patterns observed in study 5, particularly if thumb and shoulder actions were considered concentric actions and the grip force was a sustained isometric contraction.

Overall, the collective assessments suggested that rating of perceived fatigue and action tremor, on average, were highly repeatable and responsive in multiple task conditions. Postural tremor or steadiness and maximum voluntary contractions were moderately reliable and responsive. Different forms of tremor may be responsive to different task conditions. Postural tremor amplitude was found to increase over the course of an 8-hour workday in a light precision work task, and over multiple days in physically demanding work. Action tremor, on the other hand, appeared to be responsive at higher work intensities performed at a shorter duration of time. Possibly, action tremor may be more indicative of changes in the periphery, whereas postural tremor reflects changes more central in nature. Consequently, these measures should be considered for inclusion into a test battery for field use.

For the ergonomist or health and safety practitioner, this body of work provides some insight into the utility of a test battery of fatigue measures to complement current task analysis techniques. For workplace researchers, this dissertation provides insight into the temporal development of fatigue in various task conditions and the reliability and responsiveness of select measures in both short and longer-term work-studies. This research might subsequently elicit future investigations in the relationship between work exposure, fatigue development, and performance and longer-term health outcomes.

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Chapter 1

Introduction

Background

Fatigue at the workplace has been described as a multidimensional construct, affecting the overall state of the whole organism, resulting from prolonged activity and associated with psychological, socioeconomic, and environmental factors (Barker & Nussbaum, 2011; Saito, 1999). In the short term, fatigue may result in discomfort, diminished motor control, reduced proprioception, increased force variability, and reduced strength capability (Björklund et al. 2000; Côté et al. 2005; Gates and Dingwall, 2008; Huysmans et al. 2010; Slack et al. 2009; Sparto et al. 1997). These effects might lead to reduced performance, lowered productivity, deficits in work quality, and increased incidence of accidents and human errors (Eklund 1997; Kajimoto 2007; Slack et al. 2009; Caldwell et al. 2008). Fatigue, however, may serve a biological purpose, acting as a defense mechanism to maintain homeostasis and reduce physical intensity in order to prevent a *catastrophic* failure (Saito 1999; Noakes 2012).

Fatigue may also lead to longer term adverse health outcomes such as chronic fatigue syndrome, myalgia, and burnout syndromes. Mechanistically, it is hypothesized that cumulative fatigue increases adrenocortical hormone releasing factor (CRF) and reduces splenic NK cell activity, through the activation of noradrenaline, leading to compromised immune function (Kajimoto, 2007). Fatigue may also be a precursor to WMSDs – work-related musculoskeletal disorders (Iridiastadi & Nussbaum, 2006). These outcomes have been associated with future morbidity and mortality, work disability, occupational accidents, increased absenteeism, increased presenteeism, unemployment, reduced quality of life, and disruptive effects on social relationships and activities (Åkerstedt et al., 2004; Bültmann et al., 2002; Shen et al., 2006; Ricci et al., 2007).

When considering lost productivity to U.S. employers, fatigue is associated with an excess cost of $101 billion per year. The majority of this cost is due to reduced performance at work rather than absenteeism (Ricci et al., 2007). Chronic fatigue syndrome (CFS), in particular, is associated with $9.1 billion in annual productivity losses in the United States (Evengård, 2007). Ricci and colleagues (2007) found a fatigue prevalence estimate of 37.9% in the U.S. workforce. In

Sweden, fatigue has been a dominant symptom among individuals on sick leave or taking early retirement. The cost of sick leave and early retirement, in Sweden, is more than $17US billion annually (Evengård, 2007). In Japan, an epidemiological study determined that 60% of working individuals experienced fatigue and more than 50% of these individuals suffered from chronic fatigue lasting at least 6 months (Kajimoto, 2007). In Canada, persistent work-related fatigue has been reported among 15% male and 20% female workers (Winwood, Bakker, & Winefield, 2007).

Fatigue in the long-term is also debilitating at the individual level, impacting the worker's performance, increasing risk of work-related injuries, and affecting quality of life. Chronic fatigue may affect employment, which in turn bring about further financial hardship and emotional suffering. Assefi and colleagues (2003) documented the financial, occupational, and personal burden of long lasting fatigue. Half of patients with chronic fatigue were unemployed and those who remained employed had to transition jobs, work fewer hours, and/or received less pay. Many of those who were employed found it difficult to sustain employment and were unable to meet work deadlines. Huibers and colleagues (2006) found similar trends, where chronic fatigue, particularly with symptoms of physical dysfunction, was a strong predictor for inactive work status and full work incapacity. Fatigued individuals also suffered losses of personal possessions, social and recreational activities, and support from family and friends as a result of increased mood disturbances and depression (Assefi et al., 2003). Although fatigue may independently pose problems, it is important to consider that fatigue may also interact with other health conditions to increase functional impairment. Fatigue is often reported with other conditions, leading to a larger fraction of lost productivity time in the United States. There are a few hypotheses that address fatigue and its interaction with other health conditions. Firstly, co-occuring (i.e., co-morbidity) fatigue may be a surrogate for disease or symptom severity. There is speculation is that the presence of fatigue indicates greater severity. Secondly, fatigue may restrict the individual's ability to compensate physically and mentally for functional impairment caused by other health conditions. Finally, another possibility is that fatigue lowers the threshold of work impairment of an individual (Ricci et al., 2007).

Since fatigue may be a precursor to WMSDs and other long-term health outcomes, fatigue may be a relevant biomarker for cumulative exposure to repetitive and/or sustained work (Dennerlein et al., 2003; Nussbaum, 2001; Winkel & Mathiassen, 1994), which can be documented by a range of physiological and electrophysiological measurements. Consequently, fatigue may be a useful risk indicator and a design and evaluation tool (Iridiastadi & Nussbaum, 2006). However, little is known of the temporal pattern of fatigue development and its relationships with disorder risks and work performance (de Looze et al., 2009). If fatigue can be used as a biomarker for long-term health outcomes, it may facilitate the prevention of fatigue due to excessive training or work, and thus contribute to preservation and promotion of health, and control associated expenditure (Kajimoto, 2007).

Objectives

Significance of Fatigue Measurement

The measurement of fatigue has recently been of greater importance in applied research. In order to develop appropriate interventions, to reduce the extent of the acute effects of fatigue at the workplace, and to prevent possible long-term health outcomes (if fatigue is a precursor or biomarker), research must be devoted to its assessment and understanding its temporal development (de Looze et al., 2009; Kajimoto, 2007). However, since fatigue manifests itself in various forms, a single test to measure a single function might not be a feasible method. For instance, if a certain physiological function is heightened, it may only reflect a particular adaptive behaviour rather than the degree of fatigue (Saito, 1999). Because different measures provide information on different processes induced by exercise, various authors suggest that fatigue should be evaluated by a multidisciplinary approach (Vøllestad, 1997; Saito, 1999). This may include physiological and psychological measurements, which might be related to various factors that may influence fatigue (Saito, 1999).

Thesis Aims

The objective of this thesis is to identify and evaluate a battery of fatigue measures that are valid, reliable, responsive, and practical for both laboratory and field-based research. The selection of these measures will be determined using an integrative approach, and include both central and peripheral fatigue mechanisms. Additionally, this thesis will provide insight towards fatigue development in work-relevant task conditions. It is anticipated that the findings from these studies will provide insight for both researchers and practitioners in the selection of fatigue measures, interpretation of these measures as it relates to physiological mechanisms and work exposures, and provide a framework for future research. More specifically, this thesis will:

(1) Identify fatigue measures and analysis methods suitable for laboratory and field research
(2) Evaluate select fatigue measures both as a test battery and during continuous measurement for their reliability and responsiveness during different fatiguing conditions. This evaluation will also compare select novel measures with commonly used fatigue measures.
(3) Evaluate select fatigue measures over the course of a workday and multiple workdays during simulated work.
(4) Investigate factors that might affect interpretation of physiological responses (i.e., circadian effects, analysis techniques, inclusion of a test battery, residual effects detected by a test battery).
(5) Recommend a battery of measures for field applications based on the available evidence.

Thesis Overview

To address these aims, this thesis is divided into multiple sub-studies (Figure 1.1). First, a literature review of theories, mechanisms, and measures of fatigue and the impact of fatigue in industry will be presented (*Chapter 2*). Second, this thesis will identify measures and analysis methods that detect fatigue-related changes from a multi-disciplinary perspective. This data will be based from a workshop of expert fatigue researchers (*Chapter 3*). Third, I will report on an exploratory study focused on the responsiveness of a select number of measures during a workday and multiple workdays in a field setting (*Chapter 4*). Fourth, I will evaluate the selected number of measures with both commonly used and novel measures for their reliability and sensitivity in a controlled laboratory setting. This will include the responsiveness of measures during a test battery or during the fatiguing activity, and the time between cessation of activity and test battery in which measures remain responsive (*Chapter 5*). Fifth, I will evaluate whether measures detect possible circadian effects to ascertain the daylong reliability of these measures (*Chapter 6*). Sixth, measures will be evaluated under four fatiguing conditions, representing changes in type of contraction, intensity, and body segment. Furthermore, fatigue development and temporal responsiveness of measures will be described (*Chapter 7*). Finally, measures will be assessed over an 8-hour light precision micropipetting task to investigate the temporal responsiveness of measures and fatigue development. Errors will be quantified and the effects of scheduled work breaks will be reported (*Chapter 8*). And finally, I will summarize the knowledge acquired from the preceding studies and discuss insight gained towards fatigue development and measurement (*Chapter 9*).

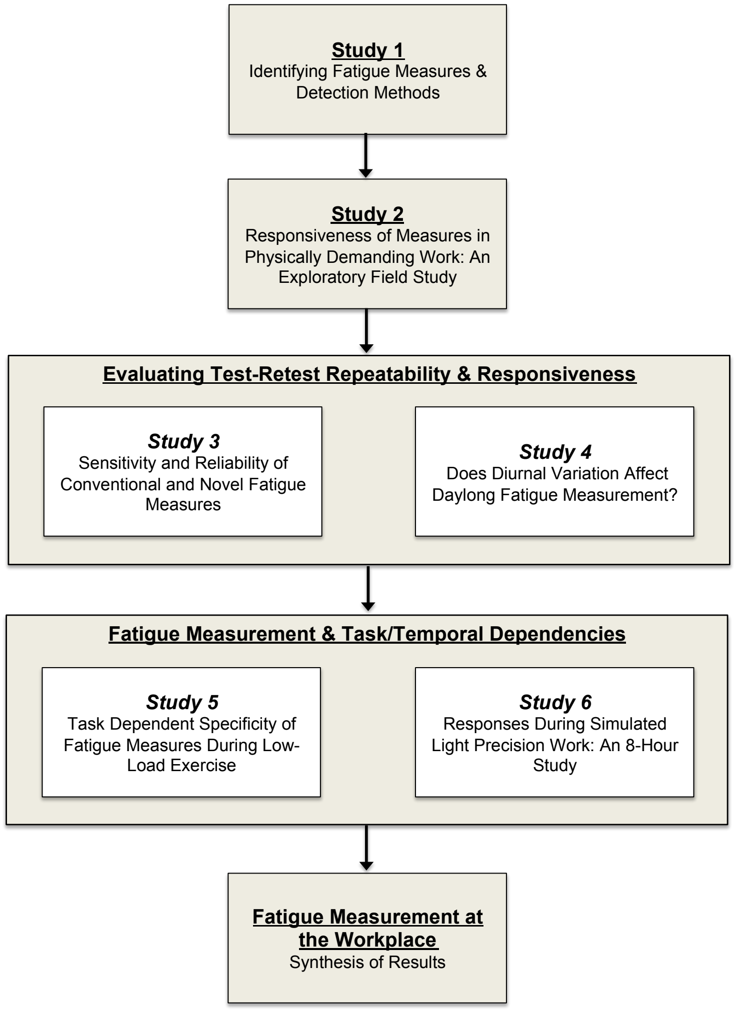


Figure 1.1 Thesis overview of studies to develop a test battery of fatigue measures.

Preliminary Studies

Study 1: Identifying Fatigue Measures & Detection Methods from a Multidisciplinary Approach

A workshop, inviting 14 researchers from Canada, United States, Sweden, and the Netherlands, was held to identify and evaluate current fatigue measures. The 14 participants represented 9 different disciplines and all had an established research interest in fatigue. Participants were asked to: (1) identify potential outcomes and/or effects of fatigue based on performance and quality, injury and disorders, illness and wellness, and discomfort, (2) identify potential causes and mechanisms related to these outcomes and effects, (3) identify fatigue measures and detection methods to monitor causes and methods, and (4) assess these measures and detection methods for their utility in both laboratory and field settings.

Study 2: Responsiveness of Measures in Physically Demanding Work: An Exploratory Study

Using a sub-set of fatigue measures selected from the workshop, an exploratory study was conducted to evaluate the responsiveness of these measures during physically demanding work. Sixteen residential plumbers were invited to participate. Fatigue was measured at the beginning of the shift, before lunch, and at the end of the workday, for 4 consecutive workdays and the following day after a weekend break (i.e., Monday). The results from this study will help inform proposed study 1.

Proposed Studies

Study 3: *Sensitivity and Reliability of Conventional and Novel Fatigue Measures*

Based upon preliminary studies 1 and 2, fatigue measures that are potentially usable in the field were selected. Fatigue measures based on strong theory with evidence of their responsiveness to fatigue were also selected. Participants were repeatedly measured with a test battery in an un-fatigued state, every 5 minutes during a 60-minute period. The same fatigue measures were then measured at 1-minute intervals during a fatiguing handgrip exercise. Simultaneously, data from some of the measures were collected continuously during the fatiguing exercise, and act as a comparison against the same measures collected as a test battery. Test battery measures were performed after the fatiguing exercise to determine the residual responsiveness of these measures (i.e., measurement responsiveness after cessation of activity to ascertain length of time in which measures may be sensitive to fatigue effects).

Hypothesis 1: Novel fatigue measures and traditional measures will show strong (i.e., $0.61 \leq \alpha < 0.8$) to almost perfect reliability (i.e., $\alpha \geq 0.80$) over successive test batteries but novel measures will be more sensitive (i.e., quicker rate of response) to the fatiguing exercise than common methods.

Hypothesis 2: The responsiveness of the fatigue measure, as a test battery, will show no difference in response than when measured continuously.

Hypothesis 3: The novel fatigue measures will demonstrate prolonged latency effects (i.e., remain sensitive to fatigue for a longer duration of time after exercise) compared to commonly used measures. It is hypothesized that commonly used measures (e.g., EMG, MVC, rating of perceived fatigue) will recover immediately after activity (i.e., within 1 minute of recovery).

Study 4: *Does Diurnal Variation Affect Daylong Fatigue Measurement?*

The selected fatigue measures used in study 3 were performed during two consecutive 12-hour periods, from morning to early evening, encompassing hours consistent with a day shift.

Hypothesis 1: Physiological responses will demonstrate diurnal effects. More specifically, there will be fatigue effects during early morning due to sleep inertia, responses will maximize or minimize during mid-day, and tend towards non-optimal responses from late afternoon to early evening.

Study 5: *Task Dependent Specificity of Fatigue Measures During Low-Load Exercise*

A subset of fatigue measures from study 1 was evaluated further under various fatiguing conditions, with and without inclusion of rest breaks, and at different body segments. Measures were taken continuously and as a test battery. Conditions represented force levels relevant to sedentary or light production work (i.e., sustained isometric handgrip contraction at 10% MVC), an intermittent isometric protocol representative of tasks characterized by time-varying changes in force (i.e., intermittent isometric handgrip contraction with mean force amplitude at 15% MVC, duty cycle 50%, cycle time 6 seconds), fatigue at a different body segment – the shoulder (i.e., intermittent isometric shoulder flexion with mean force amplitude at 15% MVC, duty cycle 50%, cycle time 6 seconds), and with and without test batteries (i.e., rest breaks).

Hypothesis 1: Based on concepts of task dependency, fatigue measures reflecting central components will be more responsive during a sustained isometric condition than an intermittent isometric condition.

Hypothesis 2: Peripheral measures will be more responsive during a condition without rest breaks (i.e., continuous intermittent at 15%MVC) than a condition with rest breaks (i.e., intermittent at 15%MVC with breaks at 10-minute intervals provided by a test battery).

Hypothesis 3: Measures will be body-segment specific, at the shoulder and at the hand/forearm. This is due to differences in morphological and fibre composition between extrinsic muscles of the forearm and primary muscles involved in forward flexion of the shoulder.

Hypothesis 4: Based on task dependency, there will be no single measure that will be most responsive in all exercise conditions.

Hypothesis 5: Central measures will be more responsive at lower intermittent force conditions (i.e., intermittent at 15% MVC) than higher intermittent force condition collected in study 3 (i.e., intermittent at 30% MVC).

Study 6: *Responses During Simulated Light Precision Work: An 8-Hour Study*

Participants will perform simulated assembly work over a typical working day (i.e., 8 hours). Measures will be taken continuously and as a test battery at 30-minute intervals from the beginning of the simulated work session. Test batteries will also be taken before the session, before and after breaks, lunch breaks, and at the end of the simulated work session. Performance measures will also be collected.

Hypothesis 1: Peripheral and central measures will respond to physiological changes over the workday. Additionally, cognitive fatigue indices will increase over the course of the pipetting task. Test battery measures will demonstrate increasing fatigue response at hourly intervals and responses will be significantly different between pre- and post- simulated work sessions.

Hypothesis 2: Although peripheral and central measures will respond over the course of the workday, central measures will be more responsive than measures reflecting peripheral responses due to the nature of the task.

Hypothesis 3: Fatigue responses will recover towards baseline values after the 15-minute morning and afternoon break, and after the 30-minute lunch break. There will be a concomitant decrease in error rates subsequent to the scheduled breaks.

Hypothesis 4: Fatigue and error rates will share similar trends. Error rates will concomitantly increase with increasing fatigue response. A decrease in error rate will follow a diminishing response in fatigue indices.

Chapter 2

A Review of Literature

Contemporary Issues in Fatigue Research

Semantics, Theories, and a Research Paradigm

Human muscle fatigue is a commonly experienced phenomenon that has been extensively studied. Fatigue research progressed in the mid 19th century with Étienne-Jules Marey's laws of human effort and efficiency, documented by his pioneering work in human movement; and Hugo Kronecker's kymographic experiments on the muscular characteristics of the frog, leading to dynamic laws of fatigue and the recognition that the intensity of muscle contractions diminishes with regularity until exhaustion (Rabinbach, 1992). Kronecker concluded that fatigue was a perfectly regular phenomenon and directly proportional to the time interval between identical electrical stimulations (Kroker, 2007). It was not until Angelo Mosso's work in the late 19th century that fatigue was explicitly studied, placing fatigue firmly within the canon of modern science, leading to classic works such as *La Fatica* (1891). Inspired by both Marey's and Kronecker's work, Mosso quantified fatigue, merging experimental physiology and psychology with the goal of improving human performance. His invention, the ergograph, was the first to measure fatigue, calibrating muscular exhaustion to the sensation of fatigue, arriving to two theories. First, fatigue is an objective phenomenon and in general, laws of fatigue are analogous to laws of energy. Second, fatigue can be measured and recorded, and demonstrates a consistent decrease in muscular force (Rabinbach, 1992). Scientific interest in human work and fatigue peaked in the 1930s, with a proliferation of empirical studies, theoretical awareness, and application of knowledge (Hockey, 2013). Since then there is a renewed interest in fatigue, but as a clinical problem, with a focus in chronic fatigue and other chronic illnesses. However, as much as *fatigue* has been within the scientific landscape, surprisingly there is no widely accepted understanding of fatigue including its process, its function, its mechanisms, the interactions between types of fatigue, and how it might be measured or detected (Hockey, 2013; Kajimoto 2007).

Extensive literature has focused on elucidating relevant processes and mechanisms. Yet there are disparities between perspectives of the most important mechanisms related to fatigue. Such disparities may be partially explained by different interpretations of studies consisting of a range of exercise models, protocols, and methods (Vøllestad, 1997). One prominent theory, dating back to the early 20th century, is based on a collection of pioneering studies conducted by Fletcher and Hopkins (1907) and Hill and Hupalov (1929). The theory conjecture is based on "limitations" or "catastrophic" models, which state that fatigue occurs after one or more bodily systems are stressed beyond their capacity. This stress leads to complete system failure, which is observed as exhaustion (Noakes et al., 2004). For instance, the catastrophic model, otherwise known as the anaerobic or cardiovascular model, postulates that skeletal muscle "anaerobiosis" leads to fatigue during high intensity exercise of short duration. "Anaerobiosis" occurs when oxygen requirement of the active skeletal muscles exceeds the heart's capacity to further increase oxygen delivery to exercising muscle. Consequently, an increase in energy generation in active muscles is derived from "anaerobic" metabolism that leads to inadequate maximum oxygen intake, lactic acid accumulation, continuous oxygen debt, exhaustion, and ultimately fatigue (Noakes & St Clair Gibson, 2004). Most importantly, catastrophic model posits that fatigue during most forms of exercise is peripherally based, due to metabolite-induced failure of skeletal muscle contractile function (Noakes & St Clair Gibson, 2004). During this time, accumulating lactate (lactic acid) was considered to be responsible for muscle fatigue, and remains erroneously the predominant fatigue mechanism in exercise sciences (Noakes, 2012).

To be both a plausible and defensible model, Noakes and colleagues (2004) note that the catastrophe model must satisfy the following conditions of maximal exercise: (1) Onset of muscle anaerobiosis is observed as a plateau in oxygen consumption, (2) A maximum cardiac output, (3) Maximal recruitment of all available motor units of the exercising muscle, and (4) Absolute state of fatigue in which complete recovery occurs after a defined period of rest. However, Noakes and colleagues (2004) argue that there is no conclusive evidence that fatigue during maximal activity fulfills any of these conditions. For instance, Noakes et al (2004) suggest that during fatigue, motor unit recruitment in the active muscle is never absolutely maximal; therefore the accumulation or depletion of metabolites cannot prevent recruitment of additional motor units. Additionally, there is little evidence that during voluntary exercise, any major organ system fails at exhaustion. On the other hand, there is greater evidence to suggest that exercise terminates while homoeostasis is maintained. Thirdly, fatigue cannot be an immediate consequence of imbalance between muscle ATP production and use. If this were true, based on the catastrophic model, ATP concentrations must fall, leading to muscle rigor. However, if muscle rigor does not develop, an alternative control mechanism must be responsible to terminate exercise despite sufficiently high muscle ATP concentrations (Noakes et al., 2004).

Instead, Noakes and colleagues (2004) proposed that regulatory centres residing in the central nervous system (CNS) continuously interact with multiple peripheral processes to control exercise performance and sensations of fatigue. This central governor model dictates that with feed forward and feedback control mechanisms, both neural command and peripheral regulatory systems control changes in any physiological variable (Noakes et al., 2004). Thus, based on the central governor model, performance is regulated to factors above the spinal cord (i.e., subconscious and conscious brain), dismissing involvement from the level of the spinal cord or motor unit (Weir et al., 2006). Subconscious regulatory strategies, by modulating the number of active motor units, thus allow completion of a task while maintaining homoeostasis and metabolic and physiological reserve capacity. For instance, in the presence of impaired skeletal muscle function, the central governor would limit the intensity of exercise by either increasing overall motor recruitment to maintain a force output, or reducing the rate of derecruitment during prolonged exercise (Weir et al., 2006). Unlike the catastrophe theory, the central governor model suggests that fatigue is not merely a physical manifestation but also a sensation.

Recent studies have critically reviewed the validity of the central governor model. Weir and colleagues (2006) argued that the central governor model disregards the effects of task dependency (e.g., exercise intensity, type of contraction, muscle groups involved, environment, training status, muscle fibre type distribution, etc.). For example, when considering a variety of fatiguing tasks, insufficient motor unit recruitment cannot explain a decrement in muscle performance in every case. This suggests that mechanisms within the muscle may partially explain the observed decrease in muscle force. Similarly, MacIntosh and Shahi (2011) criticized the central governor model for a lack of consideration of peripheral muscle fatigue, as observed when muscles diminish their contractile capability, limiting physical performance. Marcora (2008) takes this argument a step further, stating that the central governor model is internally inconsistent, unnecessarily complex, and biologically implausible. If, according to the model, conscious sensation of effort is unnecessary, subconscious control of motor unit recruitment should cause exhaustion despite conscious motivation to sustain exercise.

Alternative theories have since emerged; focusing on the notion that fatigue is a regulated process rather than a depletion of resources, accumulation of waste products, and wearing down of contractile function (MacIntosh & Shahi, 2011). One theory speculates that there is a peripheral governor, where each muscle cell has a capacity to regulate its own activation to limit the disturbance to cellular homoeostasis. Such disturbances include a fall in [ATP] where its depletion, in conjunction with an increase in ADP, can have detrimental cellular effects. MacIntosh and Shahi (2011) argued that regulation is most effective where the disruption occurs, in active muscle. The peripheral governor comprises of several redundant mechanisms including the loss of membrane excitability by activation of K^+ and Cl^- channels, decreased Ca^{2+} release by inhibition of ryanodine receptors (RyR), and decreased free [Ca^{2+}] due to calcium-phosphate precipitate. The peripheral governor model, however, does not detract from the plausibility of the central governor and its role in fatigue. For example, conscious and subconscious attenuation of motor pathways may preserve muscle homoeostasis by strategic pacing. However, ultimately, the peripheral governor has the "final say" in limiting the use of ATP by muscles (MacIntosh & Shahi, 2011).

A second emerging construct is the psychobiological model based on motivational intensity theory. As previously mentioned, the central governor model neglected perceived exertion and motivational factors, in other words, the inclusion of the conscious brain. The psychobiological model provides a simpler mechanism, where exhaustion occurs when the maximum conscious exerted effort matches the required effort. Exhaustion may also occur when the individual believes to have exerted a true maximal effort and the continuation of task is perceived to be impossible (Marcora, 2008). There is growing evidence to suggest that the psychobiological model may provide a unifying theory of exercise tolerance. If the perception of effort arises from efferent rather than afferent sensory inputs, according to this model, an increase in RPE over time is explained by increases in central motor commands required to compensate for reductions in cortical, motoneuronal, and/or muscular responsiveness (Marcora, 2008).

It has been suggested that diverging theories of fatigue are due in part to different definitions. Consequently, this may result in the use of diverse tools and procedures to measure specific fatigue processes (Enoka & Stuart, 1992; Behm, 2004). Much of this discrepancy between conventional understandings of fatigue may be a result of varying interpretations of the term from various research perspectives and disciplines. To illustrate this, fatigue, defined in the central governor model, is a sensory perception resulting from a complex integration of physiological, biochemical, and other sensory feedback, which may or may not be associated with any alteration in muscle force production. According to this definition, fatigue is a sensation rather than a response from a physical event, i.e., fatigue may be present at rest (Noakes et al., 2004). On the basis of the central governor model, fatigue is thus associated with perceived exertion, and should be measured with instruments such as the Borg scale or those that measure sensations and emotions (Weir et al., 2006). Additionally, the central governor model implies that fatigue occurs at a discrete point in time. On the other hand, fatigue defined as "any exercise-induced reduction in the ability to exert muscle force or power, regardless of whether or not the task can be sustained", has long been conceptualized as a process that occurs from the start of activity (Weir et al., 2006). Another is the function of fatigue, which is predominantly assumed as a negative state and an unwanted by-product of physical and mental work (Hockey, 2013). However, historically, there is little indication of fatigue as a negative state prior to the industrial revolution (Rabinbach, 1992). Furthermore, fatigue may serve a biological purpose, acting as a defense mechanism to maintain homeostasis and reduce physical intensity in order to prevent a *catastrophic* failure (Saito 1999; Noakes 2012). Clearly, fatigue has different institutionalized meanings across different scientific groups (Table 2.1), and not surprisingly, there is no succinct and widely accepted definition.

For many years scientists have sought, but unsuccessfully, a succinct definition of fatigue (Aaronson et al., 1999). A single and possibly dogmatic definition, although convenient for scientific investigation, may instead confirm our own biases and misrepresent the reality of fatigue (Marino et al., 2011). Such is the case with the erroneous usage of the "lactic acid theory", a phenomenon that persists despite current flaws in our understanding of metabolic acidosis (Marino et al., 2011). Additionally, given the complex redundancy in most biological systems, a single mechanism unlikely explains fatigue under all conditions. Consequently, as Weir et al (2006) suggested, the search for a grand unifying theory of fatigue, based on reductionist approaches, may be futile. A single definition cannot describe the complex interaction of biological processes, behavioural manifestations, and psychosocial phenomena (Aaronson et al., 1999); and a single theory cannot explain all observations of performance decrement (Weir et al., 2006). It is perhaps the integration of different perspectives and disciplines that may lead to a greater understanding. An integrative holistic approach has long been recognized since Bainbridge's *Physiology of Muscular Exercise* in the early 20th century. Ash (1914) stated:

> *"Fatigue is a comprehensive term which in its widest application embraces all those immediate and temporary changes, whether of a functional or organic character, which take place within an organism or any of its constituent parts as a direct result of its own exertions, and which tend to interfere with or inhibit the organism's further activities."* (Ash, 1914)

Hargreaves (2008) recognized that understanding the complex interaction between the "psyche" and neuromuscular activation is a prospective challenge. This understanding may require complex experiments to probe the fundamental underlying neurobiology between central motor drive and skeletal muscle. Ultimately this holistic approach, as advocated by Marino and colleagues (2011), may result in a new conceptual landscape to better understand the aetiology and establish possible interventions to reduce, prevent, or minimize the effects of fatigue. Case in point, in terms of aetiology, Evengård (2007) suggested that biological and psychological data could be co-analyzed with social data and environmental factors of potential influence for the pathology. In terms of interventions, glucose availability may impact multiple steps within the pathway towards neuromuscular activation, each providing viable mechanisms for the ergogenic effects of carbohydrate ingestion (Hargreaves, 2008). Glucose supplementation may thus interact with the central nervous system to enhance performance and reduce the effects of fatigue. This paper will address the mechanisms and effects of fatigue from different disciplines and perspectives, as an initial step to an integrative approach and thus a systems biology paradigm.

Table 2.1 Examples of Definitions of Fatigue Found in Literature

Perspective	Definition
Exercise Physiology	*"… 'the failure to maintain the required or expected force' or 'a loss of maximal force generating capacity' or 'a reversible state of force depression, including a lower rate of rise of force and a slower relaxation."* (Marino et al., 2011).
Muscle Physiology	*"This reversible phenomenon is denoted as muscle fatigue. …it is universally agreed that much of fatigue arises in the muscles and can therefore be studied in isolated muscle tissues."* (Allen et al., 2008).
Motor Control	*"Fatigue is a time-dependent exercise-induced reduction in the maximal force generating capacity of a muscle….Some of these 'central' [nervous system] features may disrupt performance more than the reduction in maximal muscle force."* (Gandevia, 1998).
Neuromuscular	*"…An acute impairment of performance that includes both an increase in the perceived effort necessary to exert a desired force and an eventual inability to produce this force…mechanisms underlying fatigue are task dependent."* (Enoka & Stuart, 1992).
Psychology	*"…Fatigue has been defined as a state of weariness related to reduced motivation. Psychological fatigue has been associated with stress and other intense emotional experiences and may accompany depression and anxiety…[and is] viewed as a response to internal or external demands exceeding available resources."* (cited in Aaronson et al., 1999).
Industrial	*"[Industrial] fatigue – a state of overstrain or exhaustion resulting from excessive work not being balanced by adequate rest and exhibiting itself primarily in diminished personal capacity for doing work – that is, declining productivity."* (McIvor, 1987).
Medicine	*"…a lack of energy that affects mental and physical activity, which differs from sleepiness and lack of motivation, and may be aggravated by, but is not primarily attributable to, minor exercise or diagnosable diseases."* (Evengård, 2007).

A Centralist Approach: Fatigue From The Top-Down

Activities of daily living are predominantly characterized by exposures consisting of prolonged submaximal tasks. Gandevia (1998) posits that during brief intense exercise, force is dependent on muscle and biomechanical factors. On the contrary, exercise greater than 10 seconds may be attributable to both central and peripheral factors. For instance, Kent-Braun (1999) showed that 20% of the fatigue developed after an isometric MVC, sustained for 4 minutes, was due to central factors. Millet et al (2011) stated that previous studies have systematically shown that central fatigue largely contributes to muscle fatigue during long distance running. In one study, Martin and colleagues (2010) demonstrated that central fatigue was the principal explanation for neuromuscular fatigue during a 24-hour running bout. Large central activation deficits as well as a disproportionate increase in perceived effort were observed whereas the extent of peripheral fatigue was moderate. As per the central governor model, this study adds support to the function of the central nervous system as the main mechanism for exercise limitation (Martin et al., 2010).

Manifestations of central fatigue has not only been identified by its role in driving motoneurons, but with increases in tremor, recruitment of synergetic muscles, and subjective increase in effort (Gandevia, 1998). Neuromuscular fatigue has also been associated with deleterious effects to joint and postural stability (Kennedy et al., 2011). It has been further speculated that these central features may disrupt performance more so than a reduction in maximal muscle force (Gandevia, 1998). Behm (2004) argued that the underlying mechanisms to maintain submaximal force over a sustained period is based on a compromise between fatigue-induced impairments and neuromuscular strategies to enhance and sustain performance. On one hand, inhibitory factors include supraspinal inhibition, spinal inhibition, and afferent inhibition of motoneurons. On the other hand, facilitatory factors that work to augment force production include neural potentiation, inclusion of catch-like properties, muscle wisdom, alterations in motor control, postactivation potentiation, and increased muscle stiffness.

The output of descending paths at the supraspinal level may vary during the course of a fatiguing exercise. Gandevia (2001) showed that aided by recurrent inhibition and muscle spindle "disfacilitation", motoneurons adapt their discharge rate in the initial seconds of a strong sustained contraction, resulting in a decrease in firing rate. As time progresses, reflex inputs from small-diameter muscle afferents may play an important role, depending on metabolic activity and the extent to which the contraction is ischemic. Supraspinal inhibition results in both decreased cortical excitability and slowing of impulse transit time (Behm, 2004). These supraspinal impairments may be due to changes in afferent activity and in concentrations of neurotransmitters and ammonia. It has been speculated that during exercise, tryptophan, an amino acid precursor to neurotransmitter 5-HT, is transported across the blood-brain barrier, thereby elevating 5-HT in the brain. Increases in 5-HT have been linked to possible inhibition of brain oxidoreductive processes. It has been hypothesized that 5-HT may affect arousal, lethargy, sleepiness, and mood that is linked to altered perception of effort and muscular fatigue (Davis et al., 2000; Meeusen & Roelands, 2010). Meanwhile concentrations of dopamine, found in the brain, decreases with the presence of fatigue. Davis et al (2000) hypothesized that a low ratio of brain 5-HT to dopamine leads to improved performance, including increased motivation, arousal, and optimal neuromuscular coordination, whereas a high ratio of 5-HT to dopamine leads to central fatigue (i.e. decreased motivation, tiredness, lethargy, loss of motor coordination). Noradrenaline has also been implicated to changes in performance associated with fatigue (Meeusen & Roelands, 2010). It appears that both catecholamines (dopamine and noradrenaline) have a large influence on performance during prolonged exercise, particularly when exercise is carried out in high ambient temperature (Meeusen & Roelands, 2010). Dopamine, 5-HT, and noradrenaline are all possible factors in the control of thermoregulation, including the mediation of thermoregulatory responses; thereby a shift in their concentrations may result in changes to thermal regulation and fatigue resistance (Meeusen & Roelands, 2010). Another possible mechanism is an increase in blood levels of ammonia, changing membrane permeability of certain amino acids, leading to supraspinal dysfunction.

Spinal inhibition is associated with diminished motoneuron discharge, which may be due to intrinsic motoneuronal properties, reflex inhibition and disfacilitation, Renshaw cell inhibition, and insufficient drive from supraspinal sites (Gandevia, 1998). Serotonergic cells may modulate motorneuronal behavior when serotonin and norepinephrine is released in the spinal cord from fiber systems descending from the brain stem. Serotonergic cells and other neuromodulators have been shown to depolarize motoneurons and generate a plateau potential. These effects are more evident in low-threshold motoneurons. Reflex (e.g. Group Ia inputs, reciprocal inhibition, cutaneous inputs) arising from muscle contractions may cause a decrease in motor unit firing rate. It is improbable that reflex circuitry affect individual control of motoneurons. Instead it is more probable that reflex effects are distributed across the motoneuron pool leading to a net effect of reducing firing rates. Renshaw cells provide autogenetic inhibition to a diverse set of outputs including motoneurons, Ia inhibitory interneurons, fusimotor neurons, and other Renshaw cells. Its effect on motoneuron discharge rate is dependent on discharge pattern, voluntary drive, muscle feedback, and influence on motoneuronal afterhyperpolarization (Gandevia, 2001). Renshaw cell inhibition has also been observed to decrease as descending drive to the motoneurons increases (i.e. as the strength of the voluntary contraction increases). Renshaw cell activity and their relationship to tremor and fatigue will be discussed in later sections.

Based on Hoffman reflex responses following 15-Hz stimulation, there is evidence to suggest that inhibitory afferents, arising from muscle, are involved in the down-regulation of motoneuron excitability, in both sustained and fatiguing intermittent submaximal contractions (Behm, 2004; Garland & Kaufman, 1995). Down-regulation, as a response to metabolites, acidity, pressure, pain, tension, or stretch, may diminish the chances of fatigue-induced muscle damage. Muscles are innerved by five types of sensory nerves, based on the diameter of the afferent fibres, classified as group I (Ia and Ib) through IV. However, the contribution of different sized afferents to reflex inhibition remains unresolved (Garland & Kaufman, 1995). There are, however, two hypotheses to the function of afferents during fatiguing exercise. First, input from small diameter afferents (i.e., group III and IV) decreased motoneuron activity as a result of chemical or mechanical stimuli. Hill (2000) demonstrated that Group IV afferents produced an inhibitory reflex after rhythmic contractions. Under prolonged, high-intensity contractions, chemical stimuli may excite nociceptive chemosensitive (metabosensitive) afferents. Exposure to prolonged submaximal contractions may result in the accumulation of metabolites into extracellular space, leading to reduced mechanical threshold and subsequent depolarization of Group III and IV afferents (Behm, 2004). These metabolic products include bradykinin, arachidonic acid and prostaglandin E2, potassium, and lactic acid. Secondly, there is a disfacilitation of motoneurons due to a reduction in discharge of muscle spindle afferents (i.e., group Ia and II). Disfacilitation is a decrease in fusimotor-driven feedback and a subsequent reduction in motoneuron excitation. Golgi tendon organ (Ib) afferents, during fatigue, are presynaptically inhibited and receive input from Ia, III, and IV afferents (Behm, 2004). The inhibitory effect on the motoneuron, particularly with submaximal contractions, remains ambiguous as Ib afferents fire less frequently.

The effects of muscle fatigue have led to modifications at the sensorimotor state. There is evidence to suggest that muscle fatigue affects movement coordination, alters movement or effort senses, and mental representations of actions (i.e. motor performance and action planning). Demougeot and Papaxanthis (2011) showed that fatigue significantly altered the neural drives sent specifically to the muscle of the fatigued limb, modifying the temporal features of both mental (e.g. action representation) and actual movements. Changes in the descending voluntary command, observed by Demougeot and Papaxanthis (2011) as larger efferent motor outflow, leads to changes in force estimation. Similar increases in cortical recruitment have been observed in neuroimaging studies, particularly over the major sensorimotor regions (i.e., contralateral and ipsilateral sensorimotor cortices). For instance, Tanaka and Watanabe (2011) used magnetoencephalographic (MEG) to quantitatively evaluate the movement-evoked response, reflecting sensory input and motor output, underlying physical fatigue. The authors found that during physical fatigue, ipsilateral sensorimotor and prefrontal cortex brain areas were associated with compensation mechanisms, including increased motor output. The prefrontal area, in particular, may play a central role in motor output activation to maintain physical performance (Tanaka & Watanabe, 2011). Despite increases in cortical recruitment, Yang and colleagues (2009) observed a decrease in corticomuscular coupling between cortical output centers of the brain and muscle activation level. The inverse relation between strength of the corticomuscular signal coupling and the amplitude of the efferent motor outflow may be due to a tradeoff of increasing activation level to compensate for fatigue (Yang et al., 2009). It has been speculated that decreased coupling may lead to reduced motor performance including increased force variation and reduced force steadiness. Previous studies have found that outflow signals play an important role in position and movement sense (Demougeot & Papaxanthis, 2011).

Transcranial magnetic stimulation (TMS) of the motor cortex provides the most direct evidence of central fatigue originating from supraspinal and spinal sources (Davis et al., 2000). TMS quantifies the net effects of exercise-induced muscle fatigue and the associated increased firing rate of muscle afferents on cortical inhibition and excitability of the central motor pathway (Hilty et al., 2011; Keller et al., 2011). TMS applied at intensities above the motor threshold produces short latency excitation of motoneurons. In contrast, TMS applied at lower intensities produces short latency inhibition, affecting the most direct projections from the motor cortex to spinal motoneurons (Seifert & Petersen, 2010). In 1993, Brasil-Neto and colleagues reported the first use of TMS, finding a transient depression of motor evoked potentials, 30 seconds at cessation of a fatiguing task, lasting several minutes (as cited in Kluger et al., 2012). Motor evoked potentials (MEP) are indicative of not only the excitability of cortical cells but also the overall excitability of the corticospinal pathway (Seifert & Petersen, 2010). However, Kluger and colleagues (2012) warns that MEP depression may follow, without obvious motor fatigue. After repeated central initiation of movement (e.g., tapping) and sustained central activation (e.g., motor imagery), MEP decreased, indicating that factors other than central fatigue may contribute to post-task decrements in cortical excitability. However, Kluger et al (2012) noted that the observed MEP amplitude decrements were more variable, smaller, and of shorter duration than those typically described after a fatiguing protocol, implying that MEP decrements may be related to the degree of central fatigue. Seifert & Petersen (2010) found a similar finding, where a short-latency suppression was more pronounced in the fatigued compared to the non-fatigued motor system. Cortical silent periods (CSP) are related to spinal inhibition and interruption of voluntary drive at the cortical level, which is thought to lead to inhibition of intracortical neurons and subsequently disfacilitation. Both MEPs and CSPs progressively increase during fatiguing muscle contractions (Hilty et al., 2011). Using TMS, Keller and colleagues (2011) found that after a low-force isometric fatiguing protocol, supraspinal fatigue contributed to neuromuscular fatigue, and fatigability was similar for both males and females. It is widely accepted that there are sex differences in muscle fatigue, where females are typically more fatigue resistant (Hunter, 2009). Sex-based fatigability differences may involve sex-specific actions of group III and IV afferents on the motor neuron pool of different muscle groups. The results may also imply that the observed greater fatigue resistance in women was related to muscular mechanisms (i.e., contractile properties) and the sources (supraspinal vs spinal) contributing to these sex differences may differ. Hilty and colleagues (2011) observed, with TMS, that μ-opioid receptor-sensitive muscle afferents have no net effect on the excitability of the motor pathway from the motor cortex to the muscle but might facilitate intracortical inhibition resulting in an influence on central fatigue.

As previously mentioned, neuromuscular strategies are employed to sustain performance. One facilitatory factor is neural potentiation, involving motor unit recruitment and increases and decreases in rate coding. Previous literature has showed a short-term increase in explosive force, following a series of maximum voluntary contractions, might persist for 10 minutes following the contractions. Behm (2004) attributed the facilitation of motoneuron excitation to both supraspinal (i.e., MEP facilitation at short and forceful contractions) and afferent inputs (i.e., discharge frequency from Ia afferents may contribute up to 30% of motoneuron excitation with sustained isometric contractions less than 1 or 2 seconds).

Catch-like properties are fundamental to muscle cells and not a property of the motor axon or neuromuscular junction (Binder-Macleod & Lee, 1996). These properties result in tension enhancement as a consequence of brief, high frequency bursts added to the beginning of a sub-tetanic train of pulses. The magnitude of the force augmentation is determined by the burst characteristics, both frequency and number of pulses (Binder-Macleod & Lee, 1996). Behm (2004) suggested that interspersed stimuli of less than 20 milliseconds facilitated increased peak force, increased rate of rise of force, and decreased muscle fatigability. Catch-like properties have been observed for both slow and fast twitch fibres, and its augmentation is transient within the stimulation train (Ding et al., 2003). There are two primary mechanisms of the catch-like property. One is the increase of Ca2+ release from the sarcoplasmic reticulum, and subsequently increased cross-bridge formation, as a consequence of high frequency stimulation (Duchateau & Hainault, 1986 as cited in Ding et al., 2003). Another is increased muscle stiffness, where a stiff musculotendinous system was shown to maximize performance by improving contractile component length, rate of shortening, and transmission of force from contractile component to skeletal structures (Binder-Macleod & Lee, 1996). Behm (2004) also recognized that enhanced stiffness allows muscles to sustain submaximal forces without changes in neuromuscular response. Evidence revealed that a high frequency doublet at the beginning of a catchlike-inducing train (CIT) takes up the slack in the series elastic component of muscle, increasing both muscle stiffness and Ca2+ release (Ding et al., 2003). However, force augmentation, due to catch-like properties, is dependent on the type of contraction. Binder-Macleod and Lee (1996) found that during isometric contractions, force enhancement was greater than non-isometric contractions. Between non-isometric contractions, concentric contractions produced greater force augmentation than eccentric contractions. Potentiation is similar to catch-like properties for its enhancement of skeletal muscle force. However, in contrast to catch-like properties, potentiation is most commonly seen in muscles consisting of predominantly fast-twitch fibres and its force augmentation effects last for minutes. Post-tetanic potentiation occurs after a bout of high-frequent contractions, leading to phosphorylation of myosin regulatory light chain and subsequent conformational changes in the myosin head to a more favorable position for cross-bridge binding. Catch-like properties, in contrast, are the result of brief, high frequency bursts as a result of functional electrical stimulation. Ding and colleagues (2003) argued that both potentiation and catch-like properties are not independent mechanisms. In non-potentiated muscles, catch-like inducing trains were able to augment force relative to potentiated muscle. This may be the result of the ineffective force augmentation as increased Ca2+ release and increased muscle stiffness (catch-like properties) are advantageous after the force-pCa curve has been shifted to the left (i.e., muscle is stiffer due to potentiation). Therefore, catch-like properties and potentiation share a negative linear relationship, where for non-fatigued muscles, catch-like properties were most beneficial when muscles were least potentiated, at the onset of activation (Ding et al., 2003).

Previous research has demonstrated that muscle force decreased rapidly when stimulation was maintained at a high rate. However, when the stimulus rate was reduced over time, a substantially higher force could be exerted. This has led to the third facilitatory factor, the muscle wisdom hypothesis, where a reduction in motor unit discharge rate may preserve force rather than promote fatigue. The decrease in motor unit activity has been speculated as a strategy to optimize force output of motor units as their contractile speed decreases and as a defense mechanism against peripheral conduction failure, which would subsequently affect the activation and release of Ca2+ from the sarcoplasmic reticulum (Fuglevand & Keen, 2003; Behm, 2004). A number of studies have shown that muscle wisdom (i.e., decrease in firing frequency) occurred despite increases in EMG activity, indicating a muscle-afferent reflex inhibition of motor unit firing rates (Behm, 2004). However, Fuglevand and Keen (2003) raised some doubts to the literal interpretation of the muscle wisdom hypothesis. Using a stimulation frequency rate of 30 Hz, the authors found that a decline in discharge rate of motor units enhanced rather than reduced muscle fatigue when stimulation was decreased to 15 Hz over a 60 second period. In contrast to higher stimulus rates in previous studies, 30 Hz was similar to rates that occur during voluntary effort.

Alterations in motor control may have implications in preventing excessive fatigue and preserving force based on recruitment strategies within and between muscles. Of particular interest are alterations in recruitment and derecruitment of motor units during sustained contractions, a concept known as motor unit substitution or rotation. By alternating motor unit activity in a cyclical fashion, higher-threshold motor units are recruited to replace fatigued lower-threshold motor units that have stopped firing. Westgaard and De Luca (1999) provided evidence for motor unit substitution, during a low-level static contraction, a manipulation task with mental concentration, and a computer-typing task. This study showed evidence for differential firing behavior among concurrently active motor units, without decreases in the overall EMG signal, indicating that firing behavior was not a consequence of muscles turning on or off. More recently, Manning and colleagues (2010) examined whether rotation was a consequence of increased threshold of the motoneuron or a change in posture resulting in movement artifact (i.e., electrodes picking up activity from newly activated fascicles). By observing motor unit activity during recovery periods, with the absence of additional excitation, motor units recovered. Secondly, prior to resumption of tonic behavior, motor units led to a gradual increase in firing (i.e., slow increase in excitability as neurons recover). Both observations indicate that independent of external excitation, the neurons intrinsic properties (i.e., increase in threshold) are responsible for cessation of motor unit firing (i.e., recovery).

The sensation of fatigue is often considered a signal that alerts the body from detrimental impairments including cellular damage. However, its mechanisms during physical activity are not well understood. Previous studies have focused on the above-mentioned supraspinal mechanisms, including tryptophan, which facilitates the synthesis of serotonin in the brain. An increase in serotonin synthesis has been associated with elevated activities of the sertonergic neurons and a manifestation of a feeling of fatigue (Tanaka & Watanabe, 2007). Similarly, ammonia, produced by the deamination of amino acids, has been speculated as a possible mechanism to fatigue sensation. Inoue and Fushiki (2007) described a study investigating chemical activity of the brain, namely transforming growth factor-β (TGF-β), detectable in the cerebrospinal fluid. TGF-β is a type of cytokine that transforms certain types of cells and promotes their proliferation. This multifunctional factor may also inhibit cell growth and has a role in transmission of information among cells. Inoue and Fushiki (2007) found that TGF-β induces changes in the turnover rate of neurotransmitters in brain tissues. This resulting change in brain activity may modulate the sensation of central fatigue. Through a series of experiments, the authors demonstrated that an increase in exercise intensity was related to an increased concentration of active TGF-β. An increase in TGF-β was also associated with a depressive effect on spontaneous motor activities (Inoue & Fushiki, 2007). Interestingly, TGF-β may also modulate energy metabolism of the whole body, which may be advantageous to minimize impairment when exercise must persist for an enduring time (Inoue & Fushiki, 2007).

Impaired energy utilization in the brain, induced by prolonged deprivation of rest, may lead to synaptic fatigue and is thus a feature of central fatigue (Tanaka & Watanabe, 2007). During acute exercise, serotonin and dopamine systems are activated in the central nervous system, which have been associated with sensation of fatigue. However, little is known of central fatigue effects during late stages of a severe fatiguing task, when there is a prolonged deprivation of rest. Tanaka and Watanabe (2007) found that reduced energy utilization elicits a vicious cycle of central fatigue. Reduced energy utilization consequentially decreases serotonin and dopamine turnover in synaptic terminals, as the maintenance of synaptic transmission and stimulation of synaptic release and recycling of synaptic vesicles requires ATP. Tanaka and Watanabe (2007) speculated that during prolonged fatigue, the insufficient turnover of serotonin and dopamine would lead to insufficient fatigue sensation and physical activity.

Summary (Figure 2.1):

- Central fatigue may be particularly important when activity is sustained for a prolonged period of time.
- Its underlying mechanism is based on a compromised between fatigue-inducing impairments and neuromuscular fatigue-inhibiting strategies.
- Impairments occur at three regions: supraspinal areas, spinal areas, and in the muscle afferent system.

- Supraspinal inhibition, as a result of changes in afferent activity and in concentrations of neurotransmitters, may lead to both decreased cortical excitability and slowing of impulse transit time. Dopamine, neurotransmitter 5-HT, and noradrenaline are all possible factors in the control of thermoregulation and muscle performance. Ammonia has been shown to change membrane permeability, leading to supraspinal dysfunction.
- Spinal inhibition is associated with diminished motoneuron discharge, due to intrinsic motoneuronal properties, reflex inhibition, and disfacilitation. Inhibitory muscle afferents are involved in the down-regulation of motoneuron excitability. This down-regulation may be a response to accumulation of metabolites, acidity, pressure, pain, tension, or stretch.
- The mechanism of fatigue sensation is not well understood. Yet hypotheses suggest that increases in serotonin and ammonia are possible mechanisms. Transforming growth factor- β has recently been cited to induce changes in neurotransmitter turnover rate, modulating the sensation of fatigue.

A Peripheral Approach: Fatigue At The Muscle

The previous section focused on central fatigue, which was determined to be of greater importance during prolonged low-intensity activities. At these low-level exposures, there is likely a limited effect of the metabolic changes within muscle cells. On the contrary, during activity characterized as higher intensity, intramuscular factors appear to dominate (Westerblad et al., 2010). Fatigue (i.e., peripheral fatigue) at the cellular level is the decline in contractile function as a consequence of the effects of high-energy consumption and inability of energy systems to maintain homeostasis. Peripheral fatigue may manifest as decreased isometric force production, reduced shortening speed, altered force-velocity relationship, and slowed relaxation, and can be the result of an adverse affect within the muscle contraction process during high muscle activity.

In short, the activation of skeletal muscle cells is initiated with the generation of action potentials at the neuromuscular junction. Action potentials are then propagated along the surface membrane as well as into the transverse tubular system where voltage-sensory molecules (i.e., dihydropyridine receptors) are activated. The DHPR in turn opens the ryanodine receptor (RyR) Ca^{2+} release channel in the adjacent sarcoplasmic reticulum (SR). Ca^{2+} is then released from the SR, elevating the myoplasmic calcium concentration, where it binds to and subsequently changes the configuration of myofibrillar regulatory proteins, the troponin-tropomyosin protein complex. A muscle contraction is then generated due to the interaction of actin and myosin filaments. In relaxation, action potentials cease, and cytosolic free Ca^{2+} concentration rapidly declines (Westerblad et al., 2010). Force is thus modulated by the concentration of Ca^{2+} surrounding the myofilaments (i.e., decline in tetanic $[Ca^{2+}]$ in myoplasm), the Ca^{2+} sensitivity of the myofibrillar proteins, and the force produced by cross-bridges characterized by the maximum Ca^{2+}-activated force (Allen & Westerblad, 2001). The cumulative changes acting through these three mechanisms, in principle, will result in fatigue at the cellular level (Allen & Westerblad, 2001).

Allen and colleagues (2008) examined a force trace of repeated, short tetani and associated the three mechanisms to particular phases of force change. During the initial small and rapid decline in force, the most likely mechanism is a decline in maximum Ca^{2+}-activated force. The final phase in a fatiguing contraction, where the rate of decline of force accelerates, is most likely explained by both reduced tetanic $[Ca^{2+}]$ in the myoplasm and reduced Ca^{2+} sensitivity. Nocella and colleagues (2011) discussed force loss with respect to the number of cross-bridges generating force and individual cross-bridge force. In initial stages of a fatiguing contraction, the force decline may be due to a reduction of force developed by individual cross-bridges. As exercise progresses and fatigue becomes more marked, the number of force-generating cross-bridges decreases.

As mentioned earlier, the catastrophe model focused on the contention that the accumulation of lactic acid in muscle was the predominant mechanism of fatigue. Since then, the role of lactic acid and reduced pH has been minimized in favour of a variety of metabolic (e.g., P_i, Mg^{2+}, ATP/ADP, glycogen) and non-metabolic (e.g., ROS, mechanisms related to glycogen depletion) factors, affecting different excitation-contraction processes. In fact, reduced intracellular pH may help sustain muscle excitability by reducing Cl^- conductance, thereby enabling action potentials to propagate despite fibre depolarization and Na^+ channel inactivation. Additionally, increased lactate concentration has very little effect on twitch and tetanic force responses (Allen et al. 2008). A vast number of comprehensive reviews have elegantly discussed the cellular mechanisms of fatigue, thus this chapter will briefly review important concepts and findings in the current state of the art.

During high-intensity activity, phosphocreatine (PCr) breaks down into creatine (Cr) and inorganic phosphate $[P_i]$. Resting $[P_i]$ in the myoplasm is between 1 and 5mM, increasing to 30 – 40 mM during intense contractions (Allen & Westerblad, 2001). In a review conducted by Allen and Westerblad (2001), the increased concentration of $[P_i]$ in the myoplasm was proposed to play an important role in muscle fatigue. Dahlstedt and colleagues (2001) supported this phenomenon as the authors observed changes in early fatigue, attributed to increases in $[P_i]$. In particular, tetanic force was markedly lower when muscle fibres had increased $[P_i]$. This led to the belief that increased myoplasmic P_i reduces cross-bridge force production. Elevated myoplasmic $[P_i]$ also led to an increase in tetanic $[Ca^{2+}]$, most possibly due to augmented Ca^{2+} induced SR Ca^{2+} release.

Results also indicate that increased P_i led to a reduction in myofibrillar Ca^{2+} sensitivity, slower relaxation time, and slower SR Ca^{2+} uptake. Consequently, increased P_i was shown to be involved in both fatigue-induced changes in cross-bridge function and SR Ca^{2+} handling (Dahlstedt et al., 2001). Allen and Westerblad (2001) also reviewed, with extensive evidence, increased [P_i] binding to Ca^2 in forming a CaP_i precipitate, and its role in reducing the concentration of free Ca^{2+} in the SR and increasing the rate of SR Ca^{2+} uptake. The subsequent reduction in SR Ca^{2+} release (i.e., free Ca^{2+}) may elicit a fall in force generation. It is important to note that this mechanism may play a greater role in high intensity fatiguing activities longer than 1 – 2 minutes while other mechanisms may be predominant in lower intensity activities greater than 1 hour in duration (Allen & Westerblad, 2001). However, Tupling (2004) sheds some light and questions the validity of the CaP_i hypothesis. For instance free [Ca^{2+}] may increase during fatigue development, contradicting the notion that the precipitate lowers free [Ca^{2+}]. This may suggest that other intracellular mechanisms reduce SR Ca^{2+} uptake, offsetting the positive effects of the precipitate on Ca^{2+} uptake.

Alternative mechanisms modifying SR calcium release have been proposed. One is the decline in [ATP] and consequential rise in free [Mg^{2+}] during intense exercise in fast-twitch fibres, resulting in a reduction in voltage-sensor activation of Ca^{2+} release channels. Allen and colleagues (2008) suggested possible reasons for this mechanism. First, in order for the release channels to be readily opened, ATP must be bound to a cytoplasmic regulatory site. Secondly, accumulation of ADP and AMP near the release channels may antagonize the stimulatory action of the remaining ATP, as both ADP and AMP are weak competitive agonists. Finally, increases in cytoplasmic Mg^{2+} may inhibit the Ca^{2+} release channels, thus in combination with decreased [ATP], may reduce tetanic [Ca^{2+}]. The cell, in response to marked depletion of ATP, will reduce Ca^{2+} release and in turn decrease the rate of ATP hydrolysis as there are reductions in cross-bridge cycling and SR Ca^{2+} uptake. Although a reduction in power output will be observed, the preceding mechanisms may also help in preventing complete exhaustion of all cellular ATP and the resulting rigor development and cellular damage (Allen et al., 2008). Increased ADP may act to down-regulate SERCA activity as a defense mechanism for cellular protection against large increases in ADP/ATP ratio. The relationship between ADP and SERCA activity is further exemplified as low free [ADP] reduced the efficiency of Ca^{2+} transport into the SR (Tupling, 2004).

A second mechanism is the production of reactive oxygen species (ROS) that have been shown to substantially increase during intense activity, particularly in the cytosol, extracellular space, and vascular components of the exercising muscle (Reid, 2001). Previous studies revealed that ROS scavengers reduced the rate of fatigue, implying that ROS may have a role in the mediation of muscle fatigue (Allen et al., 2008). Alessio and colleagues (2000) investigated the resulting oxidative stress after exhaustive aerobic and isometric exercise in humans. The authors found that both types of exercise resulted in oxidative stress, including increases in lipid hydroperoxides, protein carbonyls, and total antioxidants. Specifically, during exhaustive aerobic exercise, proteins were more likely to be oxidized and form carbonyls. This may be due to elevated VO_2, which produces high concentrations of oxygen free radicals. If the free radicals formation exceeds antioxidant capacity (or a deficiency in antioxidant defense), radicals may escape from the mitochondria to oxidize lipids, proteins, sugars, and other cell components (Alessio et al., 2000; Essig & Nosek, 1997). On the other hand, during exhaustive isometric exercise, lipids were more likely to undergo peroxidation (i.e., significant oxidative changes of lipid hydroperoxides). However, the functional impact of lipid peroxidation in muscle is not well understood and there remains doubt as to whether it may not be directly related to muscle fatigue. Instead, oxidation of specific proteins may be the cause of decline in contractile function (Essig & Nosek, 1997). A possible explanation for the observed oxidative stress may be hemodynamic changes (i.e., blood flow) associated with ischemia-reperfusion, with speculation that oxygen radicals might be generated after vasoconstriction. Metabolite build-up may also occur, which could contribute to fluctuations in the antioxidant/pro-oxidant balance. Another possible mechanism is mechanical stress, which contributes to exercise-induced damage of muscle fibres, even in the absence of increased VO_2. For instance, eccentric exercise initiates cytokine activity, which controls inflammation. Reactions of pro-oxidants, including LIPOX by-products, may play a causal role in inflammation. Additionally, previous studies have reported increased protein carbonyl derivatives and serum creatine kinase activity after concentric leg exercises (Alessio et al., 2000). One hypothetical mechanism is that ROS affects SR Ca^{2+} release by oxidative modification to a cysteine residue on the RyR1, reducing the rate and/or efficiency of SR Ca^{2+} transport (Allen et al., 2008). However, there remains little convincing evidence to suggest ROS modulates SR Ca^{2+} release in intact muscle during fatigue (Allen et al., 2008). Another hypothesis is that increased ROS is associated with depression in myofibrillar Ca^{2+} sensitivity (Reid, 2001). Although the exact mechanism has yet to be elucidated, possible candidates include alterations to troponin-C or oxidative damage to tropomyosin, actin, or myosin (Fitts, 2008). Brotto and Nosek (1996) found that elevated levels of hydrogen peroxide is capable of damaging one or more proteins of the ECC apparatus, resulting in low-frequency fatigue (as cited in Essig & Nosek, 1997). Reid (2001) stated that during the early phase of a fatiguing exercise, antioxidants attenuate the early force decrement, suggesting ROS involvement. Later in the fatigue process, exaggerated ROS production may mediate handling of Ca^{2+} by the SR. Prolonged exposure to ROS (e.g., hydrogen peroxide) appeared to increase SR calcium leak and slow calcium reuptake by the SR. Closely related to ROS production is the synthesis of heat shock proteins (HSPs). Essig and Nosek (1997) noted that HSPs might arise from reduced ATP activating the heat shock transcription factor or ROS directly/indirectly involved in signaling pathways. HSPs may function to protect cellular proteins from oxidative damage or denaturing during bouts of muscle contractile activity. It has been hypothesized that HSP70 and HSP32 have a myoprotective function, possibly delaying the onset of fatigue during activity and enhancing recovery from low-frequency fatigue (Essig & Nosek, 1997). HSP27 and other small HSPs have also been shown to mediate anti-oxidant protection by ablating the toxicity of oxidized proteins and reducing the number of ROS (Thambirajah et al., 2008).

Another mechanism is the relationship between glycogen and force where there is a possible link between low glycogen and decreased tetanic [Ca^{2+}]. Reduction in muscle glycogen may play an important role in demanding tasks/activities that require repeated, intense efforts, particularly with the involvement of large muscle groups (Green, 1997). These exercise intensities range from 60 to 85% of maximal aerobic power (Green, 1991). According to Sahlin and colleagues (1998), decreases in muscle glycogen are heterogeneous between fibre types. Additionally, less recruited fibres exhibited more glycogen (i.e., glycogen depleted fibres exhibit more pronounced energy deficiency). The relationship between muscle glycogen and work capacity during prolonged activity has been well established. In these models, muscle glycogen is an essential substrate in which its reduction may result in an inability to sustain glycolytic flux rate and ATP regeneration. A consequential fall in ATP concentration will culminate in the inability to meet energy demands for multiple processes in the excitation-contraction process (Green, 1991). These mechanisms, resulting in the disturbance of excitation-contraction processes, may be unrelated to metabolic alterations. It has been speculated that glycogen, acting as a non-metabolic mechanism, provides structural integrity to the SR, particularly to the triadic membrane compartment where the DHPR interacts with the RyR (Tupling, 2004). If the glycogen particle is reduced in size, they may detach from the SR and redistributed throughout the cell. Green (1991) comprehensively discussed other possible mechanisms in which glycogen serves a non-metabolic role in muscle function. One might be on the basis of myofibrillar fatigue, where endogenous glycogen reserves may protect the integrity of the sarcomere during prolonged activity. Another is the possibility that glycogen stabilizes muscle hydration level during prolonged exercise. However, there remains doubt as to the mechanistic link, and whether or not it is related to glycogen's primary role in energy metabolism (Allen et al., 2008). Surely, it may be possible that the relationship between fatigue and low muscle glycogen is not due to peripheral fatigue but rather to the reduction in the output of the α-motoneuron pool (Green, 1991). Reductions in glycogen coupled with impaired energy potential have been shown to increase metabolic by-product that in turn stimulates group III and IV muscle afferents.

Phosphorylation reactions have also been in the forefront of possible mechanisms of SR Ca^{2+} handling. As previously mentioned, myosin regulatory light chain phosphorylation, which plays a central role in post-activation potentiation, is initiated by an increase in [Ca^{2+}] during contractions via a Ca^{2+}-calmodulin-dependent activation of skeletal muscle myosin light chain kinase (skMLCK). In fast-twitch fibres, an increase in myoplasmic [Ca^{2+}] activates calmodulin kinase II (CaMKII), which may phosphorylate proteins involved in SR Ca^{2+} release (e.g., RyR, DHPR, some of their associated proteins). In slow-twitch fibres, CaMKII may act on SR Ca^{2+} ATPase and phospholamban (Allen et al., 2008). Finally, acute β-adrenergic stimulation has been shown to activate protein kinase A (PKA), which subsequently leads to phosphorylation and increased SR Ca^{2+} release (Allen et al., 2008). It is most likely that PKA phosphorylation activates RyR1 by phosphorylating Ser^{2843}, which causes a dissociation of FKBP12 from the RyR1 channel. The FKBP12 stabilizes the closed state of the RyR1 channel whereby its release increases RyR1 activity and subsequently increases Ca^{2+} release from the SR (Reiken et al., 2003). However, prolonged acute β-adrenergic stimulation may hyperphosphorylate RyR1 and lead to a release of calstabin1. It has been speculated that the release of calstabin1 may destabilize RyR1 channels and thus increase SR Ca^{2+} leakage and impair muscle function (Allen et al., 2008). Evidently, there is sufficient support to explain the effects of impaired RyR function and the associated reduction in SR Ca^{2+} release. Another hypothesis suggests that the uncoupling of the physical interaction between the α1 subunit of the DHPR and the RyR, may affect RyR function (Tupling, 2004). The physical alteration of the cytosolic physical interaction may be particularly significant in low-frequency fatigue.

Finally, muscle fatigue may also be a consequence of slowed muscle relaxation, which is most detrimental in activities that require rapid dynamic contractions (Tupling, 2004). Muscle relaxation involves the following processes: dissociation of Ca^{2+} from troponin, and detachment of cross-bridges, and SERCA-mediated Ca^{2+} removal from the cytoplasm, which may be more important in human muscle (Tupling, 2004). Nocella and colleagues (2011) observed an increased rate of tetanic force development and relaxation during the early phase of fatigue.

During later stages, however, when fatigue was more severe, the rate of force development and relaxation were slower. Impairments to SERCA-mediated Ca^{2+} activity may lead to high concentrations of free calcium. To avoid potential damaging effects of $[Ca^{2+}]_f$, Ca^{2+} is removed from the cell leading to a net loss of Ca^{2+} and reduced SR Ca^{2+} stores, which in turn may contribute to long-lasting fatigue.

Summary (Figure 2.1):

- Dysfunction at the peripheral level may be predominant during high intensity activity.
- Fatigue at the cellular level is modulated by three mechanisms: changes in tetanic $[Ca^{2+}]$ in myoplasm, Ca^{2+} sensitivity of the myofibrillar proteins, and force produced by cross-bridges characterized by maximum Ca^{2+}-activated force.
- These mechanisms are due to both metabolic and non-metabolic factors, affecting different excitation-contraction processes.
- An increase in $[P_i]$ in the myoplasm may play a prominent role in muscle fatigue, including a reduction of myofibrillar Ca^{2+} sensitivity, slower SR Ca^{2+} uptake, an initial increase in tetanic $[Ca^{2+}]$, and the forming of a CaP_i precipitate.
- Increases in [ADP] and free $[Mg^{2+}]$ have been shown to reduce voltage-sensor activation of Ca^{2+} release channels, leading to reduced tetanic $[Ca^{2+}]$.
- Reactive oxygen species (ROS) have gained momentum in recent years as a possible mechanism to reduce the myofibrillar Ca^{2+} sensitivity or the rate and/or efficiency of SR Ca^{2+} transport. Previous studies have shown prolonged exposure to ROS (e.g., hydrogen peroxide) may damage proteins in the excitation-contraction-coupling apparatus, resulting in low-frequency fatigue (LFF).
- Another important mechanism in LFF is the uncoupling of the physical interaction between DHPR and RyR, which may affect RyR function.
- Finally, muscle fatigue may also be a consequence of slowed muscle relaxation, particularly due to impairments to SERCA-mediated Ca^{2+} removal. These impairments may lead to high concentrations of free calcium, which may be detrimental in activities that require rapid dynamic contractions.

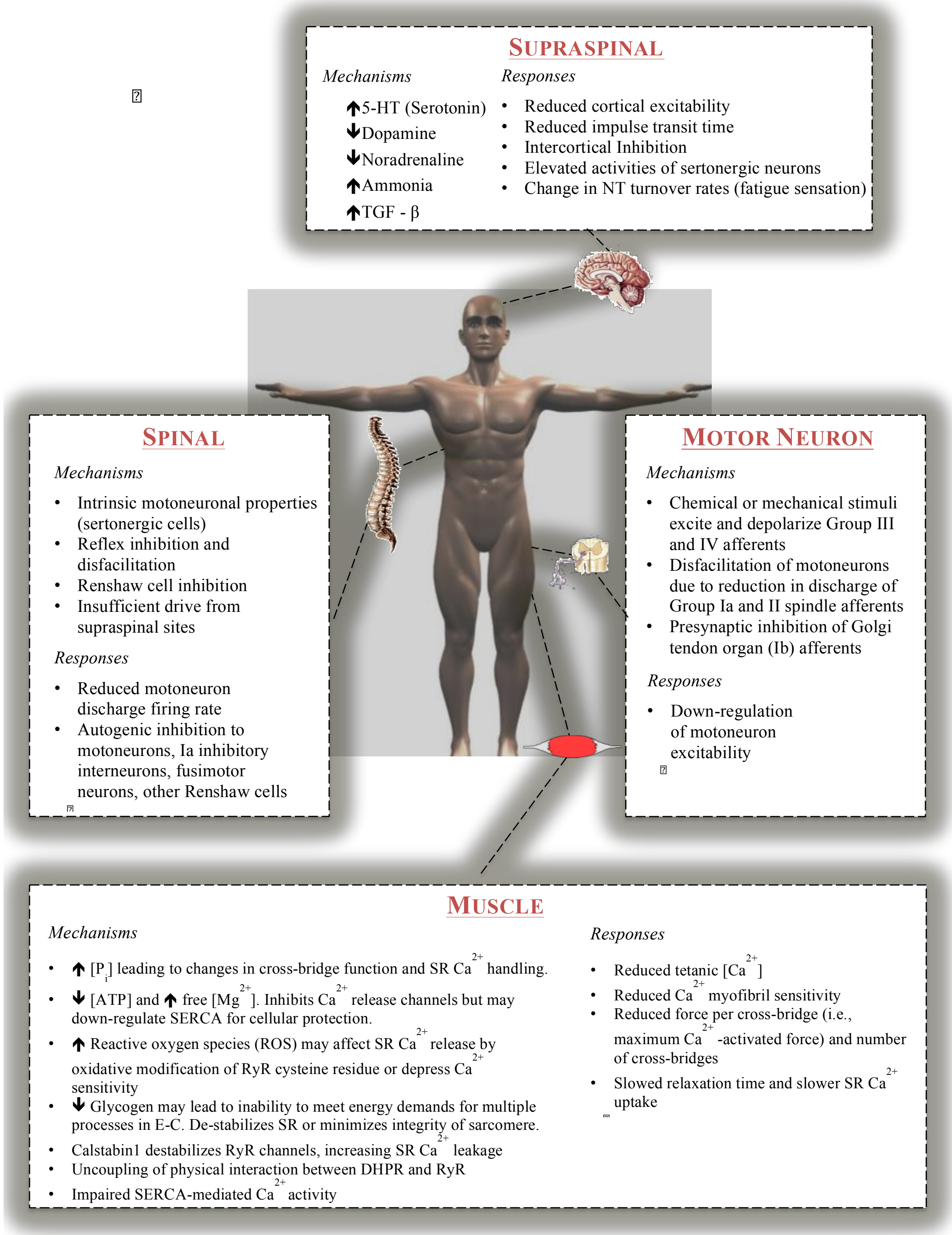


Figure 2.1 Summary of potential mechanisms and responses at different possible sites of fatigue.

Fatigue in Industry – A Historical Perspective

A main impetus in our current understanding of fatigue is its relationship to the history of work and the concept of the human body as a motor. According to Rabinbach (1992), fatigue did not appear in the scientific lexicon before the 1860s, with almost no records of medical or scientific studies on fatigue. Yet by the turn of the century, fatigue research had proliferated, with over a hundred scientific papers dedicated to muscle fatigue, exhaustion, and neurasthenia – or chronic fatigue syndrome (Evengård, 2007). The 1920s and 1930s saw a focus on cognitive *attention* and a subsequent revival in the 1960s due to the emergence of cognitive psychology. The 1950s were marked with issues on vigilance and monitoring and flourished during the second half of the twentieth century (Hockey, 2013). What might explain this increased interest in fatigue research? Historians postulate two concepts: the theorization of the laws of thermodynamics and discovery of labour power during the Industrial Revolution.

In 1847, Hermann von Helmholtz argued that forces of nature are forms of a single, universal energy, which cannot be added or destroyed, the principle of conservation of energy, forming the first law of thermodynamics. Energy became the quintessential element of all organic and inorganic experiences. Emerging in 1850 was Rudolf Clausius' second law of thermodynamics, introducing concepts of entropy, where the transfer of energy is accompanied by a decrease in total available energy. This revelation counterbalanced energy conservation, which implied that there was an inevitable dissipation of force and that entropy tends to a maximum. These laws have been applied to the human motor, which was capable of conserving and dissipating energy. Fatigue became the indicator and reminder of the body's inability for unlimited progress and productivity and was a particular instance of entropy (Rabinbach, 1992). Labour power was conceived as a result of the laws of thermodynamics, redefined from a measurement of the force of machines to the basis of all matter and motion. Work was redefined too, universalized in all mechanisms. The human body was analogous to a machine, but yielding work from muscles, nerves, and organs. Armed with the concepts stemming from the laws of thermodynamics and labour force, there was a growing awareness of the role of energy as a limiting factor in production. Fatigue and energy emerged as a modern conceptual framework to describe both work and the human body, leading to ubiquitous energy-depletion based models, i.e., catastrophe theory (Hockey, 2013).

The pervasive ideology of the human motor and the resulting fatigue-energy paradigm has endured since the 19th century. Increased output, greater work performance, and more energetic workers were coupled with efforts to eliminate industrial risk, improve health and safety, and shorten the workday (Rabinbach, 1992). McIvor (1987) elegantly discussed the evolution of industrial fatigue in Britain, between 1890 and 1918 (N.B. the term *industrial* may be dated as *work* takes a variety of forms, therefore *occupational* fatigue may be more relevant today). In the late 19th century, McIvor describes the neglect of the *human element*, the minimal regard to the limitations of human physiology and psychology in favour of production. Labour was widely regarded as a pure commodity, a factor in the production process with relatively standardized capabilities (McIvor, 1987). Most employers remained bound to traditional cost cutting techniques, as there was little evidence to accept that improving worker health could reap benefits. It was not surprising, however, that employers and government alike shared this perspective, as many were concerned about poor trade conditions and Britain's international competitive position. However, this neglect resulted in ill health, disease, premature death, deprivation, and exhaustion. Additionally, neglecting the *human element* may in fact lead to reduced productivity. Conceding that there may be greater potential for improvements in human efficiency at work, knowledge was sought to the exact measurement and analysis of work. One important study was conducted by William Mather, who investigated the relationship between overstrain and impaired productivity. Most importantly, this study concluded that decreasing working hours from 53 hours to 48 hours per week led to increased output, reduced costs, and reduced absenteeism. Later studies confirmed Mather's hypothesis that as excessive working hours were reduced (and hence industrial fatigue), productivity significantly increased. Meanwhile, in the United States, unions, women's advocates, and socialists pushed for expanded protective legislation against increased working hours (Dembe, 2009). In 1917, the landmark *Bunting v. Oregon* Supreme Court decision led to greater national attention towards ethical and medical issues associated with long working hours. The decision also helped set the foundation for passing the Fair Labour Standards Act (FLSA) in 1938, which required most government contractors to adopt an 8-hour day and a 40-hour week. Due to a combination of protective legislation, changes in production methods, and societal trends, the average workweek decreased from 60-70 hours in the 19th century, to 50-60 hours from 1900 to 1930, and has remained at 40 hours since the Great Depression (Dembe, 2009).

However, long working hours, although not mandatory, continue to persist today. With the increasing number of service and knowledge-based types of work, although the mean hour per week has not dramatically changed, there are now a greater proportion of workers in both low-hour (less than 30 per week) and in high-hour (greater than 50 per week) work schedules. Cited in

Dembe (2009), as of 2007, 18.1% of Americans worked more than 48 hours per week. In Japan, 5.77 million people worked 60 hours or more on a weekly basis, in sectors other than agriculture and forestry (Kajimoto, 2007). It is not surprising that research in *optimal* permissible working hours is currently pertinent. For instance, Nagashima and colleagues (2007) investigated the threshold amount of working hours that can be recommended to protect workers from health effects, including fatigue. The authors found that working less than 260 hours per month (i.e., 60 hours per week) resulted in a significantly lower prevalence of fatigue symptoms.

Prevention of industrial fatigue is not limited to the reduction of working hours. New forms of work have led to increased levels of physical (and mental) fatigue (Kajimoto, 2007; Saito, 1999). Such *new forms* of work include adoption of new working times (e.g., flexible working hours, shiftwork), new types of employment (e.g., temporary work, knowledge-based work), new forms of business (e.g., 24-hour businesses), globalization, and changes in work processes (e.g., lean manufacturing, work intensification). For instance, based on production systems principles, rest breaks are considered unproductive and can only be implemented up to a certain proportion of work time (Wells et al., 2007). This may have implications with previous workplace solutions that aimed to minimize fatigue via rest allowances. It is not surprising that occupational fatigue is as relevant, and its reduction more complex, in the 21st century as it was in the early 20th century.

Fatigue, Ergonomics, and Product Quality

The relationship between ergonomics and product quality has a long history (Drury, 1997). Previous studies have demonstrated relationships between a deficient work environment, i.e., ergonomic problems, and underperformance, i.e., product quality deficiencies (e.g., Eklund, 1995; Rajan et al., 1999; Axelsson, 2000; Lin et al., 2001; Wartenberg et al., 2004; Falck et al., 2010; Erdinç and Yeow 2011; Rose et al., 2013). Under poor ergonomic conditions, it has been estimated that the number of quality deficits increased 3-10 times when compared to optimal working conditions (Eklund, 1999; Axelsson, 2000). Falck and colleagues (2010) specifically found an increased risk of quality errors in highly physical (i.e., unacceptable workloads causing harmful impact on the body) and moderately physical (i.e., moderate physical stress with potential harmful impact) work. In fact, medium load assemblies showed 3.7 times higher error frequency, whereas high load work showed 3.0 times higher error frequency, when compared to low load assemblies.

Rose and colleagues (2013) indicated that deficient work environments would have an effect the system (e.g., quality, production levels), and the human (e.g., fatigue, pain, and competency). Eberhardt et al. (1993), for example, identified a very broad range of factors that could affect product quality: the configuration of the workspace, duration of the task, equipment tooling, lighting, social factors, and surface conditions as major contributors in aircraft maintenance. Hamrol et al., (2011), based on independent interviews with workers and FMEA analyses by experts, identified a range of factors including manual work, employee fatigue, time pressure (hurry), noise level (NL) perceived by the human working on the assembly line, work monotony, faulty elements, employee inattention, microclimate, not respecting work instructions, and lighting. Similarly, Village et al (2013) identified a wide range of factors including, issues of part/component design (which affects grip type), components of assembly or mating of parts (which affects matters like force and posture and number of hands required), aspects of visual demands (e.g., contrast), aspects of feedback (e.g., when a part is correctly assembled) and aspects of detection of errors/quality problems.

Falck et al., (2010) found that fatigue, as a result of tiresome and harmful work postures, was one of the most common ergonomic problems. Similarly, Hamrol et al., (2011) surveyed employees and found that worker fatigue was a main reason for assembly deficits. Recently, a systematic review conducted by Kolus et al., (2014) supported these findings, identifying fatigue as a frequent intermediary factor between poor ergonomics and quality deficits.

Improved ergonomics have been shown to directly reduce levels of mental and physical fatigue and indirectly improve health outcomes, quality and efficiency of production, and other aspects of profitability (González et al., 2003). For instance, Abrahamsson (2000) evaluated the implementation of an engineering solution in a steel manufacturing facility. Improved ergonomics led to a reduction in strenuous physical workloads, a reduction in production disturbances, improved production planning reliability, and reduced needs for maintenance. An improved work environment also led to profitability, such as fewer accidents and improved interest and motivation among employees. Rose and colleagues (2013) calculated the financial profitability of Abrahamsson's (2000) improvements and found that only 2% are attributed to sick-leave cost savings, and the remaining 98% were related to productivity and quality improvements. Yeow and colleagues (2003) assessed the cost-benefit of ergonomic interventions in workstations for electrical tests in a printed circuit assembly factory. The authors found increased productivity

(6.5%), improved quality (i.e., defect reduction of 3.0%), cost savings of US$574,560 due to better quality products, and reduced muscle fatigue.

Fatigue Measurement

Typical Measures to Detect Decrements in Cognitive Function

Although not a primary focus of this dissertation, decrements in human performance are important to consider, particularly due to changes in human information processing and cognitive aspects of fatigue. Decrements in human performance have been implicated in 80-90% of accidents. In fact, two out of three fatal occupational accidents may be caused by human error (Salminen & Tallberg, 1996), and is considered the most important single causal factor in critical incidents, including industrial accidents (Feyer, Williamson, & Cairns, 1997). Human errors are costly, as exemplified in healthcare. Medical errors costs $37.6 billion per year and preventable errors account for $17 billion in the US. It has been estimated that the incidence of medical errors can be reduced by 55% by using human factor-based initiatives (Duffy, 2009). In recent times, human factors have assumed greater importance in a diverse array of work environments, including military surveillance, air traffic control, cockpit monitoring, seaboard navigation, long-distance driving, agricultural inspection tasks, and industrial process/quality control (Warm et al., 2008). These jobs involve automation, which has led to alterations in the role of operators from active controllers to passive system supervisors. Operators now serve in a fail-safe capacity, intervening only in the event of system failure (Matthews et al., 2010).

Since information processing involve central nervous system activity and its physiological manifestations are indexes of resource mobilization, information-processing workload is measurable (Chi, Lin, & Lan, 2003). A number of terms have been used to describe the cortical activation states that impact the ability to process information. Among these terms are arousal, alertness, attention, and vigilance. In short, arousal, or wakefulness, refers to non-specific activation of the cerebral cortex in relation to sleep-wake states and is often considered an aspect of vigilance (Oken, Salinsky, & Elsas, 2006). Arousal, however, is distinct from vigilance as it involves a state of sleep-deprivation. By influencing the competition between stimuli for mental resources, arousal changes the processing for high and low priority stimuli (Mather & Sutherland, 2011). Alertness, described as phasic and tonic, is similar to arousal but includes cognitive processing. Phasic alertness is associated with orienting response while tonic alertness is synonymous with vigilance (Oken et al., 2006). Similar to arousal, even losing small amounts of sleep have been shown to significantly degrade alertness (Caldwell, Caldwell, & Schmidt, 2008). A definitive feature of attention is a focused activation of the cerebral cortex, which enhances information processing (Oken et al., 2006). Enhanced information processing may be achieved by modulating the activation of the ventral visual pathway, from the occipital lobe to the fusiform and parahippocampal region. This modulation is through increasing or decreasing attention (Chee & Chuah, 2007). Attention allows the operator to bias process incoming information in order to focus on relevant information to achieve current goals (Boksem, Meijman, & Lorist, 2005). Vigilance or sustained attention is a cognitive function that occurs when individuals maintain their focus and remain alert to a particular stimulus (visual or auditory) over a prolonged period of time (Warm, Parasuraman, & Matthews, 2008). According to Wickens and Hollands (1999), vigilance is a state of readiness to detect and respond to changes that may be intermittent, unpredictable, and infrequent. This phenomenon of decreasing vigilance level over time is known as vigilance decrement (Wickens & Hollands, 1999). There are a number of measurements to detect cognitive aspects of fatigue (Table 2.1).

Table 2.1 Human Factor Measurements

Human Factor	**Description**	**Possible Measurements**
Arousal	An aspect of vigilance, involves a state of sleep deprivation.	• EEG – Event Related Potential • Electrodermal Response (EDR) • Heart Rate • Endocrine Biomarkers – Mono-Amine Oxidase (MAO) • Body Temperature • Validated Questionnaires and Self-Reports • Critical Flicker Fusion Frequency • Auditory Evoked Responses • Pupil Dilation
Alertness	Similar to arousal, involves cognitive processing.	• Psychomotor Vigilance Test (PVT) • Functional Near Infrared Spectroscopy • EEG Frequency Bands • Validated Questionnaires and Self-Reports • Validated Scales (e.g., Stanford Sleepiness Scale, VAS) • Polysomnography • Neurobehavioural Tests • Speech Analysis (pitch, intensity, pauses, word rate) • Gaze Direction, Blink Rate
Vigilance	Focus of attention and remaining alert to a stimulus over a prolonged period of time.	• NASA-TLX (Resource Theory) • EEG and Reaction Times • Behavioural Tests • Transcranial Doppler Sonography

		• Neuroimaging (PET, fMRI) • Validated Questionnaires and Scales (e.g., Coping in Task Situations. Dundee Stress State Questionnaire, Vigilance Scale) • Eye Movements, Blink Rate • Heart Rate • Electrodermal Response • Respiration • Motor Restlessness
Attention	Bias process incoming information to focus on relevant information to achieve current goals. Actively ignore irrelevant information.	• EEG – Event Related Potential, Frequency Bands • Performance-Based Neuropsychological Tests • Validated Scales • Neuroimaging (MEG, fMRI) • Steady State Visually Evoked Potentials • Gaze Direction, Visual Fixations
Short-Term & Working Memory Failures	Factors in cognitive performance. Information processing may be limited by the capacity to retain information in short-term memory and if working memory is disrupted by other stimuli.	• Complex Span Task (e.g., Reading, Digits, Word) • N-Back Task • Pitch-Matching Paradigm Test • Validated Scales (e.g., Stanford-Binet Intelligence Scales, Wechsler Intelligence Scale – Fourth Edition) • Neuroimaging (MEG) • Saccadic Eye Movements, Gaze Direction, Smooth Pursuit Eye Movements
Cognitive Control (e.g., Slowing)	Global lengthening of processing time and may involve perceptual deficits, attentional deficits, minor cognitive deficits, and overall mental slowing.	• Graphing Mean Reaction Times Surrounding an Error • Difference in Mean Reaction Time Between Trials Post-Error and Post-Correct • EEG – Event Related Potential • Neuropsychological Tests (Symbol Digit Substitution Test, Simple Reaction Time) • Correction Saccades
Motivation	Motivation may improve action monitoring and improve overall performance by engaging the attentional system at a greater intensity and for longer duration.	• Validated Scales • Validated Questionnaires
Stress	May impact vigilance and mediate alertness via the amygdala.	• Cortisol • Subjective Workload Assessment Techniques (SWAT) • NASA-TLX • Electrodermal Response (EDR) • Heart Rate Variability • Validated Questionnaires • Validated Scales • Blood Pressure • Awkward Body Postures

Typical Measures From Laboratory Experimental Studies in Simulated Work Tasks

The majority of neuromuscular fatigue studies have been conducted in controlled laboratory settings and fewer on occupational tasks performed in real life (Table 2.2). The following section will briefly describe these measures and will provide further details for force variability and tremor, which has been measured less extensively in simulated work studies.

Extensively Studied Measures

A widely employed objective tool to evaluate muscle fatigue in laboratory-controlled studies is electromyography (Hammarskjold & Harms-Ringdahl, 1992; Bonato et al., 2002; Mathiassen & Winkel, 1996; Farina et al., 2002; Lin et al., 2004; Bennie et al., 2002; Berguer et al., 1997). Alternatively, mechanomyography (MMG) has been used to detect intrinsic mechanical properties of active muscle fibres (Søgaard et al., 2003). MMG measures the skin surface oscillations that are due to radial thickening and lateral movement of each active motor unit (Vedsted et al., 2006). Previous literature suggests that MMG, based on changes in time domain and frequency spectra values, may be indicative of local fatigue (Søgaard et al., 2003). As a complementary method to electromyography and mechanomyography, dimensional changes of muscle using sonomyography (i.e., measuring the thickness of muscle using ultrasound) appear to have some utility (Shi et al., 2007).

Measures detecting cellular and metabolic changes, including muscle biopsies and blood sampling techniques, are often recognized as "gold standard" in muscle physiology literature (Garde et al., 2003). Blood sampling is a direct method to measure these metabolites and can be used to analyze specific biomarkers. Garde and colleagues (2003) observed a progressive increase in norepinephrine concentrations during a repetitive task with blood sampling. Increases in contractile activity and metabolic work have also been assessed by non-invasive blood flow analysis, such as laser Doppler flowmetery (Larsson et al., 1995). Similarly, near-infrared spectroscopy (NIRS) monitors the balance between oxygen supply and utilization (Pereira et al., 2007).

Low-frequency fatigue (LFF), evoked by electrical muscle stimulation, may be a precursor for musculoskeletal disorders (Hagberg et al., 1995) and its recovery process may exceed 24 hours (Adamo et al., 2002). The magnitude of LFF during exercise and recovery may be calculated as the force-response ratio, dividing force responses at 20 Hz by responses at 100 Hz, and its relative decline is indicative of LFF. Mechanistically, LFF may be associated with the failure in the excitation-contraction coupling mechanism (Adamo et al., 2002) and depression in Ca^{2+} release due to the uncoupling of the physical interaction between dihydropyridine receptors (DHPR) and ryanodine receptors (RyR) (Green et al., 2004). Additionally, inorganic phosphate (P_i) might enter the sarcoplasmic reticulum (SR), forming a Ca^{2+}-P_i precipitate, lowering the free Ca^{2+} in the SR that is available for release (Tupling, 2004). According to Green and colleagues (2004), at low frequencies, a small reduction in cytosolic free Ca^{2+} ($[Ca^{2+}_f]$) can lead to reductions in force given the steep nature of the force-frequency curve. After a series of repetitive ulnar deviation tasks, low-frequency fatigue ratio decreased during the day (Dennerlein et al., 2003). Yung and colleagues (2012) also found lowered LFF ratio during recovery periods after bouts of elbow extension exercises that were in the same order of magnitude as previous studies, in terms of average force, cycle time, and duty cycle.

Other non-invasive measures, documenting global changes related to both central and peripheral mechanisms, have been studied in the fatigue literature. Position-matching tasks have been employed to determine whether kinaesthesia, the sense of limb position and movement, was affected by fatigue (Allen & Proske, 2006; Forestier et al., 2002). It was shown that the fatigued limb led to an increase muscular effort to maintain a given position, leading to greater matching errors. This decrement in proprioceptive acuity was also documented as an impairment of postural control (or increase in postural sway) by changes in centre-of-pressure as measured from a force platform (Davidson et al., 2004; Madigan et al., 2006; Mello et al., 2007, Vuillerme et al., 2002). Increased sway may be due to reduced muscular force or, more likely, decreased stability of muscle force (Davidson et al., 2004). Similarly, joint angle variability increased, including distal joints from the fatigued musculature, as monitored by motion capture systems (Madigan et al., 2006).

Force Variability

Force variability, based on changes in standard deviation and coefficient of variation, in fatiguing contractions have been documented to increase with fatigue (Leyk et al., 2006; Svendsen et al., 2010; Contessa et al., 2009). Signal complexity, calculated by sample entropy methods, has also been measured to determine predictability of the force signal. Force variability may be a reflection of underlying neurophysiological mechanisms, including the adaptation between force output and sensory input (Sosnoff et al., 2006). Less force fluctuation might indicate a lower number of error corrections and blending of pulse elements, i.e., tuning of force deviations from ideal force trajectory. According to Lin and colleagues (2014), changes in force fluctuation and complexity may reflect underlying variations in peripherally derived afferent information, variable firing rates of motoneurons, and lower of recruitment threshold of motor units.

Svendsen and Madeleine (2010) observed increases in standard deviation and coefficient of variation during a sustained 20%MVC isometric elbow flexion, until task failure. Trends also indicate increases in force complexity, but were not statistically significant. During a dynamic gripping contraction, pre- and post- fatigue, force complexity increased using sample entropy measures. Based on multi-scale entropy (MSE), complexity during long-time scales increased despite decreases in MSE area, i.e., greater regularity, during low-time scales (Lin et al., 2014). Force variability may also be sensitive to the effects of a mentally fatiguing task. Budini and colleagues (2014) demonstrated a decrease in coefficient of variation (i.e., improved force steadiness), particularly between 8 and 12 Hz frequency band, as a result of mental fatigue. The authors claimed that mental fatigue might weaken the corticomuscular coherence at 8-12 Hz, thereby reducing tremor amplitude at this frequency band.

Tremor

Changes in motor control, as a result of fatigue, may also be detected by changes in physiological tremor (Lippold, 1981). Physiological tremor is an involuntary, rhythmic, and periodic mechanical oscillation, whose dominant power lies predominantly in the range of 8 and 12 Hz. Postural tremor is a sub-category of action tremor that occurs when there is voluntary muscle activity to maintain a particular posture held against gravity (Rehman, 2000). Simply, it is the "positional wobble" (Lakie, 2010). There is, however, some conflicting evidence to the aetiology of both physiological and postural tremor (Hallett, 1998).

On one hand, tremors may be governed by central drive originating from hypothesized oscillators within the CNS, stretch-reflex activity, and motor unit synchronization (Lippold, 1981; Hallett, 1998). Elble and Randall (1976) proposed that Renshaw inhibition might be a source of the central tremor. Alternatively, Renshaw cells might act to desynchronize motorneurons, reducing physiological tremor, when firing rates were close to 10 Hz (Windhorst et al., 1978). On the other hand, the addition of Renshaw cells, particularly at motorneuron firing rates higher than 20 Hz, may increase synchrony in the motoneuron pool (Uchiyama & Windhorst, 2007). More recently, there is evidence to suggest that Renshaw cells form part of the neural system to filter out 10 Hz oscillations from motoneuron discharge, effectively reducing 10 Hz corticomuscular coherence, while increasing coherence at 30 Hz (Williams & Baker, 2009). Recurrent inhibition might thus serve as a “variable gain control”, occurring during low contraction levels, which will allow supraspinal centers to operate over a large working range to cause small changes in muscle force, thereby improving resolution in control of motor output. Over higher level of forces, a decrease in Renshaw cell inhibition will allow central command to generate larger force output for a given drive (Pierrot-Deseilligny & Burke, 2005). During a sustained contraction, recurrent inhibition is decreased, allowing for the recruitment of motoneurones to compensate for cellular impairments of fatigue (Pierrot-Deseilligny & Burke, 2005). Another proposed site and source of the 8- to 12-Hz oscillation is the inferior olive (Lamarre, 1979). The inferior olive give rise to climbing fibers that innervate Purkinje cells, which are the source of output signals of the cerebellar cortex reaching the central cerebellar and vestibular nuclei (De Zeeuw et al., 1998). A presynaptic impulse can depolarize the cell soma, spreading into the dendrites, where it activates the dendritic calcium conductance. An influx of calcium ions activates the calcium-dependent conductance and produces a plateau after depolarization. An increase in potassium conductance increases, which in turn leads to hyperpolarization of the cell, deinactivating the somatic calcium conductance. The hyperpolarization decays and a rebound depolarization occur, starting the sequence once again (Rothwell, 1998). A single action potential can elicit a train of five or six spikes (Bernardo & Foster, 1986). It has been shown that the inferior olive functions as an oscillating clock, which provides appropriate timing of command signals for the appropriate motor domains (De Zeeuw et al., 1998). Oscillating frequencies of olivary neurons may be a consequence of calcium-dependent potassium-mediated hyperpolarization, and its frequency range (i.e., up to 10 Hz) is similar to the firing rates of climbing fibers (Bernardo & Foster, 1986). Olivary neurons are dynamically electrotonically coupled by dendrodendritic synapses (gap junctions) and facilitates synchronous firing patterns generated by chemical synaptic inputs (Elble, 1998; De Zeeuw et al., 1998). This discharge produces rhythmic activation of cerebellar Purkinje cells and nuclear cells, and is correlated to the initiation and performance of movements. Tremor occurs when there is widespread and sustained olivocerebellar oscillation (Elble, 1998). Central oscillations might also originate at the thalamus, primarily as a result of thalamic low-threshold calcium spike bursts (Jeanmonod et al., 1996). Effective clinical therapy for severe tremor in movement disorders, including Parkinson’s disease and essential tremor, has provided further evidence for the involvement of the thalamus (Hua et al., 1998; Rehncrona et al., 2003). For instance, high-frequency deep brain stimulations (DBS), using implanted brain electrodes in the ventrointermediate nucleus of the thalamus, have been implemented to successfully alleviate severe tremor in non-Parkinsonian essential tremor (Rehncrona et al., 2003). In a study addressing neuronal subthalamic nucleus (STN) activity in patients with Parkinsonian rest tremor, the authors found over 50% coherence between neuronal STN activity and EMG at the tremor frequency (Amtage et al., 2008). An intrinsic property of STN neurons is its propensity to fire in rhythmic bursts; the subsequent oscillatory activity is then maintained by forming functional loops (i.e., coupling) with other centers (i.e., cortex, basal ganglia). The basal ganglia are associated with several functions, including motor control, learning, emotions, and cognition. In patients with Parkinson's disease, there are observable changes in neurotransmitter concentrations (e.g., reduced concentration of dopamine) and neuronal activity (e.g., reduced stimulation of motor cortex, inhibition of motoneurones of agonist muscles, disinhibition of motoneurones of antagonistic muscles). Using a dopaminergic agonist (antiparkinsonian drug apomorphine), Bartolic and colleagues (2010) observed a reduction in hand tremor amplitude and increase in tremor frequency variability. The authors hypothesized that the desynchronization of central oscillators in the basal ganglia, leading to out-of-phase signals that attenuate each other, reduce tremor amplitude and frequency variability. Increased frequency variability might also be due to a shift in coupling of oscillatory impulses, between the basal ganglia and motor cortex, to higher frequency ranges, and an uncoupling of synchronized central oscillators (Bartolic et al., 2010). This finding supports the notion that tremor generation may be a result of the coupling of the basal ganglia, thalamus, and other structures in the functional loop (Amtage et al., 2008). However, there remains debate as to whether movement disorders are merely exaggerated forms of physiological tremor, or different types of tremor arise from different origins. Abila and colleagues (1985) investigated the effects of thymoxamine on essential tremor and physiological tremor. A differential effect of thymoxamine was observed, suppressing essential tremor but caused significant increase in physiological tremor. Although the underlying mechanism of the thymoxamine effect on physiological tremor was unclear, Abilia et al., (1985) argued that the evidence indicates that essential and physiological tremor had different pathophysiology. Supporting this assertion of different tremor and different origins, physiological tremor has dominant frequency components between 8- and 12- Hz whereas Parkinsonian tremor has a peak of 5 Hz. This might imply that tremors due to movement disorders and physiological tremor are of different origin (Lippold, 1970). Marshall (1962), however, reasoned that essential tremor frequency decreases with age, as does physiological tremor, and therefore share the same mechanisms as physiological tremor but at higher amplitude.

On the other hand, peripheral mechanisms may best explain tremor, including changes in metabolite concentration, filtering properties of muscle, and mechanical resonance of the limb

(Raethjen et al., 2000; Lakie et al., 2004). The passive mechanical properties of a limb may be a source of damped oscillations, particularly as a result of internal or external mechanical perturbation (Elble & Koller, 1976). One possible factor involves cardiac mechanics, which has been assumed to contribute to resting physiological tremor, and to a lesser degree, postural conditions (Morrison & Newell, 2000). Cardioballistic oscillations occur as a result of the ejection of blood during cardiac systole, which provides a forceful exertion on the entire body (Elble & Koller, 1976). Morrison and Newell (2000) measured the mechanical effect of cardioballistic thrust and physiological tremor during limb-supported resting conditions. The degree of correlation between cardiac activity and tremor was small (less than 9% variance) and non-significant, leading to the assertion that the mechanical output of the heart does not markedly contribute to oscillations observed in resting limb segments. Motor unit firing has also been suggested as an explanation for increases in tremor amplitude with increasing force production, measuring tremor with both accelerometers (Bilodeau et al., 2009) and force output (Ebenbichler et al., 2000). Increases in motor unit recruitment and synchronized firing have been observed to strongly influence the 10 Hz component of physiological tremor (Endo & Kawahara, 2011). As further evidence, Bilodeau and colleagues (2009) found significant correlations between tremor amplitude and EMG amplitude, particularly of the non-dominant hand. Observed changes in tremor amplitude may also be explained by its inverse relationship with interstitial K^+ concentration. A high concentration of K^+ has a blocking effect on T-tubules, which may disrupt transmission of action potentials. Therefore, during localized exercise, an initial increase, as a result of limb ischaemia, followed by a decrease in interstitial K^+, due to blood perfusion, will promote a decrease and subsequent increase in tremor size (Lakie et al. 2004). The most common cited mechanism of tremor is stretch reflex oscillation or "instability". Lippold (1970) demonstrated similar waveforms between oscillations induced by a mechanical input and waves of a physiological tremor. Introducing a mechanical perturbation, out of phase with an ongoing waveform, has the potential to stop or reduce normal tremor. These findings provide some evidence for the role of stretch reflex servo-loop in physiological tremor. Hagbarth and Young (1979) measured muscle spindle afferent activity and EMG activity during fatigue-enhanced physiological tremor. The authors noted that the mechanism of tremor might be considered a temporal modulator, specifically a reflex modulator of the voluntarily maintained motor outflow. Rhythmical pauses in spindle inflow may lead to excitability fluctuations of the firing pool of motoneurons, which produces clustering of motor impulses in synchrony with movement cycles. These rhythmical contractions are timed with the mechanical resonant properties of moving parts. On the other hand, when assessing 8-10 Hz discontinuities in finger movement, it appeared that there was a mismatch in time between reflex response and self-generated discontinuities, i.e., EMG pattern in relation to kinematics. Additionally, reflexes appeared weak, in both spinal and long-latency components. These findings suggest that reflex responses during voluntary finger movements do not account for tremor oscillations between 8 and 10 Hz (Wessberg & Vallbo, 1996). Elble and colleagues (1987) also argued that stretch reflex plays a role in governing amplitude of oscillations but is not responsible for the 8- to 12- Hz tremor rhythm, which is most likely due to a central oscillator. Mechanical-reflex oscillations coupled with the central oscillator might in fact lead to interactions that are synergistic or competitive depending on experimental conditions. However, the authors note that possibly the enhanced tremor due to fatigue is mechanistically related to the mechanical-reflex oscillation rather than central 8- to 12- Hz oscillations (Elble et al., 1987). Nevertheless, as with fatigue mechanisms, quite possibly both central and peripheral mechanisms, to a certain degree, may contribute to tremor (Lakie, 2010).

Bousfield in 1932 suggested "the rate, amplitude, and irregularity of tremor oscillations vary directly with the degree of fatigue"; supporting Binet's (1920) assertion that tremor increases as a result of muscular contraction and becomes exaggerated under the influence of work (Bousfield, 1932). Studies have demonstrated enhanced tremor during physical and mental exertions, and after a fatiguing task. For instance, Leyk and colleagues (2006) observed a three-fold impairment of hand-steadiness with an exhaustive lift and hold task. Galinsky et al., (1990) showed increases in hand, arm, and shoulder tremor amplitude during a continuous static exertion (i.e., pointing task with the elbows extended and shoulder flexed at 90 degrees). In a finger tapping study, requiring 2.3 N of force at a rate of 200 taps/minute, Takanokura et al., (2001) measured tremor during a 10% MVC test contraction over a 120-minute period. Takanokura and colleagues (2001) found profound increases in total power of the tremor spectrum at 30 minutes of the cumulative load time. Power decreased after 60 minutes of cumulative load time and further decreased after 120 minutes. Increased tremor has been observed to persist after physically intensive work, over hours and even days (Lippold 1981). Furness and colleagues (1977) showed long-lasting increases in tremor, upwards of 4 hours after a brief, strong muscular effort. This long-lasting tremor effect may be due to central nervous mechanisms and some degree of persistence of increased synchronization of motor units (Furness et al., 1977; Lippold 1981). Tremor, however, has exhibited opposing effects during sleep deprivation. An early study by Eagles and colleagues (1955) demonstrated a reduction of tremor, particularly after 24 hours without sleep. The reduction in tremor was attributed to increased muscular relaxation.

Despite strong evidence associating fatigue and tremor, very few studies measured tremor in activities or exercise with magnitudes of force that is relevant to occupational work. Among these occupationally relevant studies, Harwell and Ferguson (1983) simulated microsurgery tasks, with participants steadily holding a wire loop with forceps under visual magnification. The authors found increases in tremor magnitude over an 8 second recording period. Slack and colleagues (2009) measured hand tremor of surgeons over the course of a working day, specifically before and after performing an operation. With accelerometers mounted on the dorsum of the hand, participants were asked to perform a micromanipulation task by holding a 2mm diameter pin, with tweezers, into a 4mm diameter hole. Slack et al., (2009) observed a small, gradual increase in hand tremor throughout the day, even when not performing physically or mentally demanding tasks. But after performing surgical tasks, hand tremor increased by a factor of 8.4.

Typical Measures From Field-Based Studies

Field-based fatigue studies have been far less extensive. Within this body of literature, many field-based studies have measured fatigue in the trapezius muscle and the duration of tasks ranged between 1 and 10 hours. A very limited number of studies measured fatigue response over multiple days (Yung et al., 2014) and the majority monitored fatigue by questionnaires or surveys (e.g., Persson et al., 2006; Boschman et al., 2013).

Of the field-based studies, electromyography is one common measure of fatigue (Bosch et al., 2007; McLean et al., 2000; Rolander et al., 2005; Hostens & Ramon, 2005; Jensen et al., 1993; Katsis et al., 2004; Finsen et al., 1998; Kimura et al., 2007; Kleine et al., 1999; Christensen et al., 1986). However, responses in both time and frequency domains, after fatiguing tasks, have been variable (Rolander et al., 2005; Hostens & Ramon, 2005; Kleine et al., 1999). For instance, there are inconsistent changes in EMG frequency and amplitude during dynamic, intermittent, and/or low-intensity exposures than during high-force contractions (Nussbaum, 2001; Søgaard et al., 2003; Yung et al., 2012). Some of the inconsistency in EMG responses may be due to potential limitations of EMG when measuring fatigue responses. Load sharing between muscles may affect the observed muscle activity. As a result, fatigue development for a particular muscle may be slowed; disturbing the relationship between endurance time and EMG-based fatigue indicators (Iridiastadi et al., 2008). Secondly, EMG may reflect changes in neural activation but lack sensitivity to cellular impairments within the muscle fiber, therefore important processes involved with fatigue development might not be reflected in the EMG signal (Vøllestad, 1997; Bosch et al., 2007). Thirdly, EMG is highly sensitive to influences other than fatigue, and despite high intra-day reliability of EMG amplitude measures, Place and colleagues (2007) expressed caution in using EMG to measure activity between days, due to changes in electrode re-positioning. And fourthly, there are inherent limitations with surface EMG, specifically crosstalk from other muscles and geometrical artifact (Yung & Wells, 2013).

Strength capability (i.e., maximum voluntary contractions) has been measured over the course of the workday. Maximum voluntary contractions are traditionally cited as the most direct assessment of fatigue, under proper test conditions and with verbal encouragement (Vøllestad, 1997). Chang and colleagues (2009) documented, among construction workers, handgrip force at the beginning and end of the work shift. However, these authors found a lack of changes between pre- and post- measures.

Self-reported fatigue or discomfort for multiple body regions has also been a frequent measure in field studies (Galinsky et al., 2000; Amick et al., 2003; Cook & Burgess-Limerick, 2004; Bosch et al., 2007; Kimura et al., 2007). Generally, increased discomfort has been perceived with the progression of work and is positively related to fatigue and reduced work capacity (Sato & Coury, 2009). However, ratings of perceived discomfort may be more strongly coupled to high frequency fatigue rather than low frequency fatigue and possibly there is dissociation between subjective and objective fatigue measures (Adamo et al., 2002). For instance, Bosch and colleagues (2007) monitored local fatigue among Dutch manufacturing workers while completing light manual assembly work. Over the course of a working day, both subjective (local perceived discomfort) and objective (EMG) estimates of fatigue were assessed and no clear relationship was found between the two indicators. However, both EMG and ratings of perceived discomfort changed, accordingly as a response to local fatigue, over the course of the day. Bosch et al., (2007) note that the relationship between local fatigue and disorders were not investigated in their study and complementary objective measures of fatigue (other than EMG and RPE/LPD) may be needed to detect differences between work conditions. Fatigue might also be measured with rating scales that measure alertness (Tucker et al., 1996) and perceived strength (Persson et al., 2006).

A number of surveys have been designed to evaluate worker health from the standpoint of fatigue (Salvendy, 1987). One such survey was developed by the Society of Industrial Medicine, which is comprised of physical complaints (e.g., pain, tired feelings, stiffness), mental symptoms (e.g., lightheaded and disoriented, anxiety, inability to concentrate), and neurosensory systems (e.g., lethargic inaccurate movements, tired eyes and inability to focus). A popular questionnaire-based assessment tool is the Swedish Occupational Fatigue Inventory (SOFI), which provides information about qualitative aspects of fatigue, for application to the work environment. This measure reflects both physical and mental fatigue based on 5 dimensions: lack of energy, physical exertion, physical discomfort, lack of motivation, and sleepiness (Åhsberg et al., 1997). SOFI has been used extensively to measure physical work, mental work, and shiftwork (Åhsberg et al., 2000). Scales and questionnaires have been developed to assess longer-term fatigue conditions (e.g., burnout, chronic fatigue syndrome, myalgia, etc.). These measures include the Maslach Burnout Inventory (MBI) that consists of 3 subscales to capture the dimensions of burnout: exhaustion, cynicism, and professional efficacy (Maslach & Jackson, 1981). MBI has been demonstrated to be both reliable and valid, and can be used in any occupational context (Bakker et al., 2002). Chronic fatigue syndrome might be measured by the Fatigue Severity Scale, which integrates dimensions of intensity and functional outcomes. And finally, the 11-point Numerical Rating Scale (NRS) have been utilized to measure the intensity of muscle pain, possibly as a result of muscle myalgia.

Finally, measures including heart rate, an index of physiological strain and metabolic rate, have been measured among high elevation construction workers (Chang et al., 2009) and road construction workers (Roja et al., 2006). In these studies, additional measures included work posture, muscular tone (myotonometry), and limb circumference. Heart rate, measured throughout the workday, was variable and may reflect changes other than physical strain, including emotional stress (Chang et al., 2009). It was shown that as fatigue progressed, muscular tone increased, which might lead to blood occlusion (Roja et al., 2006). However, there remains a lack of evidence to support the utility of myotonometry as a method to monitor fatigue.

Test Battery Vs. Continuous Measurement

Previous studies have measured physiological responses during activity on a simultaneous/continuous basis (e.g., Byström et al., 1991; Jensen et al., 1999; Hummel et al., 2005), during a test battery (e.g., Crenshaw et al., 2006; Bosch et al., 2007; Søgaard et al., 2003), and with both continuous and test battery measurements (e.g., Yung et al., 2012; Iridiastadi & Nussbaum, 2006; Rosa et al., 1985). Although continuous measurements might provide information that is representative of the workload, there are advantages with test battery measurements. First, test batteries can be administered during work breaks to avoid disruptions of the work process. Second, brief standardized measures would allow for generalization across different work settings (Rosa et al., 1985). Third, test batteries might act to control factors (i.e., muscle length, movement velocity, and magnitude of exerted force) that might lead to erroneous interpretation of physiological signals (e.g., MMG, EMG, etc.). Nonetheless, there are a number of conditions that should be satisfied for the development of an effective test battery in field research. Rosa and colleagues (1985) recommended that test batteries should be portable, easy to administer, require minimal training, and brief. Test contractions (i.e., a constant force to allow for the recording of a stationary signal), according to Søgaard et al., (2003), should be of sufficiently low magnitude, lower than force levels of the fatiguing workload. A higher magnitude of force during test contractions might mask indications of fatigue due to the recruitment of different motor units from the fatiguing workload. Finally, the order of the components of a test battery might influence the detected physiological responses. Careful consideration should be devoted to the placement of the test battery components to minimize possible carry-over effects.

Table 2.2 Typical Measures of Fatigue in Field and Laboratory Studies

Study	Monitoring Technique/Tool	Type of Study	# of Subjects	Muscle/Body Part	Test Battery or Continuous	Fatiguing Task	Fatigue Development Over Time
Allen & Proske (2006)	Position matching Movement matching Max Voluntary Force	Laboratory	8 M 7 F	Elbow Flexors	Test Battery. Pre-, post-, and 1hr after exercise.	Lifting a weight (30% MVF) with elbow flexors; 10 repetitions per set; 15 sec rest between sets; Until exhaustion	1.7° – 1.9 ° arm flexion against reference arm. No significant reduction in movement-tracking accuracy. Decrease of 30% in MVF
Forestier et al. (2002)	Position matching Electromyography	Laboratory	8 M	Ankle (Tibialis Ant., Gastroc.)	Test Battery. No fatigue and fatigue (post-exercise).	Maintain ankle flexion at 70% MVC for 40 sec and 40 sec rest between trials; Fatigue if workload cannot be maintained for more than 15 sec.	Undershoot position by 1.3°. iEMG for tibialis anterior: increase from 18 to 23%. iEMG for medial gastrocnemius: 19.5 to 22.5%. iEMG for lateral gastrocnemius: 18.0 to 18.7%
Davidson et al. (2004)	Postural sway	Laboratory	13 M	Lumbar extensors	Test Battery. Pre- and post- exercise.	Multiple sets of back extensions on a 45° Roman chair; Until 60% MVE force using high (10-minute) and low (90-minute) fatigue rates	Increase in lumbar postural sway, between 29% and 58% in time-domain sway measures. No difference between fatigue rates
Madigan et al. (2006)	Postural sway Joint kinematics	Laboratory	12 M	Lumbar extensors	Test Battery. Pre- and post- exercise.	Multiple sets of back extensions on a 45° Roman chair; Back extensions every minute, MVC every 2 minutes; 14 minute duration	Adopted slight forward lean with fatigue: 0.7 +/- 1.7 cm anterior shift in mean COM and 1.5 +/- 1.5 cm anterior shift in mean COP. Increase in joint angle variability at multiple joints including joints distal to fatigued musculature
Mello et al. (2007)	Postural sway Electromyography	Laboratory	15 M 7 F	Lateral Gastrocnemius	Test Battery (Sway). Pre- and post- exercise. Continuous (EMG)	Maximum plantar flexion until muscle failure	EMG MdPF: -0.13 Hz/s. Latency between COP displacement in relation to EMG: increase up to 1.62 seconds after fatigue
Allison & Henry (2002)	Response to Perturbation Electromyography	Laboratory	3 F 1 M	Internal/External Obliques Rectus abdominis Longissimus at L3	Test Battery. Pre- and post- exercise.	Perturbation based on sudden arm movements: instructed to raise arms as quickly as possible at onset of light. Ten trials collected post fatigue task. Fatiguing task: anterior superior iliac spines against rigid support, sustained pull at 60% MVC. Stopped if unable to maintain force above 35%	Reaction time before (181 ms, SD 70) and after (175 ms, SD 84) not significant different. A general decrease in muscle latencies post fatigue, but difference in onset detection rates may reflect individual variance and selection of reference window.
Svendsen & Madeleine (2010)	Force variability	Laboratory	10 M 10 F	Elbow Flexors	Continuous.	Maintained isometric elbow flexion at 20% MVC until failure (inability to maintain 20 +/- 2% MVC for more than 5 sec.	Both standard deviation and coefficient of variation increased with contraction time.
Kajaks et al. (2010)	Force variability Electromyography	Laboratory	7 F	Elbow Flexors	Continuous.	Trace pyramid-like template; 15 second submax exertion plateaus: 20, 40, 60, 40, 20, 0% MVC; 5 sec rest after each plateau	Changes in SD during fatiguing contractions. Greater increase in SD in 40% and 60% MVC force exertion than in 20% MVC in 1-4 and 8-14 Hz ranges. Decrease in MnPF.
Contessa et al. (2009)	Force variability Electromyography	Laboratory	4 M	Knee Extensors (vastus lateralis)	Continuous.	Isometric knee extensions by visual feedback of a series of force trajectories; Tracking tasks of repeated contractions separated by 6 sec rest; Each contraction: 50% MVC ramp at rate of 10% MVC/s, brief hold phase, target decreased to 20% MVC and maintained for 50 sec.	Force variability (CV of detrended force) increased from average of 0.67 +/- 0.18% in first contraction to average of 2.10 +/- 0.99% in last contraction before exhaustion
Lin et al., (2014)	Force variability Electromyography	Laboratory	16 M	Hand (Power Grip)	Test Battery.	Three 20-second trials of isometric power gripping (sinusoidal intermittent, 50-100% MVC, 0.5 Hz wave) before and following a fatigue intervention (several trials of 3-minute rhythmic isometric gripping, identical to test battery). Fatigue protocol continued until mean force output in the last 30 seconds of last trial lower than 60% mean force level of pre-fatigue test.	Mean frequency and mode frequency of force pulse trace in post-fatigue test (mean = 1.21 Hz +/- 0.17 Hz; mode = 0.78 +/- 0.32 Hz) lower than pre-fatigue (mean = 1.48 +/- 0.13 Hz; mode = 1.28 +/- 0.22 Hz). Sample Entropy curve of force pulse traces visible different for pre-fatigue and post-fatigue. Multi-scale entropy (MSE) area of low time scale smaller post-fatigue (12.16) than pre-fatigue (12.25). MSE of high time scale larger in post-fatigue (35.55) compared to pre-fatigue (34.05).
Shi et al. (2007)	Ultrasound Electromyography	Laboratory	8 M	Elbow Flexors	Continuous.	Elbow flexion maintained at 80% MVC; Failure when torque dropped to 70% MVC	EMG: 2.9 +/- 1.9% / second (RMS) and -0.60 +/- 0.26 Hz/s (MdPF). Overall mean deformation: 3.5 +/- 1.6% at 20 seconds after contraction
Søgaard et al. (2003)	Mechanomyography Electromyography	Laboratory	6 M	Elbow Flexors	Test Battery.	6 sec contraction at 30% or 10% MVC followed by 4 sec relaxation; 30 minute duration	Decrease in MnPF and increase in RMS for both EMG and MMG

Hammarskjold & Harms-Ringdahl (1992)	Electromyography Ratings of Perceived Exertion	Laboratory	10 M	Forearm (FDS, ECR); Upper arm (BB); Shoulder (AD, trap, infrasp.)	Continuous.	Maintain a pace of 60 rotations per minute (arm-cranking) for 45 minutes; At end of exercise 1 minute of intense cranking; immediately hammered 10 nails; 2 minutes of max cranking; sawed five pieces of pine; 2 minutes of max cranking; Screwed 5 screws	Nailing: EMG median amplitudes increased in trapezius, biceps, anterior deltoid; Sawing: EMG increases median amplitude in trapezius, deltoid, infraspinatus; Screwing: EMG median amplitude increased in anterior deltoid; RPE only increased for nailing.
Mathiassen & Winkel (1996)	Electromyography Heart Rate Blood Pressure Maximal Strength Pressure Pain Threshold Proprioception	Laboratory	8 F	Trapezius	Test Battery (Subjective Rating of Fatigue, PPT, Test Contraction). Continuous (EMG, ECG, Skin Temp).	Assembling starters for power saws; Mean task cycle time was 68 seconds = 120 methods-time measurement units; 2 hour protocols	EMG amplitudes increased during the working day; EMG test contractions increased by 10% during 6 hr work; Assembly work increased HR by 9.1 bpm; Arterial blood pressure increased 18.2 mmHg; CR10 Borg rating increased gradually to terms corresponding as "strong"; PPT decreased by 10-15% (became more sensitive); Max strengths decreased and recovered within 4 hrs; priorioceptive performance difficult to interpret (variable); Skin temp increased
Farina et al. (2002)	Electromyography	Laboratory	11 M	Left upper trapezius	Test Battery.	Participants stood with arms in five positions (arms at side of body, 45° and 90° flexion, 45° and 90° abduction) for 3 min with 1 kg load.	Increases in ARV and RMS slopes from reference position, very small increases in MnPF and MdPF.
Ebenbichler et al. (2002)	Electromyography Kinematic	Laboratory	9 M	Low back	Test Battery (static maximum force). Continuous (EMG, kinematics)	5-min lifting task (weighted box, 15% of body mass) from shelves positioned at midshank and waist height; 12 lifting cycles/min.	Significant decreases in normalized IMDF at L5, smaller changes in L1 and T10. Changes in range of motion (increase at hip, trunk, elbow and decrease at knee).
Adamo et al. (2002)	Electrically Evoked Muscle Stimulation (LFF) Subjective perception of localized muscle fatigue	Laboratory	11 M 9 F	Flexor Digitorum Superficialis	Test Battery.	Sustained at 5% MVC for 30 minutes; Intermittent (5 min work/1 min rest) at 5% MVC repeated 5 times	Twitch force decrease in sustained grip exertion; No fatigue observed in intermittent Increase of 3 points on a 7.5 pt rating scale post-work after sustained; Increase of 2 points after intermittent
Leyk et al. (2006)	Hand steadiness Heart rate Blood Sampling	Laboratory	15 M	Hand	Test Battery.	Participants lifted front part of a loaded (50 kg) stretcher-mock-up with both hands; Participants, with the stretcher, walked at a velocity of 4.5 km/h, on a treadmill, until exhaustion (dropping the stretcher).	Maximum heart rate of 172 +/- 13 min^{-1} at points of fatigue; Lactate concentrations increased from 1.4 +/- 0.4 mmol/l to 4.9 +/- 1.2 mmol/l (first 5 min of recovery); Maximum force reduced by 20% of pre-exercise values; Hand-steadiness increased 3x in both frequency and duration of contacts with device's metal wall
Hansen et al. (1998)	Vascular volume of foot Perceived discomfort Skin Temperature Electromyography Blood Pressure Heart Rate VO2 Max	Laboratory	8 F	Low Back, Feet	Test Battery (foot volume, vascular volume, MVE, EMG, COM). Continuously (Discomfort, Skin Temp., BP, HR, VO2).	Standing work: Letter sorting at 1 letter/sec; 2 hrs Standing/walking work: 20 sec standing followed by 10 sec walking; Handled bottles, carried 1 small beer crate; 2 hrs	Standing: Increased discomfort in low back from 6 to 30%, legs from 3 to 14%, feet from 8 to 31%; Foot volume increased by 3.9% mainly due to edema formation (3.0%); Skin temperature increased from 32.1 to 35.5ºC. EMG RMS constant, MnPF decreased from 146 to 140.5 Hz. Standing/walking work: Discomfort increased from 5 to 27% (Low back), 5 to 6% (legs), 8 to 27% (feet); Foot volume increased by 3.4% (both vascular foot volume and edema formation increased by 1.7%); Skin Temperature increased from 33.7 to 36ºC. No changes in EMG
Dennerlein et al. (2003)	Electrically Evoked Muscle Stimulation Ratings of Perceived Fatigue	Laboratory	10 F	Forearm Extensor (ECU)	Test Battery.	Repetitive ulnar deviation tasks; At audible tone, handle moved through 80 ° rotation; 7, 55-min segments, 5 min breaks after segments 1,3,5; 15 min breaks after segments 2,6; 30-min lunch break after segment 4; 3 hour recovery	Low-Frequency Fatigue (LFF) ratio decreased during workday; LFF did not last into the next day; Ratings of perceived fatigue increased as day progressed.
Lin et al. (2004)	Electromyography	Laboratory	13 F	Flexor Digitorum Superficialis (FDS), Extensor Digitorum Communis (EDC)	Continuous.	Typing for 2 hr without pause longer than 3 seconds.	Significant differences in EMG during max contractions before and after tasks, persistent low values thoroughout 10 min recovery time; All four muscles manifested long duration fatigue, MVE values not significantly recovered 10 minutes post-exercise; Decreasing MdPF.
Bennie et al. (2002)	Electromyography	Laboratory	13 F	Forearm Extensor (ECU)	Test Battery.	Ulnar deviation wrist movements at 15, 20, 25 repetitions/min; 4 week protocol	EMG power spectra changed in both amplitude and shape; EMG signal decreased on workdays against a control group.
Berguer et al. (1997)	Electromyography Questionnaire (Corlett)	Laboratory	3 M	Trapezius, middle deltoid, FDS, EDC	Test Battery (Questionnaire). Continuous (EMG).	Questionnaire data immediately after surgery; Three tasks: moving 1/2 inch bolts across horizontal line – six movements (BOLT), transposing rubber band between 2 horizontally placed pegs to vertical position between two other pegs, advancing long ¾ inch polyethylene tube forward.	Questionnaire: moderate/severe levels of discomfort in both shoulders post surgery; Increase in forearm flexor EMG RMS in all three tasks, non-significant increases in trapezius and deltoid
Bosch et al. (2007)	Electromyography	Field	16 F	Upper trapezius	Test Battery.	(1) Assembly of catheters; (2)	EMG mean rectified amplitude increased by 27% in (1), increased 19% in (2);

	Localized Perceived Discomfort		4 M			Picking/placing covers of shavers; 8.5 – 10 hrs.	Decrease in high frequency power by 4% in (1) and 11% in (2); MnPF decrease by 3% in (2) only
McLean et al. (2000)	Electromyography	Field	15 F 3 M	Upper trapezius, Lumbar paraspinal, Cervical extensors	Continuous.	Computer terminal work for 1 hr and 20 mins: with breaks and without breaks	No (or very minimal changes in either RMS or MnPF in all body parts)
Rolander et al. (2005)	Electromyography	Field	10 M 17 F	Left and right trapezius muscles	Continuous.	Typical dentist activities: 3 hours and 45 mcvbnmcvbncvbninutes to 4 hrs and 30 mins	Increase in EMG average rectified value by 14%, no change in MnPF.
Hostens & Ramon (2005)	Electromyography Subjective Fatigue	Field	12 M	Trapezius and deltoids, bilaterally	Continuous.	Drive during 1 hr on chosen route; rest period of 2-5 min to load EMG data to the PC at the 30-minute mark.	5/21 participants indicated more fatigue after test than before test; More than half indicated muscle stiffness; instantaneous mean frequency decreased; RMS also decreased
Jensen et al. (1993)	Electromyography MVC Heart Rate Ratings of Perceived Exertions Blood Pressure	Field	30 F	Trapezius	Test Battery (MVC, Test Contraction). Continuous (EMG)	Seven periods of typical work (8 hr) at sewing-machines; Short work cycles with average duration of less than 1 min for 70% of operators.	HR and blood pressure remained unchanged; EMG max amplitudes were unchanged; RPE ratings increased from 1 to 3; RMS increased by 3%; MPF decreased by 4%
Katsis et al. (2004)	Electromyography	Field	10 M	Biceps, forearm flexors	Test Battery.	Driving in a truck, tractor, or truck with trailor, participants drove twice in a predefined route	General decrease in MdPF (from initial values) from 9.5% to 18.9%, decrease in MnPF from 11.3% to 18.4%; RMS increase (from initial value) from 25.1% to 47.7%
Cook & Burgess-Limerick (2004)	Musculoskeletal symptom questionnaire	Field	54 F 5 M	Multiple body regions	Test Battery.	Six week duration; Typical work days; 6 week follow-up	Reports of discomfort increased slightly for all body regions (overall increasing from 71% to 75%); Significant decrease in overall discomfort for whole group 6 weeks after work
Amick et al. (2003)	Daily symptom survey	Field	192 F & M	Multiple body regions	Test Battery.	Spent in office chair, computing 5 to 6 hours per day; Three conditions: chair & training, training only, control	Beginning of day decrease in pain: Control: -0.56 points (slight pain increase); Training: 1.0, Chair-With-Training: 0.98; End of day decrease in pain: Control: 1.2, Training: 2.2; Chair-With-Training: 4.3
Finsen et al. (1998)	Working Postures Electromyography	Field	8 F	Working posture observation: back, neck, upper arms EMG: Extensor muscles of neck, trapezius		Three most common and time-consuming work tasks (based on a questionnaire study) were performed: dental examination, tooth cleaning, dental filling therapy. Work tasks average 7.8 h per week.	Work time with patients increased neck problems (OR – 4.7 – 7.0); Shoulder troubles related to total duration of breaks.
Kimura et al. (2007)	Electromyography MVC Perceived Fatigue	Field	6 M	Right trapezius	Test Battery.	Typed for 100 minutes (4 sets of 25 min each with 5-min rest between sets)	RPE: Increased from 0 (no sensation) to 3 (slight to severe); Muscle fibre conduction velocity: decreased by 13.6%; MdPF: decreased by 10.6%; RMS increased by 14.6%
Kleine et al. (1999)	Electromyography	Field	9 F	Neck; Low Back; Trapezius; Deltoid; Sternocleido-mastoid	Continuous.	Typical work (type text spoken on tape); Constantly looked at the monitor; Tape recorder controlled by foot pedal; Work for 3, 1-hr periods	Trapezius RMS greatest increase, other muscles showed no clear trends; Normalized RMS increased on average: 22% (1st hr), 17% (2nd hr), 18% (3rd hr); MdPF did not change
Christensen (1986)	Electromyography Heart Rate Questionnaire	Field	16 F 9 M	Trapezius Deltoid Infraspinatus	Test Battery.	Females: Assemble printed circuits of different kinds (40 – 120 units on one print; 75 – 100 units handled in a 5 minute period); Males: Soldered circuit boards together and assembled chasses	Questionnaire: 48% reported pain or discomfort in both neck and shoulder, 16% only in neck area, 8% only in shoulders; RPE: Females increased from 1 to 4, males from 2 to 3; Heart Rate did not change; ADPF did not change in any muscles during the day (no difference pre/post breaks); Decrease in MnPF same for three muscles (9 Hz) however infraspinatus led to higher MnPF later in the day than the morning.
Galinsky et al. (2000)	Questionnaire (level of discomfort in body regions 1-5 scale) Performance Measures (keystrokes/hr and accuracy)	Field	31 F 11 M	Discomfort ratings for: forearms, wrists, hands, elbows, shoulders, upper arms, neck, back, buttocks, legs	Test Battery.	Typical working day for data-entry tasks (keying numeric data from paper tax forms). Two variables: conventional schedule (2, 15-min breaks per shift) and alternative schedule (2, 15-min breaks and 5-min breaks supplemented throughout); 4 week period	Highest discomfort ratings: neck, back, right shoulder, upper extremities. Typically no discomfort at beginning of work shifts, increasing to the end of work period (sometimes to the highest level of 'extreme discomfort'). Performance measures only collected on daily basis (not within each day)
Roja et al. (2006)	Heart Rate Work Postures Ratings of Perceived Exertions Myotonometry	Field	20 M	Myotonometry on: m. ED, m. FCR, m. gastrocnemius, m. tibialis anterior, m. trapezius(upper)	Test Battery (Myotonometry,	Workers in road maintenance and repair (10 road workers and 10 pavers)	Subjective discomfort/pain in arms, legs, upper and lower part of lower back, shoulder. 85% of workers exceeded muscle stiffness norm (> 300N/m) after work week cycle in the extensor digitorum and flexor carpi radialis. 60% of workers exceeded norm in the tibialis anterior.

Chapter 3

Fatigue Measures Identified From A Multidisciplinary Approach: Findings from the CRE-MSD Toronto Workshop

Abstract

Fatigue is a multidimensional construct and its effects might lead to reduced performance at work, including deficits in productivity and quality. Fatigue may also be relevant in the development of chronic syndromes and disability and pain due to work-related musculoskeletal disorders. These effects and outcomes underscore the need to understand fatigue development at work. However, since fatigue manifests in various forms, a single test is not theoretically validated. A workshop was convened to identify fatigue measures that were practical, reliable, sensitive, and valid. Fifty-seven unique measures were identified. Based upon participants' ratings, four measures were recommended for both lab and field settings: maximum voluntary contractions, Borg's rating of perceived exertion or discomfort scale, questionnaires and fatigue scales, and visual analog scales. The results might serve as a resource for researchers or practitioners when selecting measures to address multiple fatigue outcome domains and to satisfy context-based practicality.

1. Introduction

Fatigue has been described as a multidimensional construct, affecting the overall state of the whole organism, and is associated with physical, psychological, socioeconomic, and environmental factors (Barker & Nussbaum, 2011; Saito, 1999). In the short term, fatigue at the workplace is linked to reduced performance, lowered productivity, deficits in work quality, and increased incidence of accidents and human errors. To support this, a recent systematic review demonstrated relationships between ergonomics factors and product or service quality, with fatigue as an intermediary factor (Kolus et al., 2014). In the longer term, fatigue may lead to compromised immune function and adverse health outcomes, including myalgia, chronic fatigue syndrome, and burnout (Kajimoto, 2007). And speculatively, fatigue may also be a precursor to WMSDs – work-related musculoskeletal disorders (Iridiastadi & Nussbaum, 2006). For example, it has been shown that fatigue of the rotator cuff muscles may lead to a narrowing of the subacromial space, which might accelerate the risk of subacromial impingement and possibly rotator cuff injury (Chopp et al., 2010).

Fatigue, defined broadly, translates to an annual cost of $330 million in lost productivity in the United States, with the majority of lost production time attributed to presenteeism, where the employee is at work but performing below their full capacity. The financial burden escalates to $101 billion when fatigue acts as a co-occurring effect with other health conditions (Ricci et al., 2007). In the U.S., fatigue is prevalent in 37.9% of the workforce. In Japan, fatigue is experienced by 60% of the working population; 50% of these individuals experienced fatigue lasting more than 6 months (Kajimoto, 2007). It has been reported that in Canada, similar to levels observed in the United States, abnormal levels of self-perceived fatigue is prevalent up to 20% of the population (Winwood et al. 2007).

2. Background

Fatigue has been firmly embedded in the canon of modern science since the mid 19th century, pioneered by Marey's laws of human effort and efficiency, Kroenecker's dynamic laws of fatigue, and Mosso's seminal work in both fatigue quantification and theories pertaining to exhaustion (Rabinbach, 1992). Since then, there has been extensive research in fatigue, culminating in a variety of theories, processes, and mechanisms. These include the catastrophic model, central governor theory, peripheral governor theory, and pscychobiological model. Consequently, this has led to a diverse set of tools and procedures to measure specific fatigue processes (Enoka & Stuart, 1992; Behm, 2004).

Meanwhile, in ergonomics and human factors research, there has been a growing interest in practical assessment methods, the temporal development of fatigue in work tasks including modern production processes (de Looze et al., 2009; Kajimoto, 2007), and ultimately its reduction. Fatigue, as a design and evaluation tool, might improve work productivity and product quality, which are both important issues with societal and firm competitiveness consequences. And, if indeed fatigue is a precursor or potential biomarker to long-term outcomes (e.g., MSDs), it may be a useful risk indicator.

However, since fatigue manifests itself in various forms, a single test to measure fatigue is not reasonable. More specifically, because different measures provide information on different processes induced by work activity, authors have suggested that fatigue should be evaluated by a multidisciplinary approach (Saito, 1999) with a complementary set of measures (Yung et al., 2014). The multitude of measures and detection methods has led to an interesting challenge in ergonomics. Given the potential complexity of fatigue, one might ask, which measures are most practical, reliable, and sensitive for the workplace?

A workshop was convened to critically evaluate current fatigue measures from different research disciplines and perspectives. The aim of the workshop was to identify a set of fatigue measures that were practical, reliable, sensitive, and valid when measuring fatigue in the workplace. By gathering expert opinion from multiple disciplines, this workshop may be an initial step to an integrative approach and thus a systems biology paradigm.

3. Workshop Participants

The workshop comprised of 14 researchers from 4 countries (Canada, United States of America, Sweden, Netherlands) and 10 graduate students representing 9 research disciplines: biomechanics, ergonomics, neuroscience, public health, muscle physiology, motor control, psychology, industrial engineering, and physiotherapy. All participants had an established research interest in fatigue and had previously conducted both laboratory- and field-based studies.

4. Workshop Structure

At the beginning of the workshop the group operationally defined fatigue to frame subsequent discussions. The workshop was then segmented based on three areas of discussion. First, participants were asked to identify outcomes potentially affected by fatigue. Four areas were identified: work performance and quality, injury and disorders, illnesses, and discomfort. Discussion centered on potential causes and physiological mechanisms for these outcomes and/or effects. Second, fatigue measurement and detection methods were reviewed to best address the quantification of the proposed causes and mechanisms. Third, the fatigue measures were then assessed for its utility in both laboratory and field research settings. Assessment of fatigue measures was conducted during and after the workshop. Each fatigue measurement and/or detection method was assigned a rating (low, medium, high) based on its practicality, sensitivity, reliability, and validity in laboratory and field settings. Measures rated “low” were *not recommended* for the specified setting. Measures rated “medium” were *recommended with reservations* while those measures rated “high” were *recommended*. This workshop structure placed the focus onto the outcomes and/or effects of fatigue and may help identify measures that are common between multiple outcomes.

5. Operational Definition of Fatigue

The multitude theories and mechanisms are due in part to contrasting definitions and institutionalized meanings across different scientific groups. Definitions range from a disciplinary-based perspective, e.g., muscle physiology – *“…fatigue is any decline in muscle* *performance associated with muscle activity…it is universally agreed that much of fatigue arises in the muscles and can therefore be studied in isolated muscle tissues"* (Allen et al., 2008), to an integrative holistic approach, e.g., *"…in its widest application embraces all those immediate and temporary changes…which take place within an organism or any of its constituent parts as a direct result of its own exertions, and which tend to interfere with or inhibit the organism's further activities"* (Ash, 1914).

The group discussed the concepts of *fatigue* – a reversible process, and *weakness* – a persistent process. Reversible fatigue was suggested to be "healthy" while a persistent process is a chronic pathway that may lead to injury. Fatigue is therefore a balance between inhibitory and facilitatory effects, and possible adaptative and maladaptive behaviour of biological tissue. However, it was stated that there is no single biomarker that could determine whether the fatigue response will lead to an adaptive or maladaptive effect or a reversible or chronic effect; and fatigue may only be problematic when coupled with another risk factor. Despite the many considerations when defining fatigue and its effects, the group agreed that fatigue over a working day might impact performance and quality at work. Fatigue over multiple days, which is cumulative over time, may be more indicative of longer-term health outcomes.

The term *capacity* was also considered, particularly for physical work. Capacity was described as the capability of doing a physical task while completing a task without getting injured. However, it was understood that capacity could decrease without activity and is task dependent. "Wellness" was suggested to be a perceptual element where it may be a motivator or an intrinsic reward after a "hard day at work". On this basis, it was argued that wellness is a causal factor rather than an outcome and should be excluded from the definition. Conversely, it was reasoned that wellbeing might affect the temporal change in capability (i.e., fatigue), over the day and between days, and may be associated with particular physiological mechanisms.

Participants believed that a general definition should not be body region specific (i.e., low back, upper extremities, etc.) or limited to a particular task or occupation. Fatigue demonstrates a degree of task dependency, influenced by the intensity and duration of activity, type and speed of contraction, muscle groups involved, environment, and physical characteristics of the worker (Enoka & Stuart, 1992; Weir et al., 2006). Work may be stereotypical and repetitive, non-cyclical, sedentary, characterized by low-level exertions, or highly forceful. A broad definition of fatigue allowed for discussion of occupations in a general context with opportunities for specificity. Participants also stated that a general definition should be based on both neuromuscular and mental aspects, but remain under the framework of occupational work.

A definition was thus conceptualized with consideration of the potential effects of fatigue in occupational tasks, its potential impact on the health and wellbeing of the individual, but did not confine fatigue to a single mechanism or impairment of a specific system. Researchers arrived to the following definition:

Fatigue is a process that results in the impairment of wellbeing, capacity, and/or performance as a result of [work] activity.

6. Potential Effects & Outcomes and Their Causes or Mechanisms Based on Domain

6.1 Performance & Quality

The workshop group identified 12 potential outcomes and effects leading to a change in work performance and quality (Table 3.1). These include types of errors, such as slips (error in execution), lapses (error in memory), mistakes (faulty plan/intention), and violations. Both slips and lapses are errors in execution while mistakes and violations are errors in planning (Reason, 1990). The type of errors were then partitioned into its potential mechanisms and/or processes, including the worker's arousal level, mental fatigue and sleepiness, reduced maximum force capability, and perceptual, cognitive, and visual/auditory errors. For instance, a slip (error in execution) may be the result of the worker's low state of arousal. Arousal, or wakefulness, refers to non-specific activation of the cerebral cortex in relation to sleep-wake states and is often considered an aspect of vigilance (Oken et al., 2006). Arousal influences the competition between stimuli for mental resources, changing processing for high and low priority stimuli (Mather & Sutherland, 2011). Pattyn and colleagues (2008) argued that the "underload" hypothesis, or the underarousal arising from insufficient workload, best account for decrements in vigilance and task disengagement.

The workshop group also addressed two speed-related variables: slow-down (slower execution) and rushed (quicker execution). Participants identified *margin of maneuver*, decrements in endurance, and reductions in power output. Margin of maneuver is an ergonomic concept reflecting the continuous adaptive process in which the worker maintains a balance between attaining production targets (i.e., task-related objectives) and preserving their health or condition (Durand et al., 2011).

The workshop group recognized the effects of endurance time, power output, and impaired motor output, which are similar to Hogan (1991) who described three dimensions that comprise the structure of physical performance: muscular strength, cardiovascular endurance, and movement quality. In Hogan (1991), muscular strength was specified into three sub-elements, including muscular power. Meanwhile, cardiovascular endurance referred to the aerobic capacity to sustain gross muscular activity over a prolonged period of time. Movement quality involved balance and neuromuscular integration and coordination, which may be comparable to the workshop's three impairments to motor output. Firstly, participants identified impairments to spatial performance (i.e., precision). In an example, hand tremor increased over the course of a day among medical surgeons (Slack et al., 2009). An increase in operative tremor, due to a combination of physical and mental fatigue, may have a pronounced effect on the accuracy of the procedure. Secondly, a change in performance and quality may be an outcome of impaired motor output that is temporal in nature. There is extensive evidence on the relationship between temporal variability (e.g., rate of force development) and sensorimotor performance (Gruber & Gollhofer, 2004). Thirdly, an impairment of motor output, based on force performance, may lead to a decrement in work performance and quality. Force variability may reflect underlying neurophysiological mechanisms, including the adaptation between force output and sensory input (Sosnoff et al., 2006).

Table 3.1 Performance & Quality Effects or Outcomes and Their Causes or Mechanisms

Effects or Outcome	Potential Causes or General Mechanisms
Slips (error in execution)	Low Arousal, Mental Fatigue, Sleepiness, Reduced Max Force Capability
Lapses (error in memory)	Mental Fatigue, Sleepiness
Mistakes (faulty plan/intention)	Visual or Auditory Errors, Cognitive Errors, Perceptual Errors
Violations	Low Arousal
Slow-Down (slower execution)	Reduced Max Force Capability, Decrements in Motor Control & Coordination, Speed-Accuracy Tradeoff
Rushed (quicker execution)	Speed-Accuracy Tradeoff
Margin of Maneuver	Reduced Max Force Capability, Contextual Antecedents, Person-Related Stressors, Speed-Accuracy Tradeoff, Work Stress, Pain or Discomfort
Impaired Motor Control (Spatial)	Reduced Proprioception, Movement Variability, Impaired Sensation
Impaired Motor Control (Temporal)	Reduced Max Force Capability, Decrements in Motor Control & Coordination, Temporal Variability, Reflex Latency
Impaired Motor Control (Force)	Reduced Max Force Capability, Tremor, Force Variability
Endurance Time	Reduced Max Force Capability, Reduced Motivation, Cardiovascular
Power Output	Reduced Max Force Capability, Speed-Accuracy Tradeoff, Motivation, Pain or Discomfort, Decrements in Motor Control & Coordination

6.2 Injury & Disorders

Workshop participants decided to categorize injury disorders into 4 outcomes, causes, and/or effects (Table 3.2). First, acute injuries may be a consequence of 7 potential processes or manifestations of fatigue. The group first acknowledged that increased muscle contraction level at a particular level of force might lead to an increased risk of muscle damage. Indeed there is a strong association between overexertion and injury (Kumar, 2001). Exertion, however, is not solely on the basis of magnitude but is also dependent on the type of contraction, the duration, the repetition, and the recovery period. For instance, sustained muscle activity, typically at low-intensity, selectively activates type I motor units, (i.e., Cinderella hypothesis). Visser and van Dieën (2006) outlined possible effects including accumulation of Ca^{2+} in the active motor units and homeostatic disturbances as a result of blood occlusion and ultimately limitations of metabolic removal. Similarly, repeated and prolonged loading may result in cumulative fatigue, reducing the tissue's stress-bearing capacity (Kumar, 2001). This damage may occur as a result of inflammation leading to remodeling of tissue and scar formation (O'Neil et al., 2001). This tissue overload may result in either acute or chronic conditions.

Second, long-term injuries were discussed to be an outcome of cellular changes and blood flow ischemia, characterized by chronic weakness, pain, or discomfort. In short, peripheral fatigue is characterized as a decline in contractile function due to the effects of high-energy consumption and inability of energy systems to maintain homeostasis (Westerblad et al., 2010). Peripheral fatigue may lead to cellular changes, which may precipitate into muscular damage and injury. Reduced blood flow and muscle tissue oxygenation may also play a role in muscle injury development. Impaired microcirculation may be the result of compression of blood arteries or increased intramuscular pressure (Visser & van Dieën, 2006). Chronic weakness may appear for days or weeks following intense activity (Green, 1997). Allen and colleagues (2008) explained this delayed recovery from fatigue as "prolonged low-frequency force depression", but is often described as "low-frequency fatigue".

Third, nerve injuries were comprised of two primary factors: repetitive strain and compression and whole body and hand/arm vibration. There is some evidence that, as a consequence of muscular fatigue, asymmetrical loading leading to a muscle imbalance cycle may result in secondary nerve compression (O'Neil et al., 2001). With respect to vibration, Adamo and colleagues (2012) found that vibration exacerbates fatigue, primarily due to an increase in muscle contraction as a result of sensorimotor and biomechanical mechanisms.

Fourth, other factors of injuries were discussed, including psychosocial (i.e., work stress), physical (i.e., work/task organization or parameters), perceptual (i.e., visual strain and fatigue), and cognitive (i.e., mental fatigue, sleepiness, and mental workload) elements. These factors may exacerbate the rate and extent of fatigue or may, in conjunction with fatigue, increase the risk of injury. For instance, Mehta & Agnew (2012) have shown that physical capacity was adversely affected by mental demand, resulting in a decrease in endurance time, increased fatigability, quicker rate of strength decrement, and slower heart rate recovery.

Table 3.2 Injury Disorders Effects or Outcomes and Their Causes or Mechanisms

Effects or Outcome	Potential Causes or General Mechanisms
Acute Injury	Increased Muscle Contraction Level (Overload) and Eccentric Contraction, Tissue Overload (Over Time), Cellular Changes, Blood Flow Ischemia, Muscle Oxygenation, Decrements in Motor Control & Coordination, Pain or Discomfort
Longer-Term Injury	Cellular Changes, Blood Flow Ischemia, Chronic Weakness, Pain or Discomfort
Nerve Injury	Repetitive Strain or Compression, Whole Body Vibration and Hand/Arm Vibration
Other Factors	Visual Strain & Fatigue, Work Stress, Mental Fatigue, Sleepiness, Work & Task Parameters

6.3 Illness & Wellness

Among the outcomes of long-term fatigue are burnout, myalgia, chronic fatigue syndrome, and impacts to quality of life (Table 3.3). Work-related burnout involves a prolonged response to chronic emotional and interpersonal stressors and is an important cause of sleep deprivation. Burnout is characterized by emotional exhaustion, increased sleepiness, loss of creativity, depersonalization, and reduced commitment and personal accomplishment (Cordes & Dougherty, 1993)

Myalgia is a multifactorial repetitive strain injury, whose symptoms include local tenderness and pain during activity (Green et al., 2011). Myalgia is associated with lower levels of muscle endurance, a high degree of perceived fatigue, and a lowered ability to relax the muscle between dynamic contractions (Larsson et al., 2000). Despite its sparsely known aetiology and pathophysiology, myalgia is often linked to both mechanical exposure and psychosocial factors (Sjörs et al., 2009).

Chronic Fatigue Syndrome (CFS) is a complex disorder that is not the result of ongoing exertion and is not substantially alleviated by rest (Fukuda et al., 1994). It is characterized by severe exhaustion, cognitive difficulties, disruption of social activities, impairments in emotional functioning, and by a number of persistent or recurring symptoms that are of new or definite onset (Wallman & Sacco, 2007). Individuals with CFS may also exhibit diminished immune function with fluctuating flu-like symptoms that persists for months or years. CFS may also mediate mechanisms that constitute a sense of effort (i.e., subjectively higher RPE) accompanying cognitive and physical exertion (Wallman & Sacco, 2007).

Fatigue in the long-term may be debilitating, impacting the individual's quality of life. The group recognized that chronic fatigue might affect full or part time employment, which in turn may bring about further financial hardship and emotional suffering. Assefi et al., (2003) documented that half of individuals with chronic fatigue were unemployed and those who remained employed had to transition jobs, work fewer hours, and/or received less pay since diagnosis. Many of those employed found it difficult to sustain employment and were unable to meet work deadlines. Huibers and colleagues (2006) found similar trends, where CFS, particularly due to physical dysfunction, was a strong predictor for inactive work status and full work incapacity. CFS patients also suffered losses of personal possessions, decrements in social and recreational activities, and support from family and friends as a result of increased mood disturbances and depression (Assefi et al., 2003).

Table 3.3 Illness & Wellness Effects or Outcomes and Their Causes or Mechanisms

Effects or Outcome	Potential Causes or General Mechanisms
Burnout	Contextual Antecedents, Person-Related Stressors
Myalgia	Cellular Changes, Disturbed Oxidative Metabolism, Increased Proportion of type I "megafibers", Work Stress, Muscle Activity
Chronic Fatigue Syndrome	Increase in mRNA, expression of metabolite-detecting receptor and adrenergic receptors. Immune Parameters (i.e., cytokines), Increased Perceived Effort, Increased Brain Activity, Slower Information Processing
Quality of Life	Chronic Fatigue Syndrome and/or Fibromyalgia

6.4 Discomfort

Workshop participants addressed causes and mechanisms of fatigue-related discomfort and pain (Table 3.4). In short, pain may be classified by its mechanism: nociceptive, peripheral neuropathic, and central sensitization. Of particular interest is nociceptive pain, which is associated with activation of peripheral receptive terminals of primary afferent neurones in response to noxious chemical, mechanical, or thermal stimuli (Smart et al., 2012). Both pain and fatigue are frequently associated with another, and has even been labeled as "sensation of muscle fatigue" (Light et al., 2010). Light and colleagues (2010) proposed that sensation of muscle fatigue is transduced, conducted, and perceived within a unique sensory system that is similar to the modality of pain.

Table 3.4 Discomfort Effects or Outcomes and Their Causes or Mechanisms

Effects or Outcome	Potential Causes or General Mechanisms
Acute Pain and/or Discomfort	Sensitization of Nociceptors

7. Measurement & Detection Methods

7.1 Performance & Quality

It was apparent that these processes, pathways, and manifestations leading to decrements in work performance and quality were derived from both mental and physical domains. Forty methods were identified as measures for performance and quality outcomes.

Situation awareness (SA) was identified as an evaluative method to measure the level of arousal and mental fatigue/sleepiness. According to Endsley (1995), SA provides a dynamic update of the environment to necessitate effective human functioning. Previous studies have shown a relationship between fatigue and information processing speed (e.g., Meijman, 1997). Generally, when SA is incomplete or inaccurate, possibly due to slower information processing speed, and when decision-making is poor, performance is reduced.

During the workshop, it was suggested that situation awareness in combination with heart rate variability might provide an effective set of measures to assess arousal, work stress, and fatigue. Heart rate variability describes variations of both instantaneous heart rate and RR intervals and provides insight into the autonomic regulation of heart rate. After vigorous activity, the normalized high frequency component of HRV was lower than pre-activity measures and returned to baseline 2 days after activity. The normalized low frequency component, however, increased on the first day after exercise, compared to the same time on the day preceding the vigorous activity. The low frequency/high frequency ratio of heart rate variability similarly increased after activity but returned to baseline, and even below baseline level, 2 days post-exercise. It was suggested that possible cardio-protective effects of cardiac vagal regulation are diminished after prolonged intense activity (Hautala et al., 2001). On the other hand, overtrained (i.e., chronic fatigue) individuals showed a marked predominance of sympathetic modulation, and a decrease in heart rate variability (Mourot et al., 2004).

Questionnaires and fatigue scales were discussed as possible measurements of mental and physical fatigue. Åhsberg and colleagues (1997) proposed that perceived fatigue could be described and measured based on 5 dimensions: lack of energy, physical exertion, physical discomfort, lack of motivation, and sleepiness. On the basis of these findings, the Swedish Occupational Fatigue Inventory (SOFI) was developed and later assessed for its internal reliability (Åhsberg et al., 1997) and content validity in physical (e.g., Åhsberg & Gamberale, 1998) and mental (e.g., Åhsberg et al., 2000) work. In general, the group felt that questionnaires and other fatigue scales proved to be an essential measure of fatigue and should be incorporated in both laboratory and field-based fatigue studies.

7.2 Injury & Disorders

Thirty-four measures were identified for this category, and reflect processes in both physical (peripheral and central mechanisms) and cognitive domains. Surface electromyography (EMG) has been used extensively to measure the neural input drive of the muscle and possibly its output force. However, responses in both time and frequency domains, after dynamic, intermittent, and/or low-intensity fatiguing tasks, have been inconsistent (Yung et al., 2012). One explanation is that load sharing between muscles may affect the observed muscle activity. As a result, fatigue development for a particular muscle may be slowed, disturbing the relationship between endurance time and EMG-based fatigue indicators (Iridiastadi et al., 2008).

More favorable are direct measures of fatigue that detect cellular changes, specifically blood sampling, urine sampling, and muscle biopsies. Studies have shown a relationship between particular biomarkers and progressive exercise and fatigue. For instance, Garde and colleagues (2003) observed a progressive increase in urinary norepinephrine concentrations during a repetitive task. In another example, Flodgren and colleagues (2006) showed significant increases in intramuscular micro-dialysate lactate and glutamate concentrations in trapezius muscle during low-load repetitive work. Unlike venous blood sampling, micro-dialysis measures local changes in substance concentrations in the muscle interstitium with minimal trauma (Flodgren et al., 2006).

7.3 Illness & Wellness

Eleven measures or detection method were discussed as measures of fatigue-related illness and wellness. Participants addressed both direct (e.g., biomarkers, muscle biopsies, blood chemistry, diagnostic imaging) and indirect (e.g., questionnaires, ratings of perceived exertion and visual analog scales, choice reaction tests, etc.) measures of burnout, myalgia, chronic fatigue syndrome, and impacts on quality of life. A wealth of literature has been dedicated to biomarker response to better understand autonomic nervous system (ANS) and hypothalamic-pituitary-adrenal axis (HPA) functioning with burnout patients. One such biomarker is cortisol where its hypersecretion and hyposecretion is indicative of HPA axis dysregulation and has been observed with workload and job strain (De Vente et al., 2003). Salivary cortisol has gained greater traction as a measure of HPA axis activity namely for its high correlation with plasma cortisol, its very short time lag between changes (1 to 2 minutes), its independence from saliva flow, and its non-invasiveness (Malamed et al., 1999).

Discussion centered on phosphorus magnetic resonance spectroscopy (P-MRS) as a non-invasive measure to assess energy metabolism. Muscle biopsies, although traditionally accepted as a gold standard measure to distinguish neuromuscular disorders, are invasive and a costly procedure. The workshop group believed that P-MRS has high utility as a measure of fatigue. Because only metabolites that are unbound and of sufficient concentration are visible by P-MRS, much of the phosphate in mitochondria and signals originating from the cytosol will be visible (Argov et al., 2000). The extensive use of P-MRS includes diagnosis or measurement of acute fatigue (Mizuno et al., 1994) and longer-term fatigue including chronic fatigue syndrome and myalgia (Wong et al., 1992; Raymer et al., 2009).

7.4 Discomfort

The group arrived at 4 possible measures of discomfort: algometer or dolorimeter, Borg's ratings of perceived exertion or discomfort scale, questionnaires or descriptors, and movement variability or movement pattern measures.

Algometers and dolorimeters are pressure-pain threshold measures that have been used to quantify pain, as an index of myofascial trigger point sensitivity, and track recovery and healing (Kinser et al., 2009). Trigger points may develop from endplates releasing excessive acetylcholine accompanied by regional sarcomere shortening. Both shortened sarcomeres and increase tension lead to ischemia and local hypoxia, which subsequently results in tissue distress (i.e., reduced ATP and release of sensitizing substances). The sensitizing substances, in turn, are responsible for nociceptive sensitization (Visser & Van Dieën, 2006).

8. Practicality & Application

Sixty measures were identified. However, measures were combined if they were similar and shared common traits. For instance, antalgic postures/movement patterns were combined with with movement variability (kinematics). Descriptors were combined with clinical tests. Lastly, fatigue scales and questionnaires were integrated. Workshop participants were thus asked to rate 57 unique measures for their use in laboratory and field-based settings (Table 3.5). Participants were instructed to rate these fatigue measures based on their previous experience and knowledge, and to only rate those that they were comfortable in providing a confident assessment.

As measures may be context-specific, duplicate measures for different outcomes and causes were first compared. Trends between context-specific measures were similar. For instance, frequency counts for heart rate variability in laboratory studies were 2, 4, and 0 for "high", "medium", and "low", respectively when assessing low arousal, while frequency counts, when assessing work stress, were 1 (high), 4 (medium), and 1 (low). In both cases, heart rate variability, in general, was categorized as "medium" for laboratory studies. After comparing trends of the same measure between different contexts, categorization of a measure into a rating group was based on averaged counts.

For field studies, 8 measures were rated high, 24 were rated medium, and the remaining 25 were rated low (i.e., not recommended). Participants also assessed the same 57 measures in laboratory settings, 17 were rated high and 40 were categorized as medium. There was no single fatigue measure that was rated low. Of particular interest are fatigue measures that were rated high in both settings (i.e., maximum voluntary contractions, questionnaires and fatigue scales, Borg's ratings of perceived exertion/discomfort, and visual analog scale). Not surprisingly, these measures are non-invasive, quick to record, and have been shown to be valid indicators of work intensity and fatigue. For instance, a maximum voluntary contraction is often used to measure force-generating capability. A decline in maximum force may be indicative of both central and peripheral fatigue (Vøllestad, 1997). Questionnaires, Borg's rating of perceived exertion/discomfort scales, and visual analog scales were also assessed as highly recommended for laboratory and field studies. These perceptual-based measures may be mediated by central mechanisms and have been used to measure both acute and chronic fatigue. To illustrate this, Sato and Coury (2009) found that ratings of perceived exertion (Borg 6-20 numerical-verbal scale) was able to identify increased workload. On the other hand, visual analog scales, measuring discomfort, was more sensitive to residual symptoms. Chronic states of physical and mental fatigue have been assessed with a variety of scales and questionnaires, including the Maslach Burnout Inventory (MBI) to measure dimensions of burnout, Numerical Rating Scale (NRS) as a measure of muscle pain, and Chalder Fatigue Scale and Fatigue Severity Scale (FSS) to assess chronic fatigue syndrome. Because of the lack of a gold standard, there must be careful consideration when selecting a suitable questionnaire or scale. For example, the Fatigue Severity Scale is a fatigue/function measure that integrates dimensions of fatigue intensity and functional outcomes. This scale is able to discriminate between individuals with different subtypes of fatigue. On the other hand, the Chalder Fatigue Scale exclusively measures fatigue intensity and lacks specificity (Taylor et al., 2000). Similarly, Ferreira-Valente (2011) compared the Numerical Rating Scale, Verbal Rating Scale (VRS), and Faces Pain Scale-Revised (FPS-R), finding the NRS as the most responsive, sensitive, and preferred for its relative simplicity and ease of administration and scoring. In field studies, a large collection of detection methods, typically requiring specialized equipment and invasive techniques, were not recommended.

Not surprisingly, methods traditionally recognized as "gold standard" in measuring cellular and metabolic changes, were assessed highly for laboratory studies but not recommended in field settings.

Questionnaires and fatigue scales, Borg's rating of perceived exertion/discomfort scales, and visual analog scales were linked to all four main outcome categories (Figure 3.1). These measures were also rated highly in both laboratory and field settings. Of the measures that correspond to 3 of 4 fatigue outcome domains, both heart rate and situation awareness were recommended with reservations (medium) in both settings; movement variability was rated medium in the field but high in the lab; and algometer and dolorimeter measurements to determine pressure-pain threshold were not recommended in the field (low) and were recommended with some reservations in the laboratory (medium). Trends indicated that measures satisfying 3 or 4 outcomes were often rated medium or high in the laboratory but led to variable ratings when assessed for field settings.

Table 3.5 Evaluated Fatigue Measures for Laboratory and Field Settings

		Field		
		High	Medium	Low
Laboratory	High	• Maximum Voluntary Contraction • Questionnaires and Fatigue Scales • Visual Analog Scale • Borg's Rating of Perceived Exertion or Discomfort Scale	• Movement Variability (Kinematics, Antalgic Postures, Movement Patterns) • Physical Variation & Motor Variation	• Electrical Stimulations – Hi/Lo Frequencies • Rate of Response (Rise Time, Rate of Force Development, Amplitude of Overshoot) • Muscle Biopsy • Phosphorus-31 Magnetic Resonance Spectroscopy • Clinical Tests (e.g., Descriptors) • Near Infrared Spectroscopy • EEG • Twitch Force • Diagnostic Imaging • Functional MRI • Blood Flow (Doppler Ultrasound)
	Medium	• Visual Attention Tests • Productivity Measures • Qualitative Assessments: Interviews • # of Errors or Product Quality	• Situation Awareness • Heart Rate Variability • Choice Reaction Tests • Heart Rate • Blood Pressure • Behavioural Observation • Tremor • MMG Amplitude • MMG Frequency • Posture Matching (Kinaesthesia) • EMG Amplitude (Changes in Efferent Neural Drive) • EMG Frequency • EMG Hi-Lo Ratio • EMG Gaps • Increased Peak EMG Amplitude Due to Large Corrective Movements • Endurance Time or Time to Complete Task • Two-Point Discrimination (Aesthesiometer) • Time Variation Pattern (e.g., Duty Cycle) • Stroop Errors • Biomarkers (e.g., Cortisol) • Force Measurements (e.g., Force Matching) • Electrodermal Response	• Critical Fusion Frequency • Oculomotor Behavioural Changes • Visuohaptic Simulations, Visuospatial Tests, Visuomotor Control • Stimuli Detection Tests • Inflammatory Responses & Oxidative Stress • Epinephrine or Norephinephrine • $\dot{V}O_2$ • Postural Sway • Orbicularis Oculi Muscle Activity • Electrodiagnostic Tests (e.g., Nerve Conduction, Somato-Sensory Evoked Potentials) • Blood Chemistry • Algometer or Dolorimeter • Loss of Sensation (Semmes-Weinstein Monofilaments) • Electromechanical Tapping
	Low			

9. Summary

This workshop addressed three areas of discussion to evaluate current concepts and measures of fatigue. By assembling expert opinion from multiple research perspectives and disciplines, a set of practical, reliable, and valid measures may be devised for laboratory and field investigations. Sixty measures were identified but 57 unique measures were evaluated. Four measures were recommended in both settings: maximum voluntary contractions, questionnaires and fatigue scales, Borg's ratings of perceived exertion or discomfort scales, and visual analog scales. Twenty-five measures were not recommended in field settings. The results of this workshop serves as a guide and it remains the researcher or practitioner's discretion to select detection methods and techniques to maximize their ability to address multiple fatigue domains and context-based practicality.

Supplementary Material

As an alternative means to present the data, Figure 3.2 is a flow chart demonstrating the linkages between fatigue outcome domains, outcomes or effects, causes or mechanisms, and measures and detection methods. Tables are presented as flow chart graphs in Appendix A.

Acknowledgements

The following were the workshop participating researchers: Tim Bosch, Jack Dennerlein, Clark Dickerson, Laura Frey Law, Howie Green, Bernard Martin, Ranjana Mehta, Michelle Robertson, and Linda Rose; and participating graduate students: Larissa Fedorowich, Chad Gooyers, Michael Greig, Thomas Karakolis, Nicholas La Delfa, Adrien Moufflet, Akram Samarikhalaj, Michael Sonne, and Amin Yazdani.

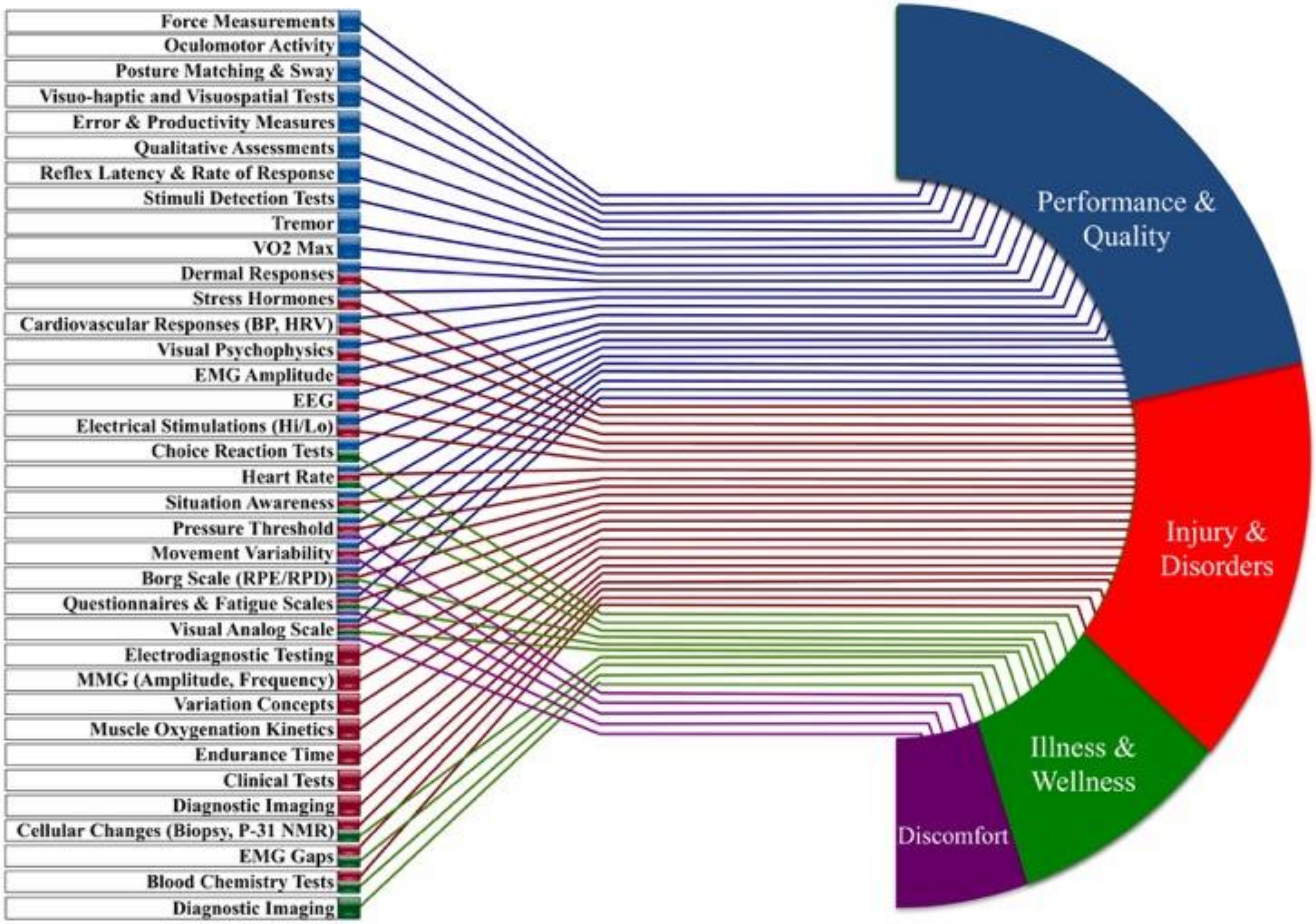


Figure 3.1 Linking fatigue measures with four fatigue outcome domains.

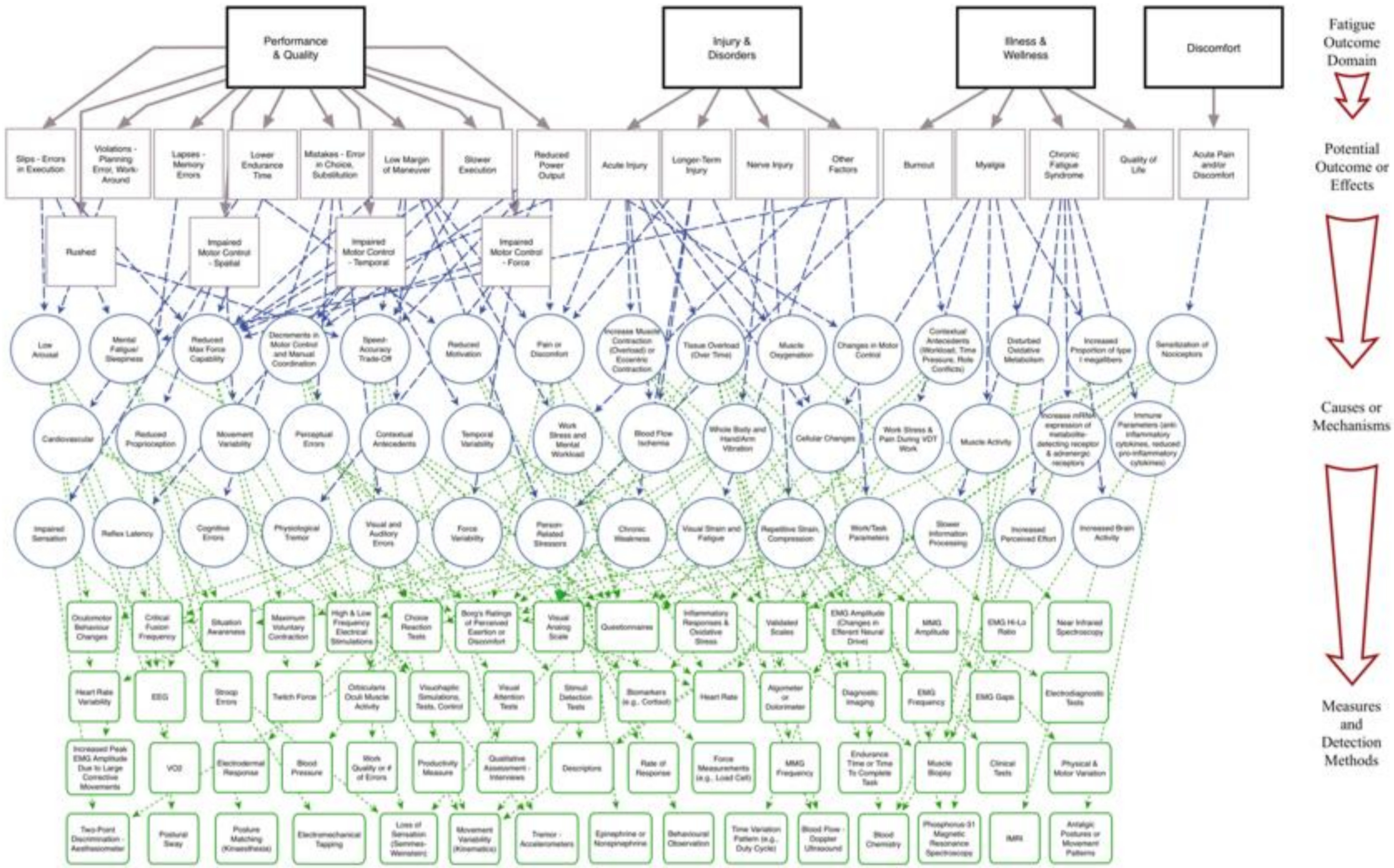


Figure 3.2 Flow chart of linkages between fatigue outcome domains, outcome or effects, causes or mechanisms, and measures and detection methods

Chapter 4

An Exploratory Study on Select Fatigue Measures in the Field: Within-Day and Between-Day Responsiveness

Yung, M., Bigelow, P. L., Hastings, D. M. & Wells, R. P. (2014). Detecting within- and between-day manifestations of neuromuscular fatigue at work: An exploratory study. *Ergonomics, 57*(10), pp. 1562-1573. DOI: 10.1080/00140139.2014.934299.

Abstract

Cumulative or persistent neuromuscular fatigue may develop over a workday and over a workweek, which might result from exposure to physical demanding work, such as repetitive and/or sustained work with insufficient recovery. The aim of this exploratory study was to document fatigue in realistic work (i.e., residential plumbing), while employing multiple measures to provide a comprehensive picture of fatigue development. We demonstrated increasing fatigue of the hand/arm over the day and persistent fatigue from Tuesday to Friday. A number of measures did not return to baseline values following a weekend break. The results from this study provide insight towards the selection of fatigue measures, test the "robustness" of these measures in a dynamic setting, and provide preliminary evidence of the temporal development of fatigue within and between multiple workdays.

1. Introduction

Exposure to physically demanding work, such as repetitive and/or sustained work with insufficient recovery, may result in cumulative or persistent fatigue. Such fatigue may reduce the stress-bearing capacity of tissue (Kumar 2001), compromise immune function (Kajimoto 2007), and serve as a precursor of ill health in the longer term (Sluiter et al. 2003). Cumulative fatigue may thus be a useful surrogate measure of injury risk and a design and evaluation tool (Nussbaum 2001; de Looze et al. 2009). However, very few studies have documented the temporal pattern of fatigue development in realistic work tasks. One particular challenge is the large diverse set of tools and procedures to measure fatigue, as a consequence of many specific fatigue processes and their manifestations (Enoka and Stuart 1992; Behm 2004). In the few studies that have documented fatigue between multiple days (e.g., Bosch et al. 2007), little changes, based on surface electromyography (EMG) indicators, were observed. The absence of changes in EMG amplitude and frequency may be explained by several factors. EMG reflects changes in neural activation and lacks sensitivity to changes within muscle fibers, therefore physiological processes that may play an important role in fatigue development might not be reflected in the EMG signal (Vøllestad 1997; Bosch et al. 2007). Additionally, EMG is highly sensitive to influences other than fatigue, and expected changes in EMG indicators have not been consistently observed in dynamic, intermittent, and/or low-intensity exposures (Nussbaum et al. 2001; Bosch et al. 2007; Yung et al. 2012). Finally, despite high intra-day reliability of EMG amplitude measures, Place and colleagues (2007) expressed caution in the use of EMG to measure activity between days, as a result of changes in electrode re-positioning. To improve discriminatory power between multiple days, a complementary set of fatigue measures may be necessary (Bosch et al. 2007).

The aim of this exploratory study was to document fatigue in physically demanding work, while employing multiple measures to provide a comprehensive picture of fatigue development. The results from this study will provide insight towards the selection of fatigue measures for the remaining studies, test the "robustness" of these measures in a dynamic setting, provide preliminary evidence of the temporal development of fatigue within and between multiple workdays, and potentially elicit issues for further investigation.

2. Physically Demanding Work: Residential Plumbing

Despite recent indications of economic downturn in both residential and non-residential construction in Canada (CANSIM Statistics Canada 2013), construction remains one of the largest industries, with at least 1.3 million Canadians employed in this sector (Canadian Construction Association 2013). Globally, construction remains a major economic activity (Van der Molen et al. 2005). Construction work, however, is a physically demanding job (Hsu et al. 2008; Choi 2012; Everett 1999), involving exposures such as heavy manual material handling, awkward postures, contact stresses, repetitive movements, vibration, and forceful exertions. In Ontario, the construction sector represented 10% of all lost time claims in 2012, 43% of those claims were due to sprains and strains (WSIB 2012).

Activities within residential plumbing follow a general sequence of tasks: plan work, measure and layout work, cut or finish a component, place or position a component to its final location, connect multiple components, and inspection (Everett 1999). The US National Health Interview Survey, as reported by Schneider (2001), indicated that 23.8% of plumbers report severe hand discomfort. Joining pipe is one particular task that may be considered *high* risk in developing WMSD (Albers et al. 2005). Assembling and joining pipe is often carried out above shoulder height while working off a ladder. Rose (2007) determined that these postures may lead to perceived discomfort in the lower back, neck, arms, and wrists, as well as mean reference contraction levels above 50% in the trapezius muscles.

Recently, in the Greater Toronto Area (GTA), cross-linked polyethylene (PEX) piping has replaced copper piping as the primary material in residential water supply piping systems. PEX piping is suitable for both hot and cold water use and is not easily damaged by frozen water (Phillips 2004). Traditionally, to install and adjoin PEX pipes, compression rings are manually crimped to secure piping with barbed fittings. Crimping tools are specific to the size of the PEX tubing (¼ inch, ½ inch, ⅝ inch, and 1 inch), but ½ and ¾ inch crimps are most common. Preliminary evidence suggests that manual crimping is associated with elevated odds ratios for reported discomfort/pain and disability of the distal upper extremities among residential plumbers in the GTA (Bigelow et al. submitted). Alternative joining methods have been introduced, including powered tools and expansive pipe connection systems. However, the expanding pipe method requires particular PEX tubing and is affected by cold-weather temperatures. According to union representatives, a typical housing unit requires between 200 and 300 crimps, and a low-rise residential plumber is expected to perform as many as 500 crimps per day (Bigelow et al. submitted).

3. Selection of Fatigue Measures

A test battery should satisfy the peripatetic nature of construction work. Measures with low power consumption were preferred as electrical power was not readily available. Robust and durable equipment was also necessary to endure changing weather and environmental conditions. Additionally, measures were also selected to reflect possible changes, as a result of fatigue, in multiple domains (i.e., central and peripheral). This exploratory study provided an opportunity to evaluate measures of interest, with their selection informed by the CRE-MSD Toronto Workshop and the *novelty* of the measure. For instance, measures were chosen not only for reliability and practicality, perceived by researchers from the CRE-MSD workshop, but also their relationship to tangible outcomes. Novelty of measures (Table 4.1) was based on the number of peer-reviewed articles, in PubMed (MedLine) database from 1950 to 2014, that cite keywords: (fatigue or muscle fatigue or local fatigue) AND (ergonomics or occupation or assembly work) AND (the measure of interest). Measures with at least 64 citations will be considered *commonly used* and remaining measures will be considered *novel*. This 64-citation threshold represents an average of one citation per year between 1950 and 2014. Of the 42 combinations of measures, 16 were considered *commonly used* and 26 were *novel*.

To fulfill the aforementioned requirements, this study's test battery will include: maximum grip strength, force variability measures, physiological and postural tremor, and Borg's rating of perceived discomfort. All measures selected in this study were linked to human performance outcomes relevant to work quality and productivity (i.e., precision and strength capability). Both maximum voluntary contractions and Borg's perceived discomfort scales were rated highly for reliability and practicality in both laboratory and field settings. Force variability was assessed high-medium in the laboratory and medium in the field. Tremor was deemed medium in both laboratory and field settings. Maximum voluntary contractions and Borg's discomfort scale were *commonly used* measures, with citations of 448 and 167, respectively. Force variability and tremor were *novel* measurements, with citation counts of 10 and 13, respectively. Finally, all measures were based on strong theory and have been shown to change with increasing fatigue. The measures reflect changes central in origin (e.g., ratings of perceived discomfort and force variability), changes to peripheral processes, or a combination of both (e.g., maximum voluntary contraction and tremor).

4. Methods

4.1 Participants

With the assistance of UA Local Union 46, residential plumbers at worksites located within the GTA were recruited to participate in this study. All plumbers adjoined PEX pipes using manual crimping methods. Plumbers were excluded from participation if they experienced current or previous injuries in the last 6 months of the dominant hand or arm. A $25 coffee card was provided at the conclusion of the study, in appreciation for their time. Participants provided informed consent for all experimental procedures and associated risks, as approved by the University of Waterloo Office of Research Ethics, prior to the experimental session. Data collection occurred between June and August of 2012.

Table 4.1 Novelty of Measures Based on Number of Article Citations as of September 2014.

Measure	# Articles	Measure	# Articles
EMG, Electromyography	275	Critical Fusion Frequency, Flicker Fusion Threshold	15
MMG, Mechanomyography	5	Diagnostic Imaging, X-Ray, MRI, Ultrasound, Sonography	91
Tremor	13	Doppler Ultrasound	2
RPE, Ratings of Perceived Discomfort, Ratings of Perceived Exertion, Discomfort, VAS, Borg	167	Movement Variability, Kinematics, Antalgic Postures, Movement Patterns	239
MVC, Maximum Voluntary Contraction, Force, Strength	448	EEG, Electroencephalography	59
Position Matching, Kinanesthesia, Sway, Proprioeeption	43	Electrodiagnostic Tests, Nerve Conduction, Somato-Sensory Evoked Potentials	10
Force Variability, Force Fluctuation	10	Endurance Time, Completion Time	148
Blood Sampling, Biomarkers	19	Error, Error Rate	102
Muscle Biopsy	19	Interviews, Qualitative Methods	71
Electrical Stimulation, Twitch, Low Frequency Fatigue	144	Inflammatory Response, Oxidative Stress	5
Steadiness, Motor Coordination	11	Epinephrine, Norepinephrine	15
Survey, Questionnaire	429	Oculomotor Behaviour	3
Heart Rate, Heart Rate Variability	217	Eye Movements, Saccades, Blink Rate	47
VO_2, Oxygen Consumption, Metabolic Rate	130	Physical Variation, Motor Variation	41
Blood Flow	23	^{31}P-NMR	1
NIRS, Oxygenation	10	Situation Awareness, Situational Awareness	412
Algometer, Dolorimeter	1	Stroop	8
Blood Pressure	65	Time Variation	33
Cortisol	20	Two-Point Discrimination, Aesthesiometer	0
Choice Reaction Tests	8	Visual Attention Tests	9
Clinical Tests	131	Rate of Response, Rise Time, Rate of Force Development, Amplitude Overshoot	67
Duty Cycle	12		

4.2 Data Acquisition & Instrumentation

A portable 16 bit, 8-channel A/D system (AI-1608AY-USB, Contec Co., Ltd., Osaka, Japan), encased in a secure enclosure, was connected to an ultraportable notebook computer. Data was monitored and collected by C-Logger (Contec Co., Ltd., Osaka, Japan) and later exported as CSV format files for further analysis. All fatigue measures were taken from a vehicle outside the immediate residential work site and data was sampled at 500 Hz. Measures were recorded from the dominant upper limb, which was defined as the primary hand when performing a cut and one-handed crimp for ¼ and ½ inch PEX pipe.

4.3 Grip Strength & Force Variability

Force variability and hand strength were measured with a handgrip dynamometer (Medical Research Ltd., Leeds, UK). Both test and maximum handgrip contractions were completed with the dominant hand, elbows flexed at 90 degrees. Participants performed a test contraction at 30% maximum handgrip force (MVC), to determine force variability, assisted by the displayed visual feedback. The 30% MVC test contraction was recorded for 15 seconds and maximum contraction for 5 seconds. Maximum handgrip contractions were executed with positive verbal encouragement.

4.4 Physiological and Postural Tremor

Physiological tremor was measured with a low profile (4mm x 4mm x 1.45mm) tri-axial ± 3 g accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA) mounted on the dorsum of the hand, on the distal part of the third metacarpal bone. The accelerometer was insulated with a high strength elastomeric liquid rubber. Participants were instructed to rest their relaxed arm on their lap, with their hand hanging freely. Accelerometer data was recorded when participants assumed this relaxed position for 15 seconds.

To assess postural tremor, a tri-axial ± 3 g accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA) was attached to a dowel to measure its steadiness during goal-directed postural pointing. Accelerometers placed on the dowel are similar to studies that have investigated postural tremor among air pistol shooters (e.g., Tang et al. 2008) and as a portable tremor measurement system to detect hand/arm muscle fatigue (e.g., Galinsky et al. 1990). When measuring postural tremor of the fingers, participants pointed the dowel towards a target, which was placed flat on a surface at approximately elbow height, with the forearms comfortably supported. The dowel was held in a dynamic tripod grasp, a functional grip traditionally undertaken in handwriting. This grasp was selected to engage intrinsic muscles of the fingers and that is common and familiar to most adults (Bergmann 1990). Participants were then asked to keep the dowel aligned upwards, perpendicular to the ground with forward shoulder flexion at 90 degrees, in order to measure postural tremor of the whole upper limb. Both hand and shoulder postural tremors were recorded for 15 seconds.

4.5 Ratings of Perceived Discomfort

Participants rated their perceived discomfort of their dominant hand/arm and shoulder using Borg's CR-10 scale (Borg, 1990).

4.6 Experimental Protocol

Due to the peripatetic nature of the plumbers work, new participants could not be recruited into the study on Monday morning. Measures were therefore collected Tuesday (Day 1), Wednesday (Day 2), Thursday (Day 3), Friday (Day 4), and the subsequent workday following a weekend break (i.e., Monday – Day 5). On the first day (Tuesday), participants performed 3 maximum handgrip contractions, separated with at least 2 minutes of rest. The average of the peaks were used to determine the magnitude of the 30% test contraction. Participants were also provided ample practice time to familiarize themselves with the test battery of fatigue measures (Figure 4.1). The test battery was administered three times per day: pre- shift (pre), mid- shift before lunch (mid), and post- shift (post). Participants were asked before the start of the work day of their intended tasks which were later verified before each test battery. The number of crimps performed was also recorded and whenever possible, participants were observed and videotaped.

4.7 Data Analysis

Force signals were low pass filtered at 10 Hz (Butterworth, 2nd Order) based on a cutoff frequency determined by residual analysis (Winter 2005). Test contractions were exerted for 15 seconds, but later windowed to the middle 12 seconds of data. Force variability and signal complexity was subsequently calculated over 3-second epochs within the 12-second window. Relative force variability was calculated by the coefficient of variation of the signal, derived from the absolute value of the mean and standard deviation of the signal. Signal complexity was determined by sample entropy. Similar to previous studies, sample entropy calculations were set to the following parameters: degree of similarity, i.e., tolerance, (r = 20% of standard deviation of force signal) and signal length for evaluative purposes (m = 2 data points). As a unit less number, the sample entropy output ranges from 0, i.e., signal is predictable, to 2, i.e., signal is complex

(Svendsen et al. 2011). Maximum handgrip contractions recorded for 5 seconds, were windowed to the middle 3 seconds of data, which were then averaged to represent force magnitude. Tremor data was bandpassed filtered between 1 and 20 Hz (Butterworth, 2nd Order), which are within frequencies of interest (Duval et al. 2001). The middle 10 seconds of the 15-second file were windowed and analyzed to determine amplitude in the time domain (i.e., root mean square amplitude). All data was processed off-line using LabChart 7 (ADInstruments, Colorado Springs, CO, USA) and Matlab 7.2 (Mathworks Inc., Natick, MA, USA).

Preliminary examination was initially undertaken to investigate the fatigue effects of crimping by stratifying data based on crimping and non-crimping tasks. However, the findings were not extraordinary compared to results from the aggregate data. This might have been due to a lack of statistical power among crimping observations. With this discovery, analysis proceeded with the full 16 participants. A repeated measures analysis using a general linear mixed model approach (Kleinbaum et al. 2007) determined whether there were statistically significant main effects and interaction effects involving two factors: Day of the work week (i.e., Tuesday, Wednesday, Thursday, Friday, Monday) and Time of the day (i.e., Pre- shift, mid- shift, post- shift), while accommodating possible missing data points. Tukey's post hoc tests were performed in the event of statistically significant main effects. All statistical analyses were performed using Statistical Analysis Software (Version 9.3, SAS Institute Inc., Cary, NC, USA).

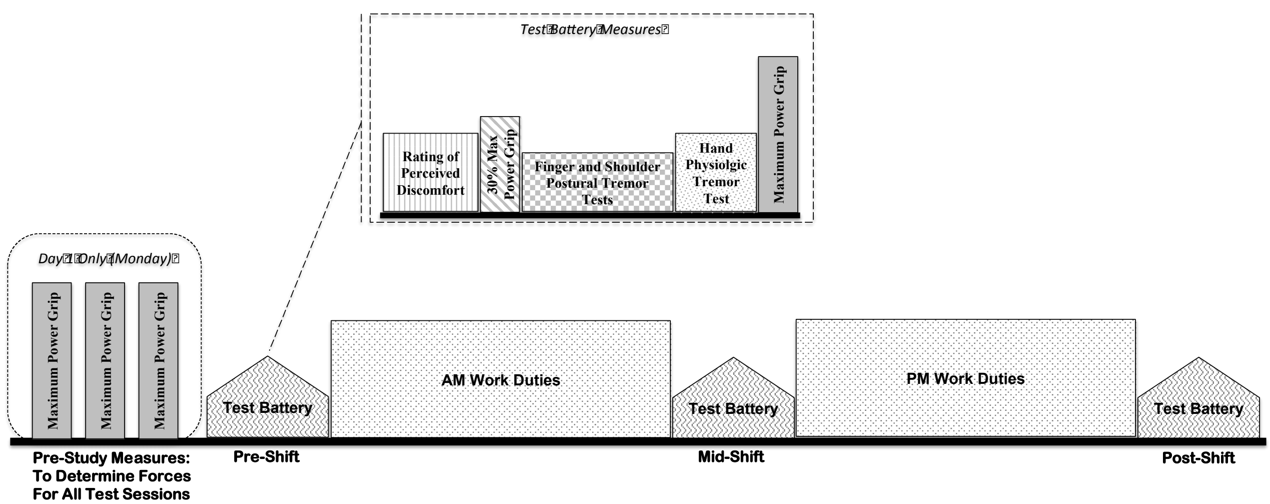


Figure 4.1 Data collection protocol

5. Results

Sixteen residential plumbers (mean age = 34.6 years, SD 13.2; 16 males) volunteered to participate in this study. A mixture of journeymen and apprentices, job experience ranged between 2 months and 40 years. All participants were right hand dominant. Two participants were paid as piece-workers while the remaining earned an hourly wage. All participants worked 5 days a week, between 7am and 3:30pm on the construction site. However, participants typically travelled, before and after work, between the employer *shop* and construction sites, to gather materials and equipment, the company vehicle, and daily work itinerary. Tasks from the sixteen participants during the morning and afternoons of the 5-day collection period are shown in Figure 4.2.

Participant	Day 1		Day 2		Day 3		Day 4		Day 5	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
1	B	B	B	I	DNW	DNW	DNW	DNW	DNW	DNW
2	B	B	B	I	B	I	DNW	DNW	B	B
3	I	I	I	DNW	I	B	B	B	I	DNW
4	I	I	I	I	I	B	B	B	I	DNW
5	B	B	T	B	B	B	B	DNW	B	B
6	B	B	T	B	B	B	B	T	B	B
7	LCI	LCI	LCI	LCI	CR	DR	DR	DR	DR	DR
8	LCI	LCI	LCI	LCI	R	I	R	DNW	DR	R
9	I	I	LCI	LCI	I	I	DNW	DNW	DNW	DNW
10	P	P	DNW	DNW	I	B	P	P	P	B
11	CR	CR	LCI	I	I	I	B	DNW	LCI	R
12	P	DR	LCI	P	I	I	LCI	P	LCI	DR
13	P	CR	LCI	P	LCI	B	CR	B	LCI	CR
14	CR	CR	DNW	LCI	LCI	LCI	CR	DNW	CR	CR
15	CR	CR	I	LCI	LCI	LCI	CR	DNW	CR	CR
16	P	P	LCI	I	LCI	LCI	CR	DNW	DR	DR

Plumbing Task:

CR	Cut and Rough-In	DR	Drops and Risers
B	Basements	P	Cutting Pipes and Piping Work
I	Installation, Finishing, Clean-up	R	Roaming
T	Testing	DNW	Did not work
LCI	Lifting, Carrying, Installing Tubs		


Cut & Rough-In


Drops & Risers


Basements (Crimping)


Installation & Finishing

Figure 4.2 Plumbing tasks performed by study participants

5.1 Grip Strength

Trends indicate peak hand strength at mid-shift and generally lower handgrip forces as the workweek progressed (Figure 4.3). Repeated measures analysis revealed both a between day ($p = 0.005$) and time of day ($p = 0.002$) effect. Significant differences were observed between days 1 ($\bar{x}$ = 438.26 N, SEM = 15.27) and 4 ($\bar{x}$ = 334.55 N, SEM = 30.54), $p = 0.016$, and days 2 ($\bar{x}$ = 396.97 N, SEM = 26.37) and 4, $p = 0.038$, and days 1 and 5 ($\bar{x}$ = 368.54 N, SEM = 31.40), p =

0.045. Time of day differences was found between pre-shift ($\bar{x}$ = 379.68 N, SEM = 18.17) and mid-shift ($\bar{x}$ = 404.28 N, SEM = 15.88), p = 0.011, and between mid- and post-shift ($\bar{x}$ = 368.54, SEM = 22.00), p = 0.031. Although not statistically significant, when considering only pre-shift handgrip strength from Tuesday ($\bar{x}$ = 425.21 N, SEM = 17.59) to Friday ($\bar{x}$ = 325.67 N, SEM = 35.62), it appeared that participants progressively exerted less force over the week. Monday pre-shift forces ($\bar{x}$ = 379.71 N, SEM = 36.51) were higher than the previous Friday but also remained lower than Day 1 pre-shift forces.

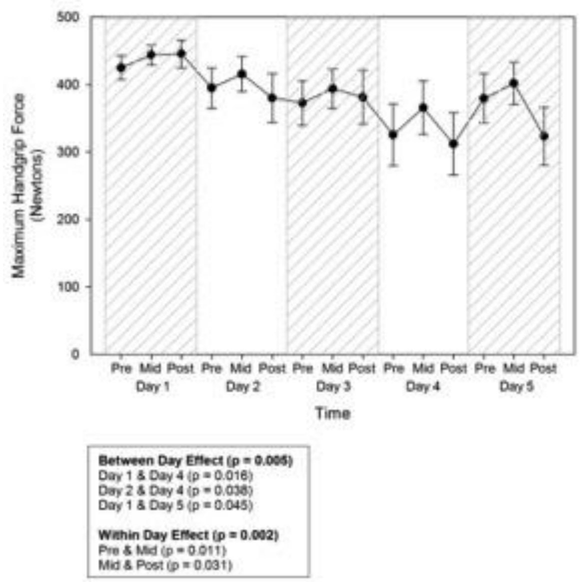


Figure 4.3 Maximum Handgrip Force Responses Within (Pre-, Mid-, Post- Shift) and Between (Days 1 – 5) Workdays.

5.2 Force Variability

Test contractions were performed and later analyzed with sample entropy calculations for complexity in the force signal (Figure 4.4). Results indicate no clear trends but a significant day effect (p = 0.050), particularly between day 1 ($\bar{x}$ = 0.023, SEM = 0.003) and day 5 ($\bar{x}$ = 0.032, SEM = 0.004), p = 0.050. Force variability, measured by relative dispersion, i.e., coefficient of variation (CV), demonstrated inconsistent trends during a workday and during a workweek (Figure 8). Further inspection of Figure 4b indicate that test contraction recordings during mid-shift were particularly dispersed with mean values slightly elevated compared to pre- and post-shift measures (i.e., 4.8% ±1.2 at mid-shift vs. 3.4%±0.1 pre-shift and 3.9%±0.01% post-shift). However, this observed trend did not show statistical significance (p=0.41).

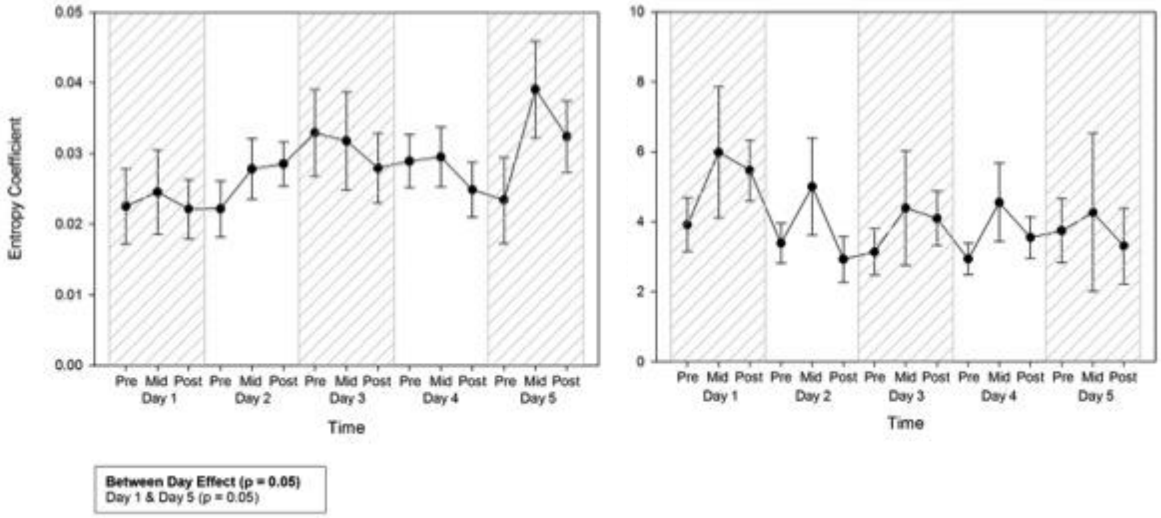


Figure 4.4 Test Contraction Force Variability Within (Pre-, Mid-, Post- Shift) and Between (Days 1 – 5) Workdays. Entropy (left) and coefficient of variation (right).

5.3 Physiological & Postural Tremor

Hand tremor amplitude generally increased over the workday and over the workweek (Figure 4.5). Specifically, there was a significant between day effect ($p = 0.019$), with significant differences between days 1 ($\bar{x}$ = 3.802 mV, SEM = 0.409) and 3 ($\bar{x}$ = 5.578 mV, SEM = 0.613), $p = 0.042$; and between days 1 and 4 ($\bar{x}$ = 5.791 mV, SEM = 0.572), $p = 0.0008$. Postural tremor of the fingers, however, did not appear to significantly change during the workday and during the workweek (Figure 9). On the other hand, an increase in amplitude of shoulder postural tremor (Figure 9) was observed over the workweek ($p = 0.0015$). Day 1 ($\bar{x}$ = 0.00342 mV, SEM = 0.00026) and day 4 ($\bar{x}$ = 0.00509 mV, SEM = 0.00050) were significantly different ($p = 0.002$) as well as day 1 and day 5 ($\bar{x}$ = 0.00435, SEM = 0.00031), $p = 0.035$.

5.4 Perceived Discomfort

Using Borg's CR-10 scale, participants rated their perceived discomfort of their dominant hand/arm and shoulder (Figure 4.6). Typically, hand/arm discomfort increased as the workday progressed. This was confirmed by a statistically significant time of day effect ($p = 0.022$) with post-hoc tests revealing a significant difference between pre- shift ($\bar{x}$ = 1.803, SEM = 0.392) and post- shift ratings ($\bar{x}$ = 3.045, SEM = 0.432), $p = 0.017$. Additionally, there was a day*time interaction ($p = 0.038$). Finally, trends indicate higher ratings of shoulder discomfort from pre-shift, mid- shift, and post- shift. However, these trends were not statistically significant.

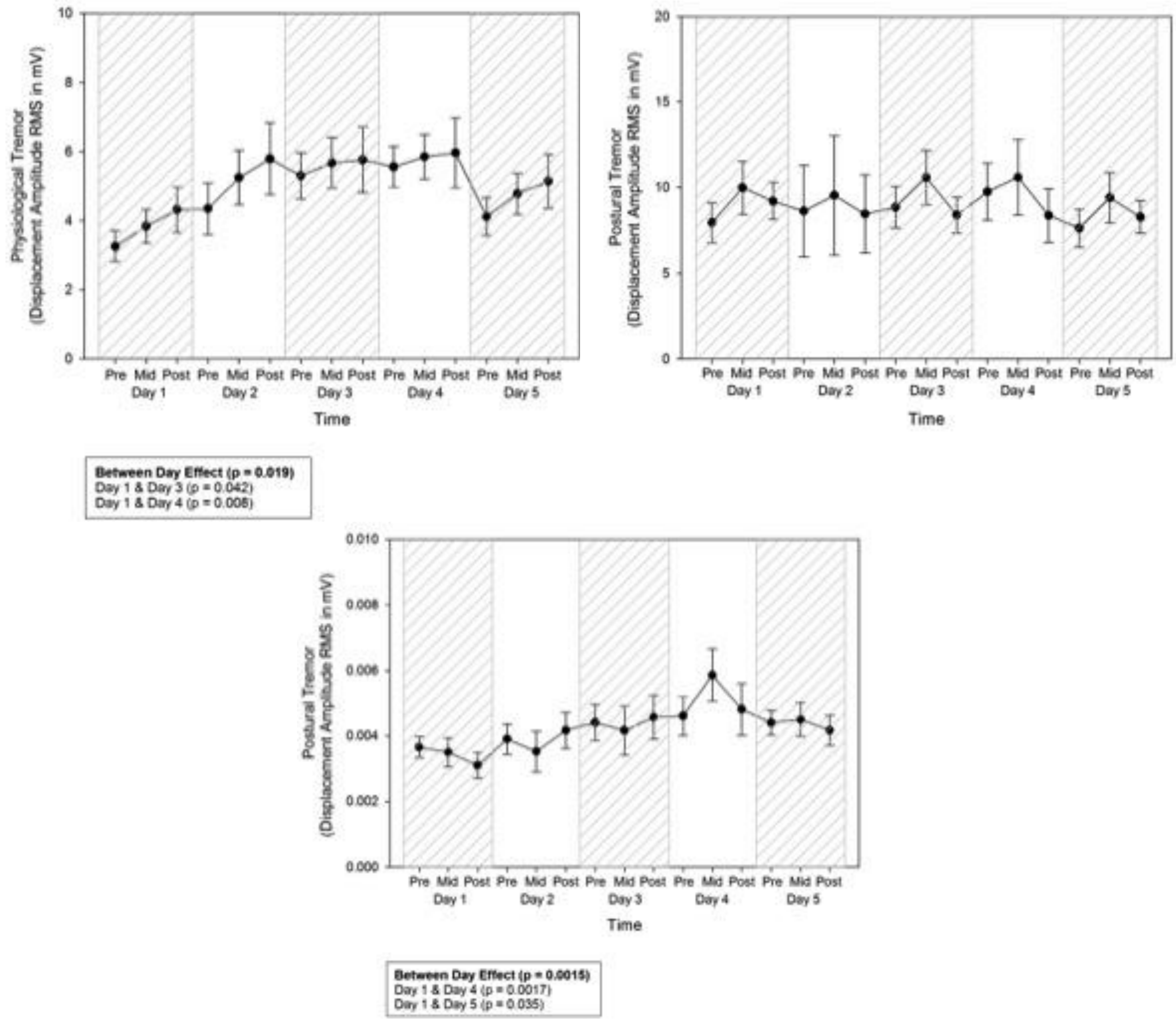


Figure 4.5 Physiological hand tremor (top left), postural tremor of fingers (top right), and shoulder postural tremor (bottom).

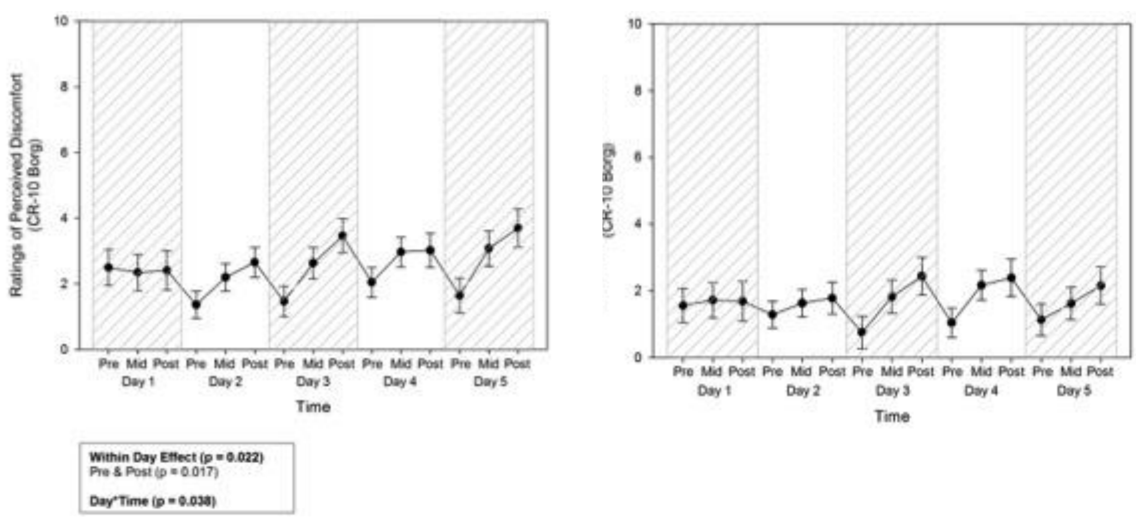


Figure 4.6 Ratings of perceived discomfort within (pre-, mid- post-shift) and between workdays (days 1-5). Ratings of the dominant hand/arm (left) and shoulder (right).

6. Discussion

Documenting fatigue in physically demanding work – residential plumbing – led to the following general observations: increasing fatigue over a workday, cumulative fatigue over multiple consecutive workdays, and preliminary evidence of insufficient recovery after a weekend break. These observations were based on a number of fatigue measures that may reflect changes in central factors, peripheral processes, or a combination of both.

6.1 Grip Strength

Maximum voluntary contractions are traditionally cited as the most direct assessment of fatigue under proper test positions and with verbal encouragement (Vøllestad 1997). In this study, precautions were employed to satisfy these requirements. Additionally, participants performed their maximum handgrip contractions under the guise of a competition between colleagues, thereby eliciting a centrally motivated response. We found a between-day effect, notably decreasing grip force from Tuesday (Day 1) to Friday (Day 4). Grip strength on the workday after a weekend break (i.e., Monday) were higher than the previous Friday, however strength remained below the force levels observed on day 1. We also found a within-day effect, with differences between pre-shift and mid-shift as well as mid-shift and post-shift grip force values.

An interesting pattern was observed, with forces typically peaking mid-shift and no significant differences between pre- and post- shift measures. Chang and colleagues (2009) observed, among electrician-plumbers working on high-elevation construction sites, higher grip force after the work shift compared to measurements taken before. The authors noted that motivation may have been a factor, but this was a clear trend within 5 different trade groups in 302 workers who perceived whole body tiredness at the end of work. To explain this unique grip strength pattern, it has been proposed that grip strength, as a function of time, may demonstrate a circadian rhythm with a minimum near waking hours, peaking in the early evening (Jasper et al. 2009). Alternatively, lowered grip strength at the beginning of work may be the result of sleep inertia phenomenon. Sleep inertia is observed for more than 2 hours after awakening, which may be due to a decline in cerebral metabolism resulting from thermal down-regulation during sleep (Jewett et al. 1999).

6.2 Force Variability

Force variability is a reflection of underlying neurophysiological mechanisms, including the adaptation between force output and sensory input (Sosnoff et al. 2006). This might also involve a reduction in corticomuscular coupling (Yang et al. 2009) and discharge rate variability of motor units (Moritz et al. 2005). Previous reports (e.g., Contessa et al. 2009; Svendsen and Madeleine 2010) have shown increasing force variability with fatigue. Svendsen and Madeleine (2010) found statistically significant increases in coefficient of variation with endurance time, measured continuously, in a sustained isometric contraction (i.e., isometric elbow flexion at 20% MVC until task failure). This study, however, did not observe this trend or any statistical significant contrasts in coefficient of variation measures.

Sample entropy measures also did not demonstrate any predictable changes over time. No clear trends were observed over consecutive workdays, but there appeared to be a significant increase following a weekend break when compared to day 1. The observed increase in force variability on Monday and the lack of predictable changes in both CV and sample entropy, however, may not be attributed to compensatory mechanisms or changes in task demands, but may reflect a lack of sensitivity to fatigue captured by discrete test contractions and by sample entropy methods. Evidently the size and structure of force variability may be dependent on the type (e.g., discrete vs. continuous) and magnitude of contraction (Sosnoff et al. 2006; Svendsen and Madeleine 2010). Although earlier reports have shown increasing coefficient of variation with fatigue (e.g., Svendsen and Madeleine 2010), this was observed *during* a fatiguing sustained isometric contraction. During a test contraction and/or with sample entropy methods, available evidence has indicated that force variability does not consistently change with increasing fatigue (e.g., Søgaard et al. 2003; Svendsen and Madeleine 2010).

6.3 Physiological & Postural Tremor

Physiological tremor's dominant power lies predominantly in the range of 7 and 12 Hz. It is an involuntary, rhythmic, and periodic mechanical oscillation. In contrast, postural tremor is a sub-category that occurs when there is voluntary muscle activity to maintain a particular posture held against gravity (Rehman 2000); simply it is the "positional wobble" (Lakie 2010). There is, however, some conflicting evidence to the possible aetiology of both physiological and postural tremor (Duval et al. 2001; Galinsky et al. 1990; Hallett 1998). On one hand, tremors may be governed by central drive originating from hypothesized oscillators within the CNS. For instance, McAuley and colleagues (1997) observed multiple peak oscillations in EMG, muscle vibration, and tremor recordings. These identical oscillations may reflect synchronization of motor units at frequencies determined within the central nervous system. On the other hand, peripheral mechanisms may best explain tremor, including filter properties of muscle, inherent characteristics of motor unit activity, and mechanical resonance of the limb (Raethjen et al. 2000). Quite possibly both central and peripheral mechanisms may contribute to tremor, to a certain degree (Lakie 2010).

Both hand physiological tremor and shoulder postural tremor increased over the workweek, with statistically significant differences between Tuesday and Friday. Hand tremor also demonstrated a significant between-day effect on days 1 and 3 while an elevated shoulder postural tremor was observed on the following Monday after a weekend break. Previous studies (e.g., Galinsky et al. 1990; Slack et al. 2009; Rehman 2000) have shown enhanced physiological tremor, particularly an increase in amplitude, during physical and mental exertions. These observed changes in tremor amplitude may be explained by its inverse relationship with interstitial K^+ concentration. A high concentration of K^+ has a blocking effect on T-tubules, which may disrupt transmission of action potentials. Therefore, during localized exercise, an initial increase, as a result of limb ischaemia, followed by a decrease in interstitial K^+, due to blood perfusion, will promote a decrease and subsequent increase in tremor size (Lakie et al. 2004). Increased tremor has also been observed after physically intensive work, over hours and even days (Lippold 1981). This long-lasting tremor effect may be due to central nervous mechanisms and some degree of persistence of increased synchronization of motor units (Lippold 1981).

Postural tremor of the fingers did not change over a work shift or during consecutive workdays. Although extrinsic hand muscles may experience loading during tripod grasps (Dong et al. 2005; de Almeida et al. 2013), the grip requires high activity in the intrinsic muscles of the hand (Ziviani 1983). A power grip, conversely, may not elicit much activity from intrinsic muscles of the hand. For instance, Greig and Wells (2008) found minimal activity from the first dorsal interosseous muscle across multiple exertions during a lateral pinch, and in particular, a power grip. Physically intensive work, including construction, typically requires bilateral power and lateral pinch hand gripping to accomplish tasks (Lau and Ip 2006). Quite possibly, intrinsic muscles of the fingers were not fully engaged during construction tasks and did not provoke fatigue-related responses including enhanced tremor.

6.4 Perceived Discomfort

Borg CR-10 ratings for the dominant hand/arm and shoulder ranged from 1 (very weak) to 4 (somewhat strong) in perceived discomfort of the hand/arm. These values were slightly lower than those observed by Rose (2007) who identified ratings between 3 (moderate) and 7 (very strong) in plumbers assembling pipes while working off a ladder. Shoulder discomfort ratings ranged between 0.5 (just noticeable) and 3, which were also lower than ratings observed by Rose (2007). In Rose's (2007) study, plumbers rated their shoulder discomfort between 1 (very weak) and 5 (strong). Lower ratings observed in this study might be due to different pipe assembly tools and the varied tasks represented in the discomfort ratings. For instance, a typical PEX ½ inch manual crimping tool is approximately 0.6 kg, whereas Rose's (2007) study observed plumbers with press jointing machines around 2 kg. Furthermore, in this study, unlike Rose's (2007) study, discomfort ratings reflected the effect of multiple tasks in addition to pipe assembly.

When investigating within and between day effects, hand and arm discomfort increased over the workday, showing a significant increase from pre- to post- shift. There were no differences between consecutive workdays but there appeared to be a day and time interaction. Shoulder discomfort increased but was not statistically different within the day or between days. Previous studies have documented perceived discomfort symptoms over a workday (e.g., Sato & Coury, 2009; Amick et al., 2003). By way of illustration, Sato and Coury (2009) found increasing ratings of perceived exertion (Borg 6-20 numerical-verbal scale) as the day progressed, particularly between pre- and post- shift measures, in a repetitive and physically strenuous manufacturing job. Perceived discomfort, measured with a visual analogue scale, however, typically increased during the work shift but no statistical differences were observed. Amick et al. (2003) investigated the level of pain or discomfort of nine body areas among employees working in sedentary computer-intensive jobs. Discomfort ratings were obtained at the beginning, middle, and end of the workday. Even in sedentary office work, participants experienced a growth of symptoms as the day progressed.

6.5 Trends Within- and Between- Work Days

Not all measures revealed increasing fatigue over the workday or over the workweek. It may be due to the selected fatigue measures reflecting different possible types of fatigue. Therefore, this study reinforces the need of a complementary set of measures, reflecting multiple domains of fatigue to attain a comprehensive picture of fatigue development.

Perceived discomfort ratings indicated increasing fatigue of the distal upper extremity from pre-, to post- shift in physically demanding work. Grip strength measures also indicated significant differences within a work day, notably when comparing peak strength capability at mid-shift with decreased handgrip strength at the end of the workday. Based on the observed responses, central components might be a principle mechanism responsible for neuromuscular fatigue during the workday. Previously, it has been shown that central factors were associated with prolonged submaximal tasks (Gandevia 1998).

Cumulative fatigue over the workweek might reflect both central and peripheral components. Based on grip strength, physiological tremor, and postural tremor measures, fatigue accumulated over the workweek, with large differences between day 1 and day 4. However, measures reflecting central mechanisms, such as self-reported assessment of discomfort, did not significantly increase over the workweek. These results were similar to Persson et al., (2006) who identified no signs of perceived fatigue accumulation from Monday to Thursday among construction workers. Conceivably, low-frequency fatigue, a phenomenon of the peripheral system, may lead to a slow recovery of force production, persisting hours or days. Low frequency fatigue may subsequently affect central drive (Keeton and Binder-Macleod 2006). However, additional studies with electrical stimulation are required to investigate this hypothesis.

Fatigue responses indicated incomplete recovery over consecutive workdays and after a weekend break. However, there are a number of factors to consider when interpreting these findings. First, activities during leisure time were not controlled and could have factored into between-day differences. A growing body of research (e.g., Sonnentag and Zijlstra 2006) has demonstrated that experiences outside work influence performance, feelings, and behaviour at work. Second, there is a prevailing notion that the first day of the working week (i.e., Mondays) is unique. Previous studies have shown a link between Mondays and peak injury rates among several injuries, including construction (Brogmus 2007). Brogmus (2007) postulated that employees might "sleep in" during weekends, therefore adjusting to a later wake time on days off. Mondays require a re-adjustment to earlier wake times, particularly in the construction sector where early morning hours are typical (Brogmus 2007), leading to reduced arousal and alertness. Additionally, as stated earlier, handgrip strength is lowest near waking hours, possibly due to circadian and sleep inertia effects. Mondays might therefore show an exaggerated decrease in grip strength, as observed in this study. Third, due to the non-routine nature of construction, workloads and ergonomic exposures vary between workdays (Paquet et al. 2005). It is possible that a higher workload fell on Monday, leading to increased fatigue response mid- and post- shift. Finally, further studies on the sensitivity and reliability of entropy during test contractions are warranted before we can draw firm conclusions.

6.6 Study Limitations & Strengths

Limitations of the study included the non-cyclic nature of construction work and the un-controlled recovery strategies between workdays and during weekends. Despite its non-routinized nature, certain tasks (i.e., assembling pipe) were regularly performed and are considered to create a high risk in developing WMSDs. We were not able to collect measures on consecutive Mondays due to scheduling challenges; comparison of the measures on consecutive Mondays would allow stronger conclusions to be drawn. Additionally, this study focused on fatigue manifested in the upper extremities, primarily the hand and arm. Although fatigue might occur in multiple body regions, residential plumbing tasks require extensive hand activity, with significant reports of hand discomfort (Bigelow et al. submitted). Finally, the variation in work activities within and between participants would tend to introduce random error into the measures, however many statistically significant effects were noted.

Strengths of the study were: First, construction work consists of many physically demanding jobs, characterized by a number of manual material handling exposures. Cumulative fatigue was documented in real-life work, which includes both scheduled and discretionary breaks and opportunities to vary muscle forces, postures, and work pace. Second, the selected fatigue test battery measures were chosen to reflected both central and peripheral components, and were field-usable, non-invasive, quick, and simple, requiring no more than two minutes to perform. These measures were also linked to human performance outcomes relevant to work quality and productivity (e.g., strength capability and precision). Lastly, this study documented multiple fatigue responses after a weekend break. To the best of the authors' knowledge, cumulative or persistent fatigue effects following two days off work have not been reported previously.

7. Conclusions

This exploratory study demonstrated increasing fatigue of the hand/arm over the day and persistent fatigue from Tuesday to Friday and that a number of measures recorded on Monday, following a weekend break, did not return to baseline values from the preceding week. This research contributes to a small body of literature documenting cumulative neuromuscular fatigue at work; it also provides insight into fatigue measurement at the workplace and supports the need of a test battery of measures reflecting multiple domains, including central and peripheral processes. Despite the potential usefulness of these measures, there remains a need for further studies to examine their utility in assessing fatigue.

Chapter 5

Sensitivity & Reliability of Conventional and Novel Fatigue Measures

Abstract
Fatigue has been linked to production quality and productivity deficits in the short term and work-related musculoskeletal disorders in the long term, and may thus be a useful risk indicator and design and evaluation tool. However, there is limited information on the reliability, sensitivity, and utility of fatigue measures as part of a test battery for field collections. This study reports on an evaluation of 11 measurement tools and their 17 parameters, selected by a group of expert fatigue researchers for their perceived validity and practicality. Eight measures/parameters were found to have test-retest ICC values greater than 0.8. Four measures were particularly responsive to an intermittent fatiguing condition with a mean force amplitude of 30% MVC. Four of five measures demonstrated comparable responses when collected continuously with the fatiguing protocol and intermittently as a test battery. Seven measures/parameters recovered from responses at exercise cessation up to four minutes into recovery. Considering all criteria, action tremor, MMG, and visual analog scale measuring perceived fatigue were found to be most reliable, most responsive, comparable to continuous measures, and sensitive after the fatiguing activity. However, there remains a need to measure responsiveness of these measures under varying exercise protocols to better ascertain measurement sensitivity.

1. Introduction

Fatigue may be a precursor to work-related musculoskeletal disorders and other long-term health outcomes, and may be a relevant biomarker for cumulative exposure to repetitive and/or sustained work (Dennerlein et al., 2003; Nussbaum, 2001; Winkel & Mathiassen, 1994). Additionally, since fatigue might be an intermediary factor between ergonomic risk factors and production quality and productivity, fatigue may be a useful risk indicator and design and evaluation tool. However, in the few studies that have documented fatigue development in realistic work tasks (e.g., Jørgensen et al., 1991; Chang et al., 2009; Persson et al., 2006; Bosch et al., 2007), the selected fatigue measures (e.g., self-reported fatigue, maximum strength capability, electromyography) have lacked discriminatory power to measure fatigue within- and between- workdays.

Using a complementary range of physiological and electrophysiological measurements (e.g., perceived fatigue, maximum strength capability, force variability, physiological and postural tremor), it may be possible to attain a comprehensive picture of fatigue development (Yung et al., 2014). In Yung and colleagues' (2014) study of the upper limbs among plumbers, measures were selected to reflect possible changes, as a result of fatigue, in multiple domains (i.e., central and peripheral), and to reflect human performance outcomes relevant to work quality and productivity (i.e., precision and strength capability). These measures had previously been rated highly by a multidisciplinary group of researchers for their perceived reliability and practicality as a fatigue detection method (Study 1). Indeed over a workday of physically demanding work, measures reflecting central mechanisms were most responsive. Over consecutive workdays, measures reflecting a combination of both central and peripheral-based measures indicated cumulative fatigue effects (Yung et al., 2014). Although the selection of these measures was based on strong theory and on evidence of responsiveness to fatigue, there is a lack of information on the sensitivity and reliability of these measures.

Detecting fatigue in realistic work tasks requires the selection of measures that are field-usable; specifically, measurement methods that are portable, easy to administer, require minimal training, brief, minimally intrusive and encumbering, and robust (Rosa et al., 1985). Additionally, as part of the selection process, measures may be collected continuously during work activity, or as a test battery during discrete time periods. Although continuous measurements might provide information that is representative of the workload, there are advantages with test battery measurements. First, test batteries can be administered during work breaks to avoid disruptions of the work process. Second, brief standardized measures would allow for generalization across different work settings (Rosa et al., 1985). Third, test batteries might act to control factors (i.e., muscle length, movement velocity, and magnitude of exerted force) that might lead to erroneous interpretation of physiological signals (e.g., MMG, EMG, etc.). Despite the numerous advantages of a test battery, there is little information on the representativeness of test battery data when measuring fatigue. More specifically, we ask whether measures collected as a test battery are comparable to responses as a continuous measure, and whether measures are able to detect fatigue responses after the task.

The aim of this study was to: (1) compare the reliability and sensitivity of selected fatigue measures that were identified and rated strongly by a multidisciplinary group of researchers and were shown responsive to physically demanding work; (2) investigate the degree to which test battery measures approximate continuous measures; and (3) examine measurement responsiveness after cessation of activity to ascertain the length of time that measures may be sensitive to fatigue effects.

2. Methods

2.1 Participants

Sixteen healthy university-aged students (8 males, 8 females, mean age=24 years, mean height=171.6 cm, mean weight=70.7 kg) were recruited to participate in this study. Participants had no current or past injuries of their elbows, upper arms, and forearms. Two participants (1 male, 1 female) were left hand dominant. Participants provided informed consent for all experimental procedures and associated risks, as approved by the University of Waterloo Office of Research Ethics, prior to the experimental session.

Participants were seated at a desk facing a computer monitor that displayed visual feedback of handgrip force when performing test contractions and the fatiguing protocol. The chair was adjusted so that participants were seated comfortably when performing test battery measures and the fatiguing protocol. When necessary, participants were asked to rest their elbows and forearms onto the chair's armrest. Test batteries and fatiguing protocol were performed by the participant's dominant hand.

2.2 Test Battery of Fatigue Measures

Fatigue measures were selected due to their responsiveness to physically demanding work (Yung et al., 2014); due to their perceived validity, reliability, and practicality; and due to their relationships to performance, including work productivity and quality (Study 1). Measures shown to be responsive to physically demanding work include maximum voluntary contractions (MVCs), physiological tremor, and postural tremor (Yung et al., 2014). Typical measures from field studies were also included, such as electromyography (EMG) and rating of perceived fatigue using a visual analog scale (VAS). Mechanomyography (MMG) was also selected as a complementary measure of mechanical oscillations to electrical activity measured by EMG (Madeleine et al., 2001). And as a complementary measure to both EMG and MMG, tremor measures during an isometric contraction were also recorded (i.e., action tremor). Measuring action tremor minimizes signal contamination from other sources, as compared to resting tremor, and enables comparisons to EMG and MMG during a clearly defined and measurable muscle activity (McAuley et al., 1997). Finally, psychomotor tests (i.e., fixed pace tapping test) and handwriting analysis were selected for inclusion to the test battery. The fixed pace tapping test provided a measure of sensorimotor synchronization (SMS), and hence sensorimotor coordination and audio-motor coupling (van der Steen & Keller, 2013); whereas handwriting tests might reflect changes in cognitive and motor demands (Longstaff et al., 2003; Jasper et al., 2009).

The test battery of fatigue measures consisted of 11 measurements that were completed successively. A full test battery, with all 11 measurements, required approximately 2 minutes to complete. Measures were performed in the following order:

2.2.1. Visual Analog Scale (VAS) – Perceived Fatigue

Perception of fatigue was obtained using a 10-cm visual analog digital scale. Visual analog scales have been shown to have psychometric validity and reliability and have been widely used to assess anxiety and mood states, pain, and "musculoskeletal" fatigue (Leung et al., 2004). Anchor points represented "no fatigue at all" and "complete exhaustion". Perceived fatigue was expressed as a value between 0 and 100.

2.2.2. Physiological Tremor

Placed on the dorsum of the hand, on the distal part of the third metacarpal bone, a tri-axial ±3 g accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA sensitivity=300 mV/g, noise density=250 µg/rtHz, 4mm x 4mm x 1.45mm) recorded physiological tremor. Participants were instructed to adopt a seated posture, with their dominant elbow and forearm supported on the armrest and their hand fully relaxed for a period of 12 seconds. Additionally, participants were asked to observe the monitor display to avoid looking at the hand due to possible visual-dependent peaks in hand tremor (McAuley et al., 1997). Signals were bandpassed filtered (Butterworth, 2nd Order, 1 and 20 Hz) and analyzed in the time domain. Instantaneous root mean square amplitude was calculated at 1-second windows and averaged for the middle 10-seconds.

2.2.3. Postural Hand Tremor

A ±3 g tri-axial accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA, sensitivity=300 mV/g, noise density=250 µg/rtHz) was mounted onto the distal end of the tapping probe (see psychomotor tapping test). Participants held the probe vertically with a dynamic tripod grasp, and pointed towards a target (a 1 cm diameter hole) positioned on the desk surface at approximately elbow height, with the elbows comfortably supported. Participants inserted the probe into the 1cm diameter hole but hovered above a touch-registering plate for collection duration of 12 seconds. Tremor was bandpassed filtered (Butterworth, 2nd Order) between 1 and 20 Hz. The instantaneous root mean square amplitude was calculated at 1-second windows and averaged for the middle 10-seconds.

2.2.4. 30% Maximum Voluntary Contraction (MVC) Test Contraction

A test contraction at 30% of the participant's maximum handgrip force was performed for 17-seconds. Participants exerted handgrip forces using a handgrip dynamometer (Medical Research Ltd., Leeds, UK) with the assistance of visual feedback (LabView, National Instruments Corporation, Austin, TX). The handgrip dynamometer was mounted vertically on a custom fabricated apparatus (Department of Kinesiology, University of Waterloo), within comfortable reach of the participant. Surface electromyography (EMG), mechanomyography (MMG), action tremor, and force variability were collected during the test contraction.

2.2.4.1 Surface Electromyography

Electromyography was recorded using bipolar surface electrodes (Ag-AgCl electrodes, Ambu Blue Sensor N, Denmark) with an inter-electrode distance of 20 mm, placed on the belly of the extensor carpi radialis (ECR) and flexor carpi radialis (FCR). Both muscle belly sites were marked with an indelible felt tip pen to ensure consistent placement between both days. Hair was removed by razor and skin abraded with ethanol and prepared with NuPrep Gel (Weaver and Company, CO, USA). EMG signals was collected with an eight-channel data system (Bortec, Calgary, AB), a common mode rejection ratio of >115 dB, and a band-pass filter between 10 and 1000 Hz. Signals were amplified and sampled at 2048 Hz. Root mean square amplitude was calculated at 1 second intervals and averaged over the middle 15 seconds.

2.2.4.2. Mechanomyography

A low profile tri-axial ± 3 g accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA; sensitivity=300 mV/g, noise density=250 μg/rtHz, weight = 3 grams) recorded mechanical responses of extensor digitorum (ED) muscle. In accordance with Watakabe et al., (2003), the accelerometer weighed no more than 5 grams to minimize signal distortion based on accelerometer weight. The accelerometer was placed on the muscle belly of the flexor digitorum superficialis (FDS) with double-sided tape, which was marked with an indelible felt tip pen. MMG signals were Butterworth, 2nd order bandpassed filtered between 5 and 100 Hz, and average root mean square amplitude was calculated at 1-second epochs for the middle 15 seconds of data.

2.2.4.3. Action Tremor

The tri-axial accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA) attached on the dorsum of the dominant hand also served to measure action tremor during a handgrip contraction. The accelerometer was placed on the distal part of the third metacarpal bone, mounted with double-sided tape and loosely secured with transpore medical tape. Action tremor signals were bandpassed (Butterworth filter, 2nd order) between 1 and 20 Hz. Amplitude of the signal was calculated as the root mean square (RMS) over the middle 15-seconds of data, and averaged.

2.2.4.4. Force Variation (Coefficient of Variation)

The recorded force signal was analyzed to determine fluctuations, which may be indicative of changes in motor control. Force signal during the test contraction was filtered with a Butterworth 2nd order dual lowpass filter at 10 Hz. The variation of force was determined by calculating coefficient of variation (%) of the test contraction as the average of 1-second epochs of the middle 15-seconds.

2.2.5 Maximum Voluntary Contraction

Participants exerted maximum voluntary handgrip forces with a handgrip dynamometer (Medical Research Ltd., Leeds, UK). With verbal encouragement, participants exerted a ramped maximum contraction for 5 seconds. The middle 3-seconds of the 5 second MVC was windowed and values were averaged.

2.2.6. Psychomotor Sensorimotor Synchronization Test (Fixed Pace Tapping)

A custom fabricated tapping device (Department of Kinesiology, University of Waterloo) consisting of a pointer/probe, a metal template, and a metal plate, provided a measure of sensorimotor synchronization (SMS), and hence sensorimotor coordination and audio-motor coupling (van der Steen & Keller, 2013). The finger-tapping task has been shown to provide an index of fatigue (Wells, 1908), and as a variant, this arrangement also provided a measure of precision. The template consisted of 9, 1-cm holes oriented in a circle and overlaid onto a metal plate. Since all components were connected to the same power source, if the probe touched either template or metal plate, a closed electric circuit was formed, and touches were registered (frequency and duration). Touches on the template were considered an error and touches on the underlying metal plate were successes. Participants performed the fixed-paced tapping test at 90 beats per minute for 17 taps, in a clockwise direction, a comfortable pace determined by pilot studies. This tapping rate falls within the upper inter-onset interval (IOI) limit of 1.8 seconds (i.e., 108 beats per minute) for sensorimotor synchronization, i.e., referential behavior involving temporal coordination of motor rhythm with an external rhythm (Repp, 2005). Additionally, this frequency closely approximates the average spontaneous motor tempo (SMT) or self selected personal tempo, which has a period of 600 msec (Fraisse, 1982). The test required approximately 30 seconds to complete.

2.2.7 Handwriting Tests

Handwriting involves a complex interaction between several cognitive and motor processes, including syntactical, semantic, and lexical processing. It is a highly automated, over-learned sensorimotor skill, typically performed on a daily basis (Jasper et al., 2009). Handwriting can be analyzed for its kinematics, smoothness, and variability of consecutive movements, reflecting changes in cognitive and motor demands (Longstaff et al., 2003; Jasper et al., 2009). Participants drew on a digitized tablet (Bamboo CTH 470, Wacom Co., Ltd., Japan), which measured participants' handwriting kinematics as they traced a stereotyped movement pattern (e.g., circle). Circles or spirals are well-learned tasks, reducing variability due to motor learning (Longstaff et al., 2003), rendering any differences due to changes in motor control. Participants traced a 3-cm diameter concentric circle, five times consecutively, as fast and as accurately as possible in a clockwise direction. Handwriting data was analyzed with commercially available MovAlyzeR handwriting software (Version 6.1, NeuroScript, Tempe, AZ). The following parameters were then calculated for each trial: absolute peak vertical velocity (APVV), straightness error, average absolute velocity (AAV), average normalized y jerk per trial (YJerk), average normalized jerk per trial (Jerk), and average pen pressure. Handwriting tests were recorded for 20 seconds.

2.3 Feedback System

Participants performed test contractions and the fatiguing protocol using force control with the assistance of a visual feedback system (LabView, National Instruments Corporation, Austin, TX). Visual feedback has been shown to be comparable to proprioceptive feedback (i.e., position control) in long-term response (Søgaard et al., 2003). However, visual feedback may involve a complex control loop, which may increase the amount of variation in motor unit recruitment pattern (Søgaard et al., 2003). Auditory feedback was provided to indicate timing for contraction and relaxation periods during the fatiguing protocol (i.e., a two-tone beep, one indicating contraction and the other for relaxation).

2.4 Protocol

Participants arrived to the laboratory on two separate days. Prior to all experimental days, participants were given ample time to familiarize themselves with the test battery.

Reliability assessments of the fatigue measures were conducted on day 1. Participants performed three maximum voluntary contractions, using a power handgrip, with 2 minutes of rest between contractions. The middle 3-seconds of the 5-second contraction was averaged and the highest force value was used to determine the absolute magnitude of the 30% MVC test contraction. Averaged biophysical data collected during the maximum voluntary contraction served to normalize EMG, MMG, and active tremor signals. After time to practice the test battery, participants were asked to perform a test battery at 5-minute intervals for 60 minutes. Therefore, with a baseline measure at time 0, a total of 13 trials were collected. However, the last 12 trials were analyzed to avoid potential learning effects. During the 5-minute rest period, participants viewed standardized video programming to mitigate boredom and cognitive fatigue effects. A 5-minute interval period was selected, which is beyond 3-minute resting times suggested by Lim and Kong (2014) to minimize consequences of fatigue in consecutive trials of maximum grip contractions. Therefore, 5-minutes may be sufficient to ensure minimal fatigue between trials.

The second day was dedicated to evaluating the sensitivity of fatigue measures. Test batteries were collected at 1-minute intervals during a fatiguing intermittent handgrip exercise. The fatiguing exercise consisted of a mean force of 30% MVC, a duty cycle of 50%, and a cycle time of 6 seconds. These work variables are in the same order of magnitude as previous studies, both in terms of cycle time and duty cycle (Yung et al., 2012), and is within the force magnitude relevant to fatigue effects (Westgaard & Winkel, 1996). Additionally, the mean magnitude of force (30% MVC) was higher than mean handgrip force levels during intermittent contractions evaluated by Byström & Fransson-Hall (1994), who found that an intensity of 17% MVC increased anaerobic metabolism, systemic effects (i.e., heart rate and blood pressure), ratings of perceived exertion, and a loss in functional capacity. The selection of 30% MVC ensured the manifestation of fatigue when evaluating the sensitivity of the selected fatigue measures.

Forces, electromyography, and action tremor were measured continuously during the fatiguing protocol and were compared to test battery measures. Participants performed the intermittent fatiguing protocol until volitional fatigue or until an observable degradation of performance, i.e., 50% decrease of force output during fatiguing protocol over consecutive contractions and reduction of MVC to less than 60% MVC.

2.5 Statistical Analysis

Two way random effects model intraclass correlation coefficient [ICC(2,1)] analysis were performed to measure the degree of consistency for each measure (IBM Corp., IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY). Single measure ICC values were recorded, which reflects the reliability of an individual measure rather than the mean of values. Complete agreement between trials was indicated by an ICC score of 1, whereas no agreement is denoted by a score of 0. Generally, for interpretation, an ICC score less than 0.20 indicates poor agreement, between 0.21 and 0.40 indicates fair agreement, between 0.41 and 0.60 reflects moderate agreement, between 0.61 and 0.80 reflects strong agreement, and scores greater than 0.80 indicates almost perfect agreement (Bain et al., 1993).

To evaluate sensitivity, test battery measures, at 1-minute intervals during the fatiguing protocol, were plotted over time, normalized, and fitted with a logarithmic regression function [$y = a + b \text{ Log } (x)$]. This was similar to Yung et al., (2012) who found that non-linear regression achieved on average the highest coefficient of determination across all measures. For reference, when slopes were greater than 0, an increase by a multiplicative factor in x is associated with an estimated increase of b Log (x) units in the mean of y. The slopes (b) from the logarithmic function were then used as the dependent measure in a mixed-model analysis to compare battery measures during the fatiguing protocol. To ensure equitable comparisons, the magnitudes of slopes were compared to account for opposing direction of response, expected during fatigue (e.g., increases in EMG RMS vs. decreases in MVC output). Tukey post-hoc tests determined any statistical differences between measures if a significant main effect was identified.

A mixed-model repeated measures analysis compared non-normalized measurement values at baseline, at cessation, and during 15 minutes recovery: every minute for the first 5 minutes and every 2 minutes for the remaining 10 minutes. Since visual analog scale data was obtained as continuous intervals, perceived fatigue was analyzed with parametric statistical analysis. Continuous measurements during the fatiguing protocol were plotted over time, normalized, and fitted with logarithmic regression. Paired samples t-tests allowed for comparisons between continuous and test battery rate of responses for EMG, MMG, force variation, and action tremor. All statistical analyses, unless otherwise stated, was performed using Statistical Analysis Software (Version 9.3, SAS Institute Inc., Cary, NC, USA) at an alpha level of 0.05.

3. Results

3.1 Test-Retest Reliability

Mean intraclass correlation coefficient scores for test battery measures (Figure 5.1) ranged between 0.184 (poor agreement) and 0.984 (almost perfect agreement). Straightness error (i.e., normalized standard deviation from a straight line) during handwriting achieved the highest ICC score. The lowest ICC score was found with the tapping test frequency rate. Remaining handwriting parameters demonstrated strong to almost perfect agreement: absolute peak vertical velocity (ICC = 0.920), average absolute velocity (ICC = 0.927), normalized Y jerk (ICC = 0.836), normalized jerk (ICC = 0.848) and pen pressure (ICC = 0.776). Almost perfect agreement was also observed in action tremor (ICC = 0.834), MMG amplitude (ICC = 0.825), and perceived fatigue (ICC = 0.808). Strong agreement was found with maximum voluntary contraction (ICC = 0.666) and EMG amplitude measures for both FCR (ICC = 0.768) and ECR (ICC = 0.734). Postural tremor (ICC = 0.587) and force variation (ICC = 0.412) led to moderate agreement, whereas physiological tremor (ICC = 0.302) and number of errors during the tapping test (ICC = 0.338) indicated fair agreement.

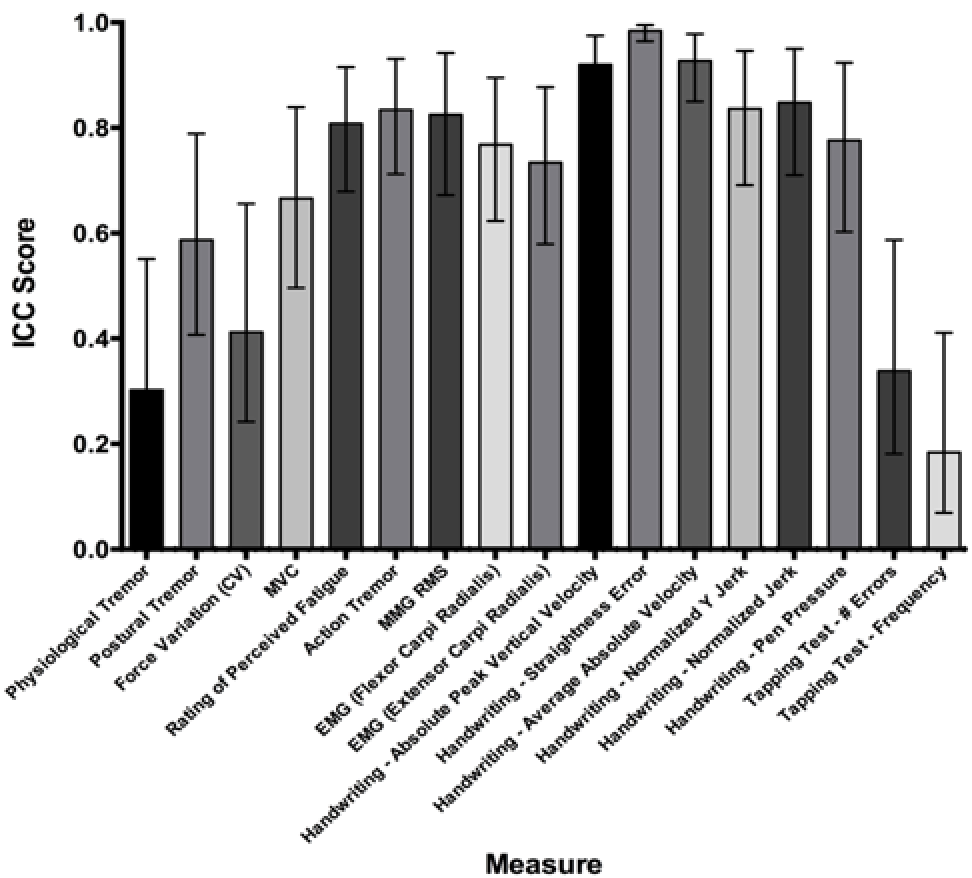


Figure 5.1 Test-Retest Reliability of Test Battery Measures

3.2 Sensitivity

The mean endurance time to complete the fatiguing task was 15.31 minutes. For the 17 detection methods and measurement parameters (Figure 5.2), the mean rate of response ranged from 0.0145 normalized units/Δtime (handwriting normalized jerk) to 1.459 normalized units/Δtime (action tremor).

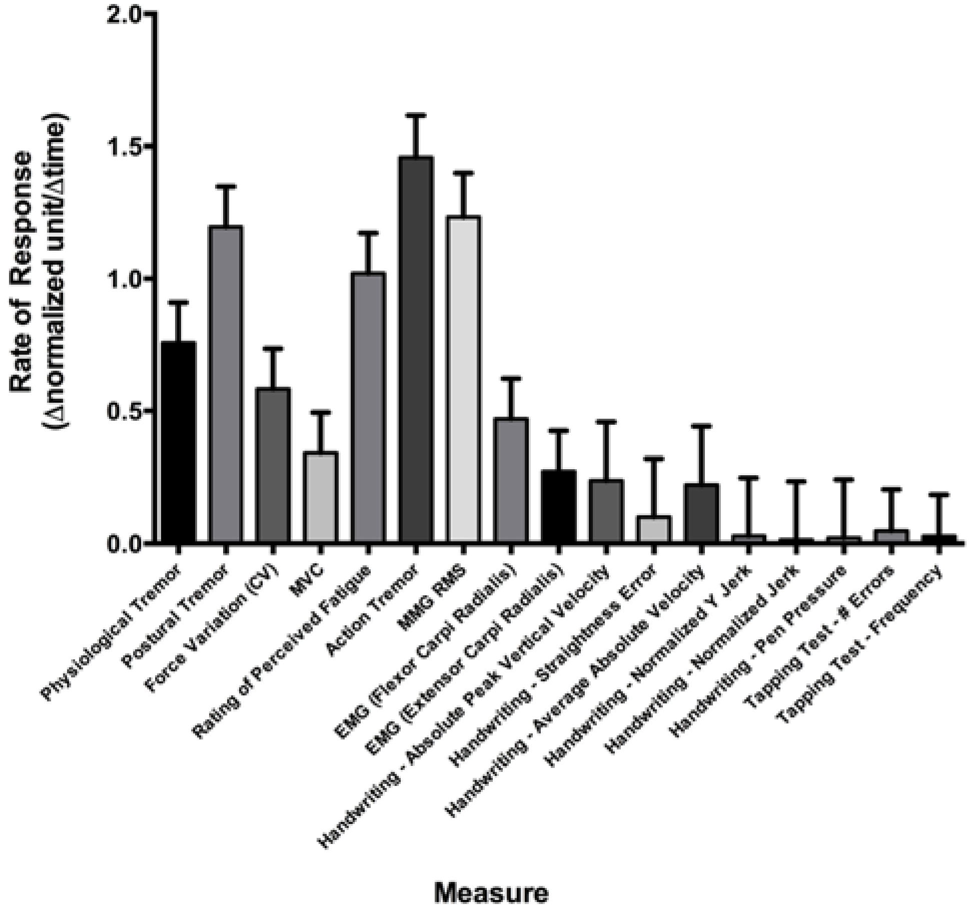


Figure 5.2 Responsiveness of Test Battery Measures

Action tremor was statistically different from physiological tremor ($\bar{x}$ = 0.7575*[1], p = 0.0038), force variability ($\bar{x}$ = 0.5826*, p = 0.001), MVC ($\bar{x}$ = 0.3414*, p = 0.001), EMG amplitudes – FCR ($\bar{x}$ = 0.4698*, p = 0.001) and ECR ($\bar{x}$ = 0.2726*, p = 0.001), handwriting parameters – APVV ($\bar{x}$ = 0.2378*, p = 0.001), straightness error ($\bar{x}$ = 0.1003*, p = 0.001), YJerk ($\bar{x}$ = 0.02832*, p = 0.001), Jerk (p = 0.001), and pen pressure ($\bar{x}$ = 0.0217*, p = 0.001), and number of errors ($\bar{x}$ = 0.0478*, p = 0.001) and frequency ($\bar{x}$ = 0.0277*, p = 0.001) during the tapping test. We also observed multiple significant effects with MMG RMS amplitude ($\bar{x}$ = 1.233*) and MVC (p = 0.002), EMG amplitudes (FCR: p = 0.022, ECR: p = 0.001), APVV (p = 0.015), AVV (p = 0.012), straightness error (p = 0.002), YJerk (p = 0.001), Jerk (p = 0.001), # of errors (p = 0.001), and tapping frequency (p = 0.001). Similarly, postural tremor ($\bar{x}$ = 1.196*) led to a quicker rate of response than MVC (p = 0.002), EMG FCR (p = 0.019), EMG ECR (p = 0.001), handwriting

[1] normalized units/Δtime

parameters (APVV: p = 0.016; Straightness Error: p = 0.002; AVV: p = 0.013; YJerk: p = 0.001; Jerk: p = 0.001; Pen Pressure: p = 0.001), and tapping tests (# errors: p = 0.001; frequency: p = 0.001). The rate of response for perceived fatigue ($\bar{x}$ = 1.020*) was statistically quicker than MVC (p = 0.045), EMG ECR (p = 0.014), straightness error (p = 0.027), YJerk (p = 0.004), Jerk (p = 0.005), pen pressure (p = 0.009), tapping errors (p = 0.001), and tapping frequency (p = 0.001). Model fits (r^2) ranged between 0.174 and 0.875.

3.3 Measurement Latency

Seven measures demonstrated significant differences between baseline and cessation (Figures 5.3 to 5.6 – for graphical purposes, figures indicate normalized values from baseline). MMG amplitude recovered to values closer to baseline within 1 minute of recovery (p = 0.7397 at 1 minute). All tremor-based measurements were significantly different from baseline within 3 minutes of recovery. Interestingly, handwriting pen pressure revealed significant differences between baseline and recovery 2-3 minutes after cessation of activity (Recovery 2: p = 0.0504; Recovery 3: p = 0.0039). Perceived fatigue, MVC, MMG amplitude, and physiological, postural, and action tremors led to significant differences between cessation and recovery, upwards of 15 minutes. Action tremor, however, did not demonstrate significant differences between cessation and the first minute of recovery (p = 0.7229). Generally, with the exception of pen pressure, handwriting parameters and tapping test measures did not exhibit significant differences between baseline, cessation, and recovery.

3.4 Test Battery vs. Continuous Measurement

Generally, trends indicate quicker rate of responses when measured continuously than as a test battery with accelerometer-based measurements (i.e. tremor and MMG). On the other hand, trends in force fluctuations based on coefficient of variation and EMG amplitudes were found to have a quicker rate of response when measured as a test battery (Figure 5.7). There were no significant differences between rate of response of action tremor simultaneous with the fatiguing protocol ($\bar{x}$ = 2.5865*, σ = 3.5006) and as a test battery at 1-minute intervals ($\bar{x}$ = 1.459*, σ = 1.2355), p = 0.2885. Similarly, no significant differences were found between force fluctuation

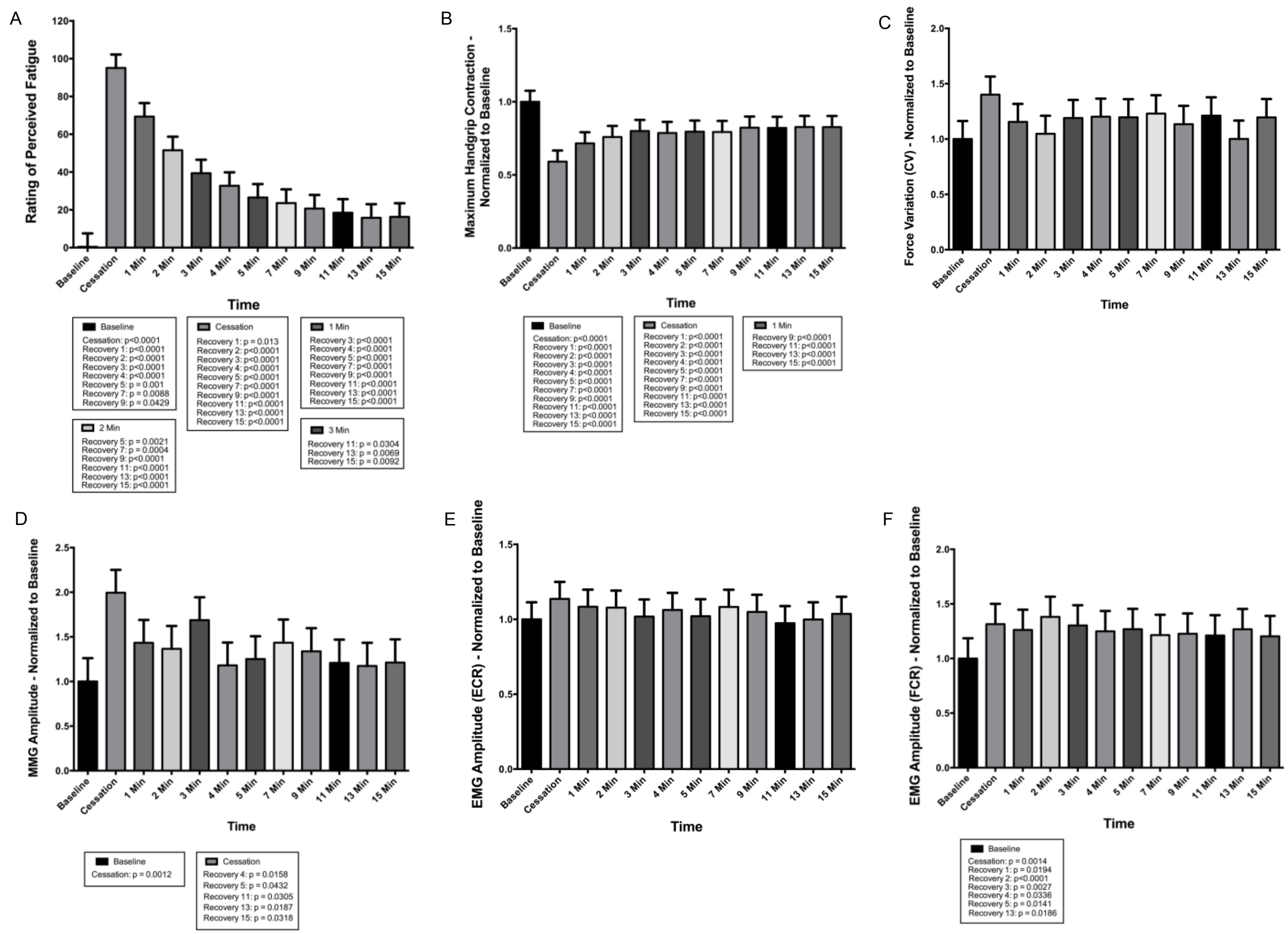


Figure 5.3 Measurement responses at baseline, cessation, and during recovery.

(A) Ratings of perceived fatigue, (B) Maximum voluntary contraction, (C) Force variation, (D) MMG amplitude, (E) EMG amplitude of extensor carpi radialis and (F) flexor carpi radialis

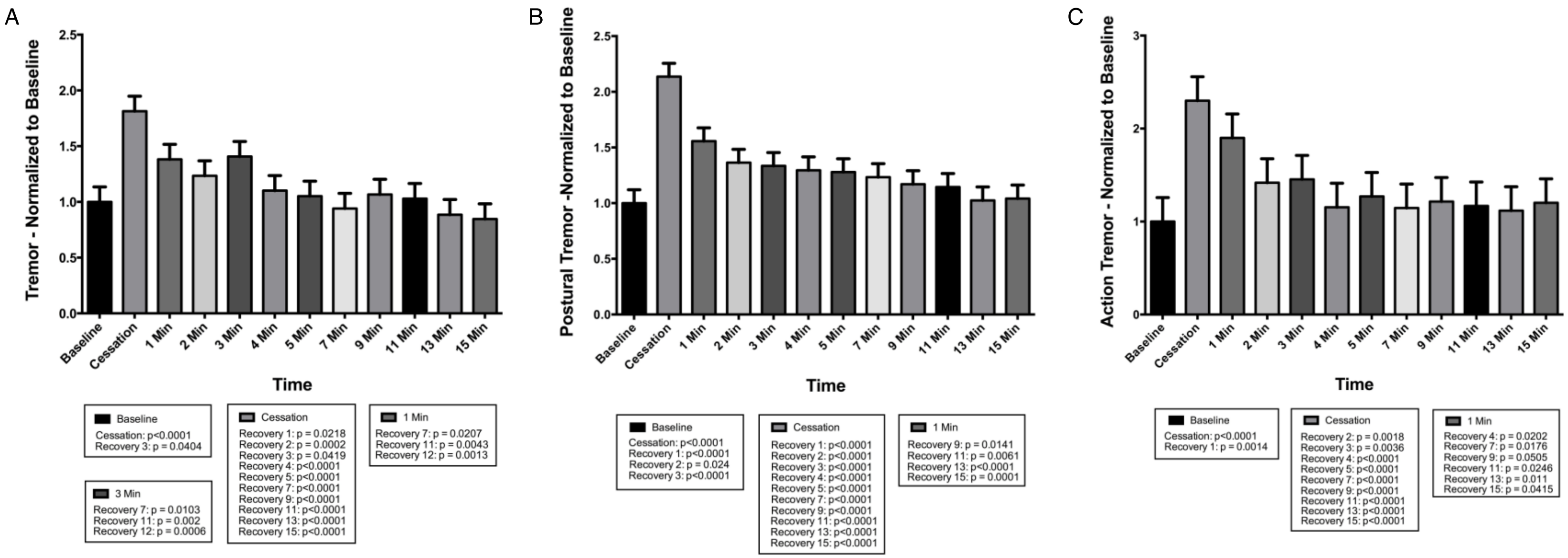


Figure 5.4 Tremor-based measures at baseline, cessation, and during recovery.

(A) Physiological tremor, (B) Postural tremor, (C) Action tremor during an isometric handgrip test contraction at 30% MVC

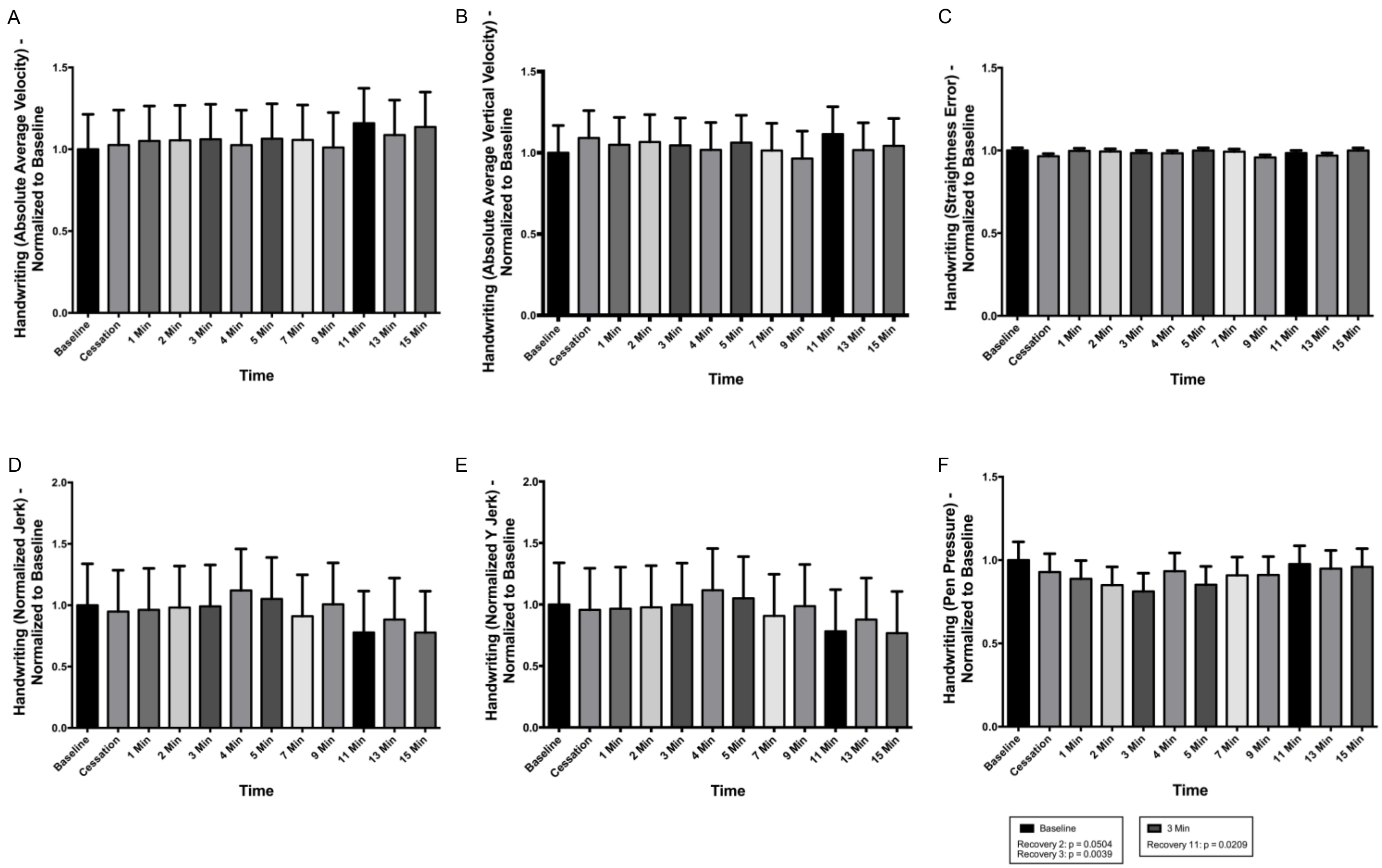


Figure 5.5 Handwriting kinematic and kinetic characteristics at baseline, cessation, and recovery.

(A) Absolute average velocity, (B) Absolute average vertical velocity, (C) Straightness error, (D) Normalized jerk, (E) Normalized jerk in the y-direction, and (F) Pen pressure

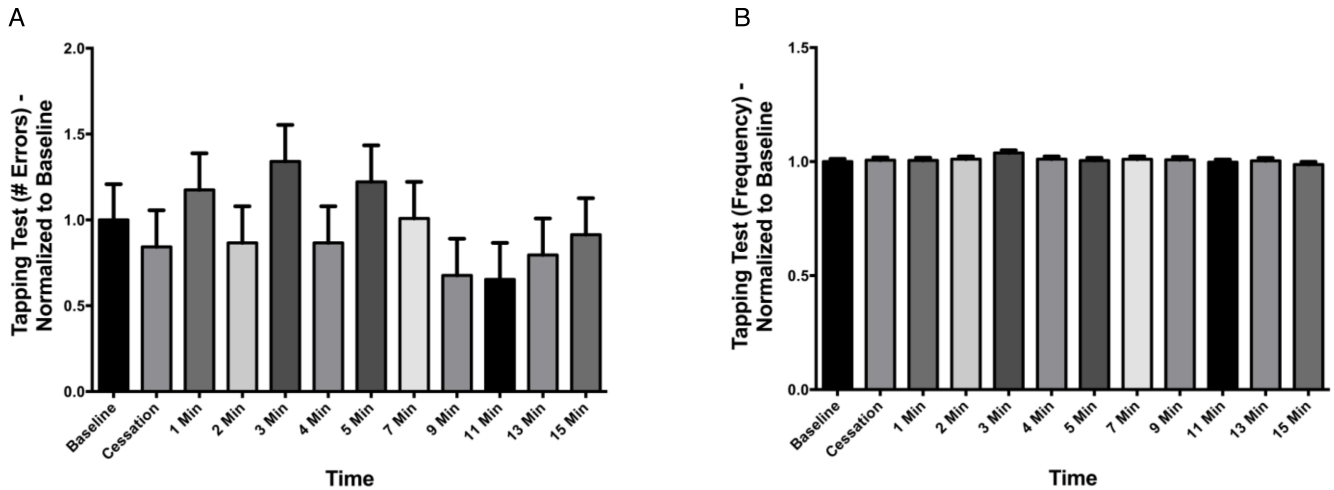


Figure 5.6 Tapping test number of errors and frequency at baseline, cessation, and during recovery.

(A) Number of errors and (B) Frequency.

measured during a test contraction ($\bar{x}$ = 0.5826*, σ = 0.5603) and during the fatiguing protocol ($\bar{x}$ = 0.4569*, σ = 0.4632), p = 0.4359. Differences between MMG amplitude during the fatiguing protocol ($\bar{x}$ = 2.5996*, σ = 3.5278) and as a test battery ($\bar{x}$ = 1.233 *, σ = 1.1662) did not lead to but approach statistical significance (p = 0.085). EMG amplitudes, however, demonstrated a degree of statistical difference between continuous and test battery measures. Although ECR during test battery ($\bar{x}$ = 0.2726*, SD = 0.3924) and continuously ($\bar{x}$ = 0.0896*, σ = 0.2203) were not statistically different (p = 0.055), EMG of the FCR led to differences between test battery ($\bar{x}$ = 0.4698*, σ = 0.4589) and muscle activity taken continuously ($\bar{x}$ = 0.1726*, σ = 0.2269), p = 0.007.

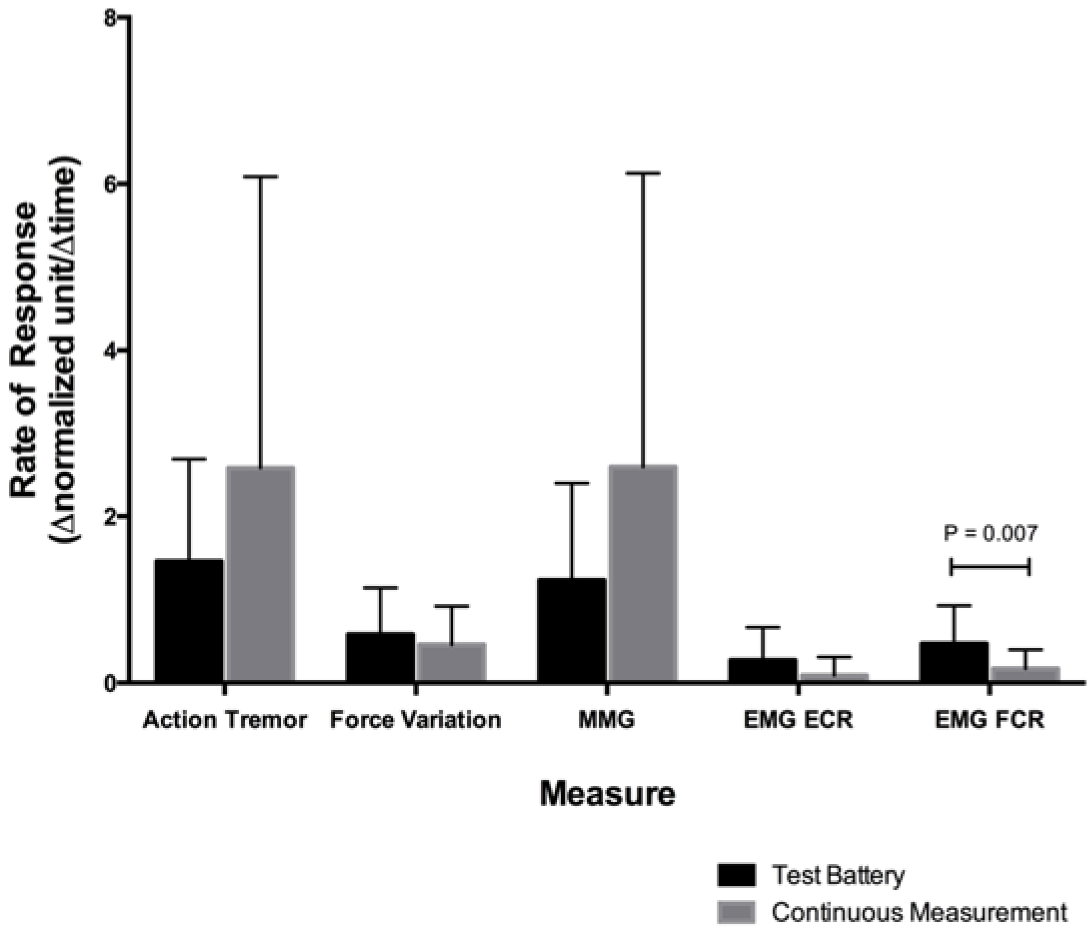


Figure 5.7 Comparing Test Battery and Continuous Measurements

Data plotted over time in both test battery and continuous measurements were normalized and fitted with logarithmic regression. Paired samples t-test between test battery and continuous measurement demonstrated significant effect in EMG of the flexor carpi radialis.

4. Discussion

4.1 Test-Retest Reliability

Handwriting parameters were highly repeatable, displaying almost perfect agreement between 13 consecutive trials. Handwriting, including its execution, has been shown to be reliable, such as consistent peak grip forces of the thumb, index, and middle fingers in the selected writing grasp (Hsu et al., 2013). The results from this study lend support that drawing circles and spirals are well-learned tasks and can be performed with a high degree of accuracy by healthy individuals who have no motor dysfunctions (Longstaff et al., 2003). Straightness error, in particular, was highly reliable. Interestingly, the repeatability of test-retest trials based on pen pressure was observed to achieve strong agreement (ICC = 0.776) but was lower than pen tip forces (ICC = 0.98) previously found by Hsu and colleagues (2013). In that study, a force transducer recorded axial force from the pen tip. Mergl et al., (1999) recorded kinematic parameters in a single test-retest situation for a series of handwriting tasks, including concentric circles as fast as possible for 30 seconds. The authors, who measured reliability twice with a 1-week interval, found Pearson's correlation values of r = 0.587 for mean peak velocity and r = 0.676 for mean number of changes of direction of velocity. The higher agreement found in this study might be due to measuring reliability over successive trials, the use of intraclass correlations, and minimization of potential diurnal effects.

Tremor-based measurements were variable; action tremor and MMG amplitude demonstrated almost perfect agreement, postural tremor displayed moderate agreement, and physiological tremor indicated fair agreement. Louis et al., (2000) measured postural tremor over four test-retest repetitions with a similar test arrangement to this study. A Pearson's correlation between r = 0.82 and 0.94 (high agreement) was observed for the steadiness test with a 0.312 inch hole, which was inconsistent with this study's ICC coefficient of 0.587 (moderate agreement). The difference in agreement might be due to methods in which postural tremor was attained. Louis and colleagues (2000) measured tremor from the number of contacts between the stylus and the wall of the metal hole, whereas postural tremor was assessed in this study by accelerometry on the distal end of the stylus. The methods employed in this study may be more sensitive to changes in postural tremor, trial to trial. Similarly, in another study, Letz and Gerr (2000) found average postural hand tremor in both left and right hands to be highly reliable (ICC >0.80), particularly based on its amplitude (i.e., RMS acceleration). In that study, participants were asked to hold a 2-axis accelerometer mounted in a stylus, positioned in front of their navel while seated. Test-retest reliability was estimated with Pearson product moment correlation for 2 trials with each hand. The current study, on the other hand, estimated reliability over multiple trials. MMG reliability has been previously assessed by Al-Zahrani and colleagues (2009) who found ICC values between 0.84 and 0.96 for root mean square amplitude at 75% MVC for 40 seconds, with 5 minutes of rest in between. These values were comparable to the ICC value (ICC = 0.825) observed in this study.

Studies have assessed reliability of EMG parameters for muscles of the lower back (e.g., Peach et al., 1998), the lower extremities (e.g., Kellis & Katis, 2008), neck and shoulder (e.g., Jensen et al., 1996), and distal upper extremity (e.g., Oskouei et al., 2013). Oskouei and colleagues (2013) measured both intra- and inter-day reliability for select forearm muscles at various contraction levels of maximum voluntary grip force. A comparable force of 20% MVC led to a single measure ICC(2,1) value of 0.716 for flexor carpi radialis, which approximates the reliability observed in this study (ICC = 0.768). Although extensors were excluded from Oskouei et al.'s (2013) study, the average single measures ICC value for all studied forearm muscles and at all contraction levels was 0.666, which can be interpreted as strong agreement. Both FCR and ECR muscles in this study fall within this ICC category.

As expected, perceived fatigue measured with a visual analog scale was highly repeatable, demonstrating an ICC value of 0.808 in test-retest situations. Five-minute rest period was introduced to minimize fatigue but repeated trials led to increased perceived fatigue towards the end of the test session. Test-retest reliability assessments have been performed for acute pain (e.g., Bijur et al., 2001) and chronic musculoskeletal pain (e.g., Boonstra et al., 2008), with varying degree of reliability, ranging between 0.60 and 0.97.

4.2 Sensitivity

Of the selected fatigue measures that were analyzed, action tremor, MMG RMS amplitude, postural tremor, and rating of perceived fatigue were highly responsive, with rates of responses greater than 1 normalized unit per change in time. These measures were statistically different from the least responsive measures. The least responsive measures, including handwriting and tapping parameters, led to responsiveness value magnitudes closer to zero. MMG RMS amplitude have been shown to be responsive as part of a test battery during five isometric elbow extension protocols with identical mean force amplitude of 15% MVC (Yung et al., 2012). In Yung and colleagues' (2012) study, test batteries were obtained at 15-minute intervals, for protocols lasting upwards of 60 minutes. Increase in MMG root mean square amplitude ranged between 16.1% per test battery during an intermittent condition, up to 112% per test battery during a sustained 15% MVC condition. An increase of 1.233 normalized units was observed in this study during an intermittent protocol at a mean amplitude of 30% MVC. The observed MMG response might be due to the high intensity of work performed by muscles associated with higher mean amplitude of force. An increase in internal work may lead to greater accumulation of metabolites, which might impair cross-bridge function (Binder-Macleod & Russ, 1999). Impairments in cross-bridge cycling are reflected by changes in MMG amplitude (Shinohara & Søgaard, 2006). This study also involved concentric intermittent handgrip contractions, in comparison to isometric time varying approaches in Yung et al., (2012). Different types of contractions might account for differences between MMG responses, where concentric contractions may involve pronounced peripheral impairments followed by central fatigue development. Isometric contractions, on the other hand, may follow the inverse pattern (Babault et al., 2006). Yung et al., (2012) observed quicker rate of response with MMG measures than EMG, similar to this study's results. Indeed, previous literature has shown inconsistent changes in EMG responses during dynamic, intermittent, and/or low-intensity exposures (Nussbaum, 2001; Søgaard et al., 2003).

Action tremor was found to be highly responsive, significantly different from 13 remaining measures, with the exception of postural tremor, perceived fatigue, and MMG amplitude. Postural tremor was similarly responsive as action tremor, and was significantly different than MVCs, EMG, handwriting parameters, and tapping test parameters. However, physiological tremor did not appear to be as responsive as action tremor, but it was more responsive than tapping test parameters. In the literature, there is some conflicting evidence to the aetiology of tremor (Hallett, 1998). On one hand, tremors may be governed by central drive originating from hypothesized oscillators within the CNS, stretch-reflex activity, and motor unit synchronization (Lippold, 1981; Hallett, 1998). Nonetheless, tremor has been shown to increase as a result of muscular contraction and after a fatiguing task. For instance, Leyk and colleagues (2006) observed a three-fold impairment of hand-steadiness with an exhaustive lift and hold task. Galinsky et al., (1990) showed increases in hand, arm, and shoulder tremor amplitude during a continuous static exertion (i.e., pointing task with the elbows extended and shoulder flexed at 90 degrees). In a finger tapping study, requiring 2.3 N of force at a rate of 200 taps/minute, Takanokura et al., (2001) measured tremor during a 10% MVC test contraction over a 120-minute period. Takanokura and colleagues (2001) found profound increases in total power of the tremor spectrum at 30 minutes of the cumulative load time. Power decreased after 60 minutes of cumulative load time and further decreased after 120 minutes. Furthermore, increased tremor has been observed to persist after physically intensive work, over hours and even days (Lippold, 1981). Furness and colleagues (1977) showed long-lasting increases in tremor, upwards of 4 hours after a brief, strong muscular effort. This long-lasting tremor effect may be due to central nervous mechanisms and some degree of persistence of increased synchronization of motor units (Furness et al., 1977; Lippold 1981).

Although handwriting parameters did not appear to be overly responsive, the nature of the fatiguing task might not have elicited responses detectable by handwriting analysis. Handwriting requires precise and rapid manipulation, and is performed by intrinsic muscles and simultaneous proximal stability (Cornhill & Case-Smith, 1996; Naider-Steinhart & Katz-Leurer, 2007). A common grip, often cited as the optimal grasp for handwriting performance, is the dynamic tripod grasp, which requires distal control from intrinsic hand muscles. Atypical grips (e.g., lateral tripod, etc.), however, still requires activity from intrinsic hand musculature, dynamic wrist control, and distal finger control of the writing tool (Dennis & Swinth, 2001). A power grip, performed in the fatiguing task, has been shown to not elicit significant activity from intrinsic muscles of the hand (Greig & Wells, 2008).

Psychomotor sensorimotor synchronization tests did not lead to extraordinary changes in both accuracy and frequency. These results might not be surprising according to previous studies investigating motor performance outcomes and short-term fatigue. Côté and colleagues (2008) found little changes in movement duration (i.e., frequency) after a fatiguing task, which might be preserved and compensated by the nervous system, specifically adaptions in interjoint and intermuscular coordination. Similarly, Hammarskjöld and Harms-Ringdahl (1992) found little change in work movement frequency while performing carpentry tasks, after fatiguing the arm and shoulder. Despite minor changes in movement frequency, the authors observed decrements in work quality, increased perceived exertion while performing carpentry tasks, and increased muscle activity.

4.3 Measurement Latency

Although recovery responses are specific to the preceding exposure, comparisons between measurement latencies may provide insight into the sensitivity of these measures after exposure to a fatiguing exercise or task. Seven measures that were shown to be responsive based on rate of response also demonstrated differences between baseline and cessation. These measures were:

perceived fatigue, MVC, MMG amplitude, EMG amplitude (FCR), physiological tremor, postural tremor, and action tremor. Of the remaining 10 measures, one measure – handwriting pen pressure – resulted in a significantly lower value relative to baseline, three minutes into recovery. The remaining nine measures did not demonstrate any differences between baseline and cessation, and were generally less responsive during a fatiguing exercise with mean amplitude of 30% MVC, cycle time of 6 seconds, and duty cycle of 50%.

Yung et al., (2012) measured recovery using central and peripheral-based fatigue measures. In that study, when compared to baseline, maximum voluntary contraction was significantly different at cessation and recovered within 15 minutes after an intermittent contraction at a mean amplitude of 15% MVC. Søgaard et al., (2003) found a decrease in MVC from baseline up to 30 minutes of recovery, after an intermittent contraction between 0 and 30% at a duty cycle of 60% and cycle time of 10 seconds. Recovery of MVC in this study was consistent with the previous literature, with maximum voluntary contractions significantly lower than baseline upwards of 15 minutes. The same two previous studies also examined recovery of EMG and MMG. Søgaard and colleagues (2003) observed no differences in EMG and MMG from baseline, 10 minutes into recovery, at a test contraction of 5% MVC. Yung et al., (2012) found a significant increase in MMG amplitude at cessation but recovered quickly within 15 minutes. EMG amplitude did not appear to be significantly higher than baseline at cessation or during recovery. The current study found similar trends. MMG amplitude was significantly higher than baseline at cessation but was not significantly different thereafter. However, recovery values remained elevated relative to cessation until 4 minutes in recovery. EMG amplitude of the ECR was similar to Yung et al., (2012) and Søgaard et al., (2003), where amplitude at cessation and recovery was significantly different from baseline. However, EMG of the FCR, revealed significant differences from baseline at cessation and recovery upwards of 5 minutes and at 13 minutes. Interestingly, recovery responses remained elevated and were not statistically different from cessation values.

Perceived fatigue remained elevated, relative to baseline, until 11 minutes post-exercise. Perceived fatigue at cessation, however, significantly decreased from the first minute of recovery. Four minutes into recovery, ratings of perceived fatigue begin to approximate values at 15 minutes, as there were no statistical differences between these time periods. These results suggest that measurements at cessation provide the best estimate of fatigue and decreased significantly thereafter. If immediate RPE recording was not attainable, measurement up to three minutes did not provide extraordinary results (i.e., significantly different from baseline and from 15 minutes recovery). Selen et al., (2007) measured ratings of perceived exertion with a 10-point Borg scale, administered before, during, and after a fatiguing protocol. The authors found an increase in RPE following the fatiguing protocol but recovered immediately. Adamo and colleagues (2009) found the highest ratings of fatigue at cessation of both sustained and intermittent fatiguing conditions. The perception of fatigue, however, returned to baseline values after 15 minutes. Adamo and colleagues (2009) asserted that perceptual measures of fatigue are of short duration, compared to muscle twitch force.

Tremor measurements were statistically higher at cessation than baseline. Postural tremor persisted from baseline until the third minute of recovery. Physiological tremor was different from baseline, three minutes after cessation of exercise. Action tremor quickly recovered, within the first minute of recovery. In all tremor measurements, the highest fatigue response was observed at cessation and quickly decreased during recovery. Action tremor, however, had cessation values that were higher than 2 minutes of recovery and onward, which might indicate that responses at 1 minute of recovery may approximate physiological responses at cessation. Using a hand-steadiness device, Leyk and colleagues (2006) measured postural tremor after a lift and carriage of a loaded stretcher. Postural tremor was measured before exercise, during the first minute of recovery, 30 minutes, 1 hour, 4 hours, and 24 hours post-exercise. Based on the number and duration of wall contacts between probe and board, there were significant threefold increases, one minute into recovery. These values returned to baseline data after 30 minutes of recovery. Results from this study were consistent with Leyk et al., (2006), who found a multiplicative increase (i.e., twofold) in postural tremor at cessation and recovery within the minutes of post-exercise.

Comparisons between studies, however, should be approached with caution, as measurement latency is dependent on recovery from the preceding fatiguing exercise. If fatigue response is indeed task dependent, the selected exercise/work parameters may affect recovery rates of central and peripheral mechanisms, and thereby affect the observed measurement latency responses. Therefore, the observed measurement latencies may not be generalizable and are specifically for an intermittent handgrip contraction with mean amplitude of 30% MVC, 50% duty cycle, and 6-second cycle time. Nonetheless, the observed similarities between this study findings and previous literature indicate that some measures demonstrate consistent responses, regardless of fatiguing exercise.

4.4 Test Battery vs. Continuous Measurement

Previous studies have measured physiological responses during activity on a simultaneous/continuous basis (e.g., Byström et al., 1991; Jensen et al., 1999; Hummel et al., 2005), during a test battery (e.g., Crenshaw et al., 2006; Bosch et al., 2007; Søgaard et al., 2003; Barwick et al., 2012), and with both continuous and test battery measurements (e.g., Yung et al., 2012; Iridiastadi & Nussbaum, 2006; Rosa et al., 1985). Of the previous studies that collected both continuous and test batteries measurements, Iridiastadi and Nussbaum (2006) and Rosa et al., (1985) used different measures for continuous and intermittent collections. Yung et al., (2012) collected a set of identical measures (e.g., MMG and EMG) both simultaneously and as part of a test battery, but did not compare these methods. This current study found that for most of the measures, there were no statistical differences between test battery and continuous measurement. EMG of the FCR muscle was statistically different, as rate of response during test battery was quicker than as a continuous measurement. EMG of the ECR muscle was approaching statistical significance, with continuous responses leading to quicker rate of response than test battery measurements. Similarly, MMG responses between continuous and test battery measurements was approaching statistical significance. EMG and MMG measure activity of particular muscles that work in synergy to exert a force. At elevated levels of grip force (i.e., above 50% maximum grip force), forearm flexor activity has been shown to exceed or is similar to that of extensor activity. However, at lower grip forces, Mogk and Keir (2003) observed the contrary, greater extensor muscle activation than flexor activation. Since a test contraction at 30% maximum handgrip force was performed, to elicit participating motor unit activity from the fatiguing contractions, it is possible that a lower test contraction magnitude elicited greater contributions from extensors than during the fatiguing exercise. If that was the case, with increasing fatigue there is an increase in muscular effort, and a concomitant increase in contribution from forearm flexors to maintain a 30% maximum handgrip force test contraction. Greater involvement of the flexors over time might be one explanation of the statistically significant increase in EMG FCR root mean square amplitude during a test battery. Another possible explanation is the capability of test contractions to standardize force output for equitable comparisons between test batteries. Although participants were asked to meet the targeted force level, during the fatiguing protocol, the actual force output may vary with each contraction. Coefficient of variation analysis revealed higher dispersion of targeted force output during continuous measurement (CV = 7.99%) than test battery (CV = 1.74%). Changes in muscle forces, muscle length, and muscle contraction velocity may influence fatigue-related changes in EMG amplitude or frequency (de Looze et al., 2009). Action tremor and force fluctuations, on the other hand, measure fatigue of entire body segments or reflect changes in motor output. These global effects may be less susceptible to issues including load sharing between muscles during a fatiguing task.

4.5 Selection of Measures Based on Criteria

The current study provides evidence for fatigue measures and their estimates of reliability, responsiveness, comparability with continuous measurement, and post-exercise sensitivity. These measures were recognized by an expert group of researchers as potentially useful in measuring fatigue in occupational settings and were measures based on strong theory. Selection of fatigue measures, however, does not rely solely on one criterion, but of the collective assessments (Table 5.1). With this in mind, we found action tremor to be reliable, responsive, comparable to continuous measurement, and moderately sensitive to fatigue post-exercise. However it should be noted that action tremor was measured with an isometric contraction while using a rigid fixation, i.e., handgrip dynamometer. Quite possibly, tremor oscillations were attenuated at higher frequencies (bias towards lower frequencies) compared to an elastic resistance, which raises mechanical resonance frequency and facilitates detection of higher frequency tremors. Despite this limitation, the method chosen in this study provides a number of advantages. First, action tremor measured with a rigid fixation is directly linked to performance-related fatigue outcomes, such as precision and accuracy. Forces in occupational tasks are less likely applied with elastic resistance. Second, the peak oscillation frequencies (10, 20, 40 Hz) may be neuromuscular in origin (i.e., central oscillators). Any changes to mechanical properties when loading the limb may amplify rather than generate peak oscillations (McAuley, 1997).

Mechanomyography also appeared to satisfy the assessed criteria, more specifically *almost perfect* test-retest reliability, high responsiveness, comparability to continuous measurement, and prolonged recovery from cessation. However, MMG may be susceptible to similar limitations as electromyography. First, MMG signals may be influenced by changes in muscle length and force (Orizio et al., 1989). Second, MMG signals may be susceptible to geometric artifact, and therefore crosstalk between muscles (Islam et al., 2014). And lastly, this study measured mechanical activity from a single extensor muscle. Possibly, MMG might demonstrate similar variability as EMG, if multiple muscles were measured. On the contrary, previous literature has demonstrated similar repeatability (Al-Zahrani et al., 2009), responsiveness (Yung et al., 2012), and post-exercise sensitivity (Søgaard et al., 2003) when measuring mechanical activity of multiple muscles.

Table 5.1. Summary of Reliability and Responsiveness Criteria for Test Battery Fatigue Measures.

Measure	Reliable?	Responsiveness (Normalized Units/Δ Time)	Comparable to Continuous?	Difference Pre- & Post- Exercise? (Normalized to Pre)	Time to Recover Back to Baseline	Time to Recover from Cessation
Perceived Fatigue (VAS)	Almost Perfect (ICC = 0.808)	1.020	N/A	Yes – Pre: 0.42, Post: 95.11	9 minutes	1 minute
Physiological Tremor	Fair (ICC = 0.302)	0.758	N/A	Yes – Pre: 1.00, Post: 1.81	3 minutes	1 minute
Postural Tremor	Moderate (ICC = 0.587)	1.196	N/A	Yes – Pre: 1.00, Post: 2.14	3 minutes	1 minute
Action Tremor	Almost Perfect (ICC = 0.834)	1.459	Yes – TB: 1.459, Cont: 2.587	Yes – Pre: 1.00, Post: 2.29	2 minutes	2 minutes
Surface EMG*	Strong (ICC = 0.751)	0.371	Variable$^{\beta}$	Variable$^{\beta}$	0 – 13 minutes	1 minute
MMG	Almost Perfect (ICC = 0.825)	1.233	Yes – TB: 1.233, Cont: 2.599	Yes – Pre: 1.00, Post: 1.99	1 minute	4 minutes
Force Variation	Moderate (ICC = 0.412)	0.583	Yes – TB: 0.583, Cont: 0.457	No	0 minutes	0 minutes
Maximum Voluntary Contraction	Strong (ICC = 0.666)	0.341	N/A	Yes – Pre: 1.00, Post: 0.59	15 minutes	2 minutes
Tapping Errors	Fair (ICC = 0.338)	0.048	N/A	No	0 minutes	0 minutes
Tapping Frequency	Poor (ICC = 0.184)	0.028	N/A	No	0 minutes	0 minutes

Handwriting – APVV	Almost Perfect (ICC = 0.920)	0.238	N/A	No	0 minutes	0 minutes
Handwriting – Straightness Error	Almost Perfect (ICC = 0.984)	0.100	N/A	No	0 minutes	0 minutes
Handwriting – AAV	Almost Perfect (ICC = 0.927)	0.222	N/A	No	0 minutes	0 minutes
Handwriting – YJerk	Almost Perfect (ICC = 0.836)	0.028	N/A	No	0 minutes	0 minutes
Handwriting – Jerk	Almost Perfect (ICC = 0.848)	0.015	N/A	No	0 minutes	0 minutes
Handwriting – Pen Pressure	Strong (ICC = 0.776)	0.022	N/A	No	3 minutes	0 minutes

* Mean between flexor and extensor muscle.
$^{\beta}$ Differs between muscles of interest

Perceived fatigue using a visual analog scale similarly fulfilled reliability, responsiveness, comparability, and post-exercise sensitivity assessments. There are many advantages of using a visual analog scale to measure fatigue. Particularly, it is simple, easy, and quick to administer (Lee et al., 1991). These psychometric scales are also related to fatigue and reduced work capacity (Sato & Coury, 2009) and reflect central mechanisms (Allman & Rice, 2003). For instance, perceptual measures of fatigue have been related to EMG amplitude (Fontes et al., 2010) and its frequency spectra (Iridiastadi & Nussbaum, 2006). On the other hand, there are limitations in using visual analog scales. First, the degree of familiarity of the task might affect psychological cues related perception (Mital et al., 1994). Second, perceived fatigue might be strongly coupled to high frequency fatigue rather than low frequency fatigue (Adamo et al., 2002). Third, perception of fatigue may be difficult to detect at the beginning and end of exercise (Springer & Pincivero, 2010; Hancock et al., 2012). By way of illustration, studies (e.g., Springer & Pincivero, 2010; Yung et al., 2012) have demonstrated maximal ratings of fatigue before volitionally terminating exercise due to exhaustion.

One major limitation of this study is the use of a single exercise protocol to assess responsiveness of the fatigue measures. Fatigue responses, and therefore measurement, are task-dependent and might be influenced by physical exposure parameters, including duty cycle and cycle time (Byström & Fransson-Hall, 1994), intensity (Gandevia, 1998; Westerblad et al., 2010), type and speed of contraction, and muscle groups involved (Enoka & Stuart, 1992; Weir et al., 2006). As a first step to assess sensitivity, this study provides information on one aspect of responsiveness using mean force amplitude relevant to occupation and fatigue effects and duty cycle and cycle time similar to previous studies. Further studies are required to assess the sensitivity of these measures under different exercise profiles.

5. Conclusion

Fatigue has been frequently cited as an intermediary factor between poor ergonomics and production errors and as a possible precursor to the development of work-related musculoskeletal disorders. Devising a set of practical fatigue measures is one step towards detecting and documenting fatigue. However, there is limited information on the sensitivity, reliability, and utility of fatigue measures as a test battery. The current study evaluated 11 measures and their 17 parameters, selected for their perceived validity and practicality for field collection. Action tremor and mechanomyography collected during a test contraction, and perceived fatigue assessed by a visual analog scale, were found to be most reliable, most responsive, comparable to continuous measures, and sensitive after the fatiguing activity. This preliminary evidence suggests that these measures should be considered with other measures of interest, as part of a test battery when measuring fatigue. However, there remains a need to measure responsiveness of these measures under varying exercise protocols to better ascertain measurement sensitivity.

Chapter 6

Does Diurnal Variation Affect Daylong Fatigue Measurement?

Abstract

Diurnal changes of physiological functions might influence the interpretability of fatigue measures over the course of a workday. These changes are endogenously generated, predictable, and occur at regular periodic intervals. Unfortunately, there is sparse evidence of how diurnal variability might affect select fatigue measures over a normal, minimally fatiguing workday. This study aimed to investigate the effects of 12-hour diurnal variation on select fatigue measures in a traditional time-of-day protocol. Mechanomyography root mean square amplitude (MMG RMS) and action tremor root mean square amplitude (Action Tremor RMS) demonstrated rhythmic behaviour, with significant time effects from 08:00 to mid-afternoon and early evening. Circadian rythmicity was also observed in overall muscle activity and the aggregate of all measures. Although trends of remaining measures were generally consistent with findings reported in previous literature, they did not show significant time of day effects or rhythmical circadian behaviour. Therefore, additional analytical considerations might be required when interpreting daylong responses of MMG and action tremor, whereas the remaining measures were not significantly affected by intrinsic diurnal variability.

1. Introduction

A growing interest in the relationship between fatigue and its acute (e.g., deficits in motor control, reduced proprioception, increased error) and longer-term outcomes (e.g., work-related musculoskeletal disorders, chronic fatigue syndrome, myalgia) has brought greater attention to its temporal development (de Looze et al., 2009). By understanding the temporal pattern of fatigue and its relationships with disorder risks and work performance, fatigue may be a useful risk indicator and workplace design and evaluation tool (Iridiastadi & Nussbaum, 2006). However, studies that have documented fatigue at the workplace are often limited to comparisons before and after work, which may not be sufficient to draw firm conclusions. For instance, Chang and colleagues (2009) observed *increased* strength at the end of work compared to the beginning of the shift, despite increases in self-perceived tiredness. In one of the few studies that measured fatigue over multiple periods of the working day, strength similarly demonstrated a minimum at the beginning of work and a peak during mid-day (Yung et al., 2014). Perceived strength also appeared to follow this diurnal pattern (Persson et al., 2006). Diurnal fluctuations of physiological functions might underlie these observations and challenge the interpretation of fatigue measures and their responses over the course of a workday (Saito, 1999).

These diurnal fluctuations are predictable, occurring at regular, periodic intervals over the course of 24 hours, regulated by endogenous pacemakers (Refinetti & Menaker, 1992; Jasper et al., 2009). These rhythms are often associated with variations in body temperature, which has been hypothesized as a consequence of the evolutionary need to provide energetic savings during inactive phases (Refinetti & Menaker, 1992). Rhythms are at a minimum early morning, increase during the day, at a maximum in the afternoon/early evening (acrophase), and decreases prior to sleep (Crowley et al., 1972). However, circadian rhythms do not always parallel body temperature rhythm due to changes in wakefulness and status of the circadian system (Carrier & Monk, 2000). Refinetti and Menaker (1992) described that even among individuals or populations with similar wakeup and bedtimes, the phase relationships are variable. This may be due to differences in occupational schedules, photoperiod, and other uncontrolled factors (Refinetti & Menaker, 1992). Several studies have shown that circadian rhythms might be regulated by a pacemaker in the suprachiasmatic nuclei and modulated by endogenous melatonin levels (Cagnacci et al., 1992).

Under laboratory conditions, there appears to be some evidence for diurnal variations of a range of physiological processes. These variations have been shown in carefully controlled laboratory studies with a constant routine methodology, which control external and internal influences that might conceal endogenous circadian factors, and traditional time-of-day protocols over a normal working day. Kraemer et al., (2000) measured several dimensions of cognitive attention and found statistically significant time-of-day variations of several indicators. However, not all of the selected indicators were homogenous, signifying that multiple parameters of the same physiological function may follow different time-of-day variations due to underlying circadian and homeostatic mechanisms. Fatigue is similarly multi-dimensional and a complementary set of fatigue measures have been recommended to properly reflect fatigue responses at multiple sites (Bosch et al., 2007; Yung et al., 2014). The aim of this study was to better understand the effects of diurnal changes on recorded signals for a range of fatigue measures. This study documented responses measured by a test battery of fatigue measures over two consecutive 12-hour periods.

2. Fatigue Measurement

A single test to measure fatigue might not be a sufficient (Saito, 1999). Because different measures provide information on different processes induced by exercise, various authors suggest that fatigue should be evaluated by a multidisciplinary approach (Vøllestad, 1997; Saito, 1999). This might include physiological and psychological measurements, which may be related to various factors that may influence fatigue (Saito, 1999). To support this, Yung and colleagues (2014) documented fatigue in physically demanding work using a test battery of measures that reflects central and peripheral mechanisms. Since different measures were responsive over the workday and over the workweek, the authors argued for a complementary set of measures to give a comprehensive picture of fatigue development.

In study 3, we evaluated a test battery of novel and commonly used measures of fatigue for their reliability and sensitivity during a fatiguing task. These measures were selected for their responsiveness to physically demanding work in realistic work tasks (Yung et al., 2014) and for their perceived validity, reliability, and practicality by an expert group of fatigue researchers (Study 1). This test battery consisted of 11 measurements: rating of perceived fatigue using a visual analog scale (VAS), physiological hand tremor, postural hand tremor, a 30% maximum voluntary contraction test contraction while measuring surface electromyography (EMG) of the extensor carpi radialis (ECR) and flexor carpi radialis (FCR), mechanomyography (MMG) of the flexor digitorum superficialis (FDS), action tremor of the hand, force variation, maximum voluntary handgrip contraction, a fixed pace tapping test, and handwriting tests. These 11 measures were subsequently analyzed to generate 17 parameters (e.g., amplitude in the time domain, frequency, etc.). The authors found moderate agreement (i.e., ICC value greater than 0.4) among 14 measures/parameters, eight of which achieved a test-retest ICC value greater than 0.8, indicating almost perfect agreement. Six measures achieved responsiveness greater than 50% normalized units per change of time. Four measurements/parameters (action tremor, MMG, perceived fatigue, and postural tremor) demonstrated responsiveness greater than 100% normalized units per unit time during an intermittent handgrip protocol with mean amplitude of 30% maximum voluntary contraction, 6-second cycle time, and 50% duty cycle.

To further investigate the reliability of the 11 test battery measures in study 3, we evaluated the same 11 measures for possible diurnal-related effects.

3. Methods

Methods are similar to a study reported in study 3. For this current study, participants were asked to return on two consecutive days, after the reliability study. This ensured that participants were familiarized to testing procedures and all test battery measures were well practiced to reduce variability introduced by learning effects. Three maximum voluntary handgrip contractions (MVC) were performed prior to all test sessions to determine force levels for the 30% MVC test contraction.

3.1 Participants

Sixteen healthy university-aged students (8 males, 8 females, mean age=24 years, mean height=1.72 m, mean weight=70.7 kg) were recruited to participate. Participants had no current or injuries of their elbows, upper arms, and forearms in the previous 6 months. Two participants (1 male, 1 female) were left hand dominant. Participants provided informed consent for all experimental procedures and associated risks, as approved by the University of Waterloo Office of Research Ethics, prior to the experimental session.

3.2 Test Battery of Fatigue Measures

The full test battery, with all 11 measurements, required 2 minutes to complete. Participants were asked to wear EMG electrodes, secured with adhesive dressing, over the course of the day. Accelerometers were mounted on placement sites each time participants return to the laboratory to perform the test battery. Placement sites for electrodes and accelerometers were also marked with an indelible felt tip pen at the beginning of each day and at the end of the first day. This ensured consistent placement between days and ensured consistent placement of accelerometers over the test session. All measures were acquired at a sampling frequency of 2048 Hz and unless otherwise stated, analyzed with LabChart 7 (ADInstruments, Colorado Springs, CO, USA) and MATLAB 7.2 (Mathworks, Inc,. Natick, MA. USA). Measures were performed in the following order:

3.2.1. Visual Analog Scale (VAS) – Perceived Fatigue

Perception of fatigue was obtained using a 10-cm visual analog digital scale. Anchor points represented “no fatigue at all” and “complete exhaustion”. Perceived fatigue was expressed as a value between 0 (no fatigue at all) and 100 (complete exhaustion).

3.2.2. Physiological Tremor

A ±3 g tri-axial accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA; sensitivity=300 mV/g, noise density=250 µg/rtHz, 4mm x 4mm x 1.45mm) was placed on the dorsum of the hand, on the distal part of the third metacarpal bone. Participants were instructed to adopt a seated posture, with their elbow and forearm supported on the armrest and their hand fully relaxed for a period of 12 seconds. Participants were asked to avoid looking at the hand due to possible visual-dependent peaks in hand tremor (McAuley et al., 1997). Signals were bandpass filtered (Butterworth, 2nd Order, 1 and 20 Hz) and analyzed in the time domain. Instantaneous root mean square amplitude was calculated at 1-second windows and averaged for the middle 10-seconds.

3.2.3. Postural Hand Tremor – Hand Steadiness

A ±3 g tri-axial accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA, sensitivity=300 mV/g, noise density=250 µg/rtHz) was mounted onto the distal end of the tapping probe. Participants held the probe with a dynamic tripod grasp over a target (i.e., a 1 cm diameter hole), positioned on the desk surface at approximately elbow height, with the elbows comfortably supported. Participants inserted the probe into the 1cm diameter hole but hovering above a touch-registering plate for collection duration of 12 seconds. Signals were bandpass Butterworth filtered (2nd Order) at cutoff frequencies of 1 and 20 Hz. The middle 10-seconds was analyzed by calculating the instantaneous root mean square amplitude at 1-second epochs.

3.2.4. 30% Maximum Voluntary Contraction (MVC) Test Contraction

A test contraction at 30% of the participant's maximum handgrip force was performed for 17-seconds using a handgrip dynamometer (Medical Research Ltd., Leeds, UK) with the assistance of visual feedback (LabView, National Instruments Corporation, Austin, TX). The handgrip dynamometer was mounted vertically on a custom fabricated apparatus. Surface electromyography (EMG), mechanomyography (MMG), action tremor, and force variability were collected during the test contraction.

3.2.4.1 Surface Electromyography

Electromyography was recorded using bipolar surface electrodes (Ag-AgCl electrodes, Ambu Blue Sensor N, Denmark) with an inter-electrode distance of 20 mm, placed on the belly of the extensor carpi radialis (ECR) and flexor carpi radialis (FCR). Both muscle belly sites were marked with an indelible felt tip pen to ensure consistent placement between both days. Hair was removed by razor and skin abraded with ethanol and prepared with NuPrep Gel (Weaver and Company, CO, USA). EMG signals was collected with an eight-channel data system (Bortec, Calgary, AB), a common mode rejection ratio of >115 dB, and a band-pass filter between 10 and

1000 Hz. Signals were amplified and sampled at 2048 Hz. EMG electrodes remained mounted on the participant, over the 12-hour day, to minimize signal variability as a result of electrode re-positioning. The average root mean square was calculated in the time domain, of the middle 15-seconds at 1-second epochs of the 17-second test contraction.

3.2.4.2. Mechanomyography

A low profile tri-axial ± 3 g accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA; sensitivity=300 mV/g, noise density=250 µg/rtHz) recorded mechanical responses of flexor digitorum superficialis (FDS) muscle. The accelerometer was placed on the muscle belly with double-sided tape, which was marked with an indelible felt tip pen. Signals were bandpass filtered between 5 and 100 Hz (Butterworth, 2nd Order) and amplitude was calculated as the average root mean square amplitude at 1-second epochs over the middle 15 seconds of data.

3.2.4.3. Action Tremor

The tri-axial accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA) attached on the dorsum of the hand also served to measure action tremor during the 30% MVC handgrip contraction. The accelerometer was placed on the distal part of the third metacarpal bone, mounted with double-sided tape and loosely secured with Transpore medical tape. Action tremor signals were band-pass filtered (Butterworth filter, 2nd order) between 1 and 20 Hz. Amplitude of the signal was calculated as the average of the root mean square (RMS) over the middle 15-seconds of data.

3.2.4.4. Force Variation (Coefficient of Variation)

The recorded force signal was analyzed to determine fluctuations, which may be indicative of changes in motor control. Force signal during the test contraction was filtered with a Butterworth 2nd order dual lowpass filter at 10 Hz. Force variation was analyzed with coefficient of variation (%) – the standard deviation divided by the mean – at 1-second intervals and averaged for the middle 15 seconds of data.

3.2.5 Maximum Voluntary Contraction

Participants exerted maximum voluntary handgrip forces with a handgrip dynamometer (Medical Research Ltd., Leeds, UK). With verbal encouragement, participants exerted a ramped maximum contraction for 5 seconds. The force signal was low-pass filtered at 10 Hz (Butterworth, 2nd Order, dual passed). The middle 3-seconds of the 5 second MVC was windowed and values were averaged.

3.2.6. Psychomotor Sensorimotor Synchronization Test (Fixed Pace Tapping)

A custom fabricated tapping device (Department of Kinesiology, University of Waterloo) provided a measure of sensorimotor synchronization (SMS), sensorimotor coordination, and audio-motor coupling (van der Steen & Keller, 2013). A template, consisting of 9, 1-cm holes oriented in a circle, overlaid a metal plate. Since all components were connected to the same power source, if the probe touched either template or metal plate, a closed electric circuit was formed, and touches were registered (frequency and duration). Touches on the template were considered an error and touches on the underlying metal plate were successes. Participants performed the fixed-paced tapping test at 90 beats per minute for 17 taps, in a clockwise direction, a comfortable pace determined by pilot studies. This tapping rate falls within the upper inter-onset interval (IOI) limit of 1.8 seconds (i.e., 108 beats per minute) for sensorimotor synchronization, i.e., referential behavior involving temporal coordination of motor rhythm with an external rhythm (Repp, 2005). Additionally, this frequency closely approximates the average spontaneous motor tempo (SMT) or self selected personal tempo, which has a period of 600 msec (Fraise, 1982). The test required approximately 30 seconds to complete.

3.2.7 Handwriting Tests

Handwriting is a highly automated, over-learned sensorimotor skill, performed on a daily basis (Jasper et al., 2009). It involves a complex interaction between several cognitive and motor processes, including syntactical, semantic, and lexical processing. A digitizing tablet (Bamboo CTH 470, Wacom Co., Ltd., Japan) measured participants' handwriting kinematics as they traced a stereotyped movement pattern (a 30 mm diameter circle), five times consecutively, as fast and as accurately as possible. Participants used their dominant hand to draw circles in an outward direction, i.e., clockwise direction. Outward direction circular movements can be performed at a quicker speed than inward movements, possibly due to "an easier biomechanical and sensorimotor implementation than the inward direction" (Semjen et al., 1995). Handwriting data was analyzed with MovAlyzeR handwriting software (Version 6.1, NeuroScript, Tempe, AZ). The following parameters were then calculated for each trial: straightness error, average absolute velocity (AAV), and average pen pressure. Handwriting tests were recorded for 20 seconds.

3.3 Protocol

Diurnal effects were collected on two consecutive, 12-hour days, from 08:00 to 20:00 hrs. Each day, participants were asked to return to the lab every 2 hours to perform the test battery (i.e., 08:00, 10:00, 12:00, 14:00, 16:00, 18:00, and 20:00 hrs). At the beginning of each day, participants were asked to exert three maximum voluntary contractions to normalize EMG muscle activity during test batteries performed at 2-hour intervals. A 12-hour period was chosen to reflect variations in performance over a normal working day. When participants were not in the lab, they were allowed to assume their regular daily duties, but were asked to refrain from physically intensive activity including physical exercise and intensive physical manual tasks involving the upper extremities. Participants were also asked to refrain from caffeine consumption before, during, and in between the 12-hour sessions. Although this protocol is not a constant routine, i.e., constant bed rest under constant illumination with scheduled meals, refraining from hand intensive activity and caffeine might reduce external and internal influences that mask true endogenous rhythms. Additionally, a number of studies have shown possible diurnal variations in strength and other physiological responses using a traditional time-of-day protocol representing a normal working day (e.g., Wright, 1959; Lyddan et al., 1971).

Participants were comfortably seated at a desk facing a computer monitor that displayed visual feedback of handgrip force (LabView, National Instruments Corporation, Austin, TX). The visual feedback allowed participants to perform 30% MVC handgrip test contractions. When necessary, participants were asked to rest their elbows and forearms onto the chair's armrest to perform tremor tests. The test battery was executed with the dominant hand.

3.4 Statistical Analysis

Test battery measurements were compared between the seven periods of time: 08:00, 10:00, 12:00, 14:00, 16:00, 18:00, and 20:00 hrs. In order to minimize any effects of possible inter-individual differences, measurement values were standardized for each participant across both testing days. Z scores were calculated by using the overall mean and standard deviation of the test-specific value. Therefore a z score of zero was indicative of the mesor (or mean level) of a circadian rhythm and scores above or below reflect a higher or lower than average physiological response, respectively. Data was then evaluated for normality by plotting data as a histogram, drawing Q-Q plots, and the Shapiro-Wilk test. If data deviated from a Gaussian distribution, nonparametric approaches were considered (Friedman's test for repeated measurements and Wilcoxon-signed-rank test for paired comparisons between time periods). Bonferroni corrections were applied to control familywise error rate of multiple comparisons ($\alpha = 0.05$, adjusted $\alpha = 0.05/21 = 0.0024$). Otherwise, a one-way repeated measures ANOVA and subsequent Tukey post-hoc tests were calculated to determine differences between time periods. Effect sizes (i.e., partial eta squared, η_p^2) were calculated during repeated measures ANOVA testing. Nonparametric and parametric one-way analyses for repeated measurements were performed on these Z scores to test the main effect of time with an alpha set at $p < 0.05$. Statistical analyses were performed using Statistical Analysis Software (Version 9.3, SAS Institute Inc., Cary, NC, USA).

Cosinor analysis is a technique to detect the rhythmicity of circadian rhythms by fitting, using least square methods, cosine curves with known periods to estimate the pattern of a smooth rhythm (Refinetti et al., 2007). It has the equation:

$$X_i = M + A\cos(\theta_i + \varphi) + e_i \qquad \text{Equation (1)}$$

Where M is the rhythm-adjusted mesor (Midline Estimating Statistic of Rhythm), A is the amplitude defined as half the height of oscillation approximated by the fitted cosine curve, φ is the acrophase which is the phase in relation to a fixed reference time, and e_i is an error term assumed to be independent and normally distributed with mean zero and fixed unknown variance. θ_i corresponds to trigonometric angles corresponding to sampling times t_i, and computed as $\theta_i = (2\pi\, t_i)/P$. Period, P, is assumed known. The resulting outputs for each point X_i are: mesor, amplitude, and acrophase. Zero-amplitude testing were performed as an F test where $F = (MSS/2)/(RSS/(N–3))$, MSS = model sum of squares and RSS = residual sum of squares. In zero-amplitude testing, the null hypothesis that the amplitude is zero (i.e., there is no rhythm) is rejected at a significance level set at $\alpha = 0.05$. Single cosinor analysis was performed on the averaged values of all participants at each time period.

4. Results

Prior to both days, participants were asked to report the number of hours they slept prior to the session. Leading up to the first test day, participants slept on average 6 hours and 38 minutes ($\overline{x}$ = 397.63 minutes, σ = 59.11 minutes). An average of 7 hours and 30 minutes was reported prior to the second test day ($\overline{x}$ = 450.31 minutes, σ = 53.62 minutes).

Preliminary analysis found no significant differences between day 1 and day 2, therefore measurement values were averaged at each time period, between the two days, for each individual. This data management process was completed after calculating z scores, but prior to repeated measures testing. A summary z score was calculated as an indicator of overall diurnal effect based on all fatigue measures, calculated from the mean of Z scores for each participant and each time period (Figures 6.1 and 6.2). Summary z scores were also calculated for measures grouped by common traits (Figure 6.3). For instance, the mean of hand steadiness, physiological tremor, and action tremor were categorized as overall tremor (Fig 6.3A). The mean of two electromyography measurements and mechanomyography reflected overall changes in muscle activity (Fig 6.3B). Measurements recorded during a maximum handgrip contraction, including MMG, EMG, action tremor, and force were averaged and the mean was considered an overall measure of neuromuscular activity during a maximal exertion (Fig 6.3C). The mean of absolute average velocity, straightness error, and pen pressure reflected changes in overall handwriting (Fig 6.3D). Z score signs of straightness error and pen pressure were switched to better reflect performance (i.e., $z > 0$ indicative of above-average handwriting performance). Tapping error and frequency values were averaged and categorized as a measure of tapping (Fig 6.3E). Similar to handwriting performance, tapping error signs were switched to better reflect tapping performance. Finally, an overall summary measure was devised based on simple means of all fatigue measures (Fig 6.3F).

There were no statistical differences between the 7 intervals of time in perceived fatigue ($p = 0.299$), physiological tremor ($p = 0.696$), hand steadiness ($p = 0.650$, $\eta_p^2 = 0.045$), FCR EMG muscle activity ($p = 0.397$, $\eta_p^2 = 0.066$), ECR EMG muscle activity ($p = 0.907$, $\eta_p^2 = 0.023$), force variation ($p = 0.498$, $\eta_p^2 = 0.057$), maximum handgrip contraction ($p = 0.786$, $\eta_p^2 = 0.034$), tapping errors ($p = 0.339$, $\eta_p^2 = 0.076$), tapping frequency ($p = 0.653$, $\eta_p^2 = 0.047$), handwriting absolute average velocity ($p = 0.530$, $\eta_p^2 = 0.055$), handwriting straightness error ($p = 0.295$), and handwriting pen pressure ($p = 0.295$). Measurements recorded during maximum handgrip contractions also demonstrated no statistical significance between time periods: MMG ($p = 0.5147$, $\eta_p^2 = 0.076$), EMG FCR ($p = 0.538$, $\eta_p^2 = 0.057$), EMG ECR ($p = 0.981$, $\eta_p^2 = 0.013$), and action tremor ($p = 0.408$, $\eta_p^2 = 0.069$). Action tremor during a 30%MVC, on the other hand, demonstrated a time effect [$F\ (15,6) = 2.78$, $p < 0.05$, $\eta_p^2 = 0.166$] with statistical differences between 08:00 and 16:00 ($p = 0.015$), and 08:00 and 18:00 ($p = 0.028$) after Tukey post-hoc adjustments. MMG of the flexor digitorum superficialis also demonstrated a significant time effect [$F\ (15,6) = 2.76$, $p < 0.05$, $\eta_p^2 = 0.206$), with significant differences between 08:00 and 12:00 ($p = 0.048$) and 08:00 and 16:00 ($p = 0.013$) pairs.

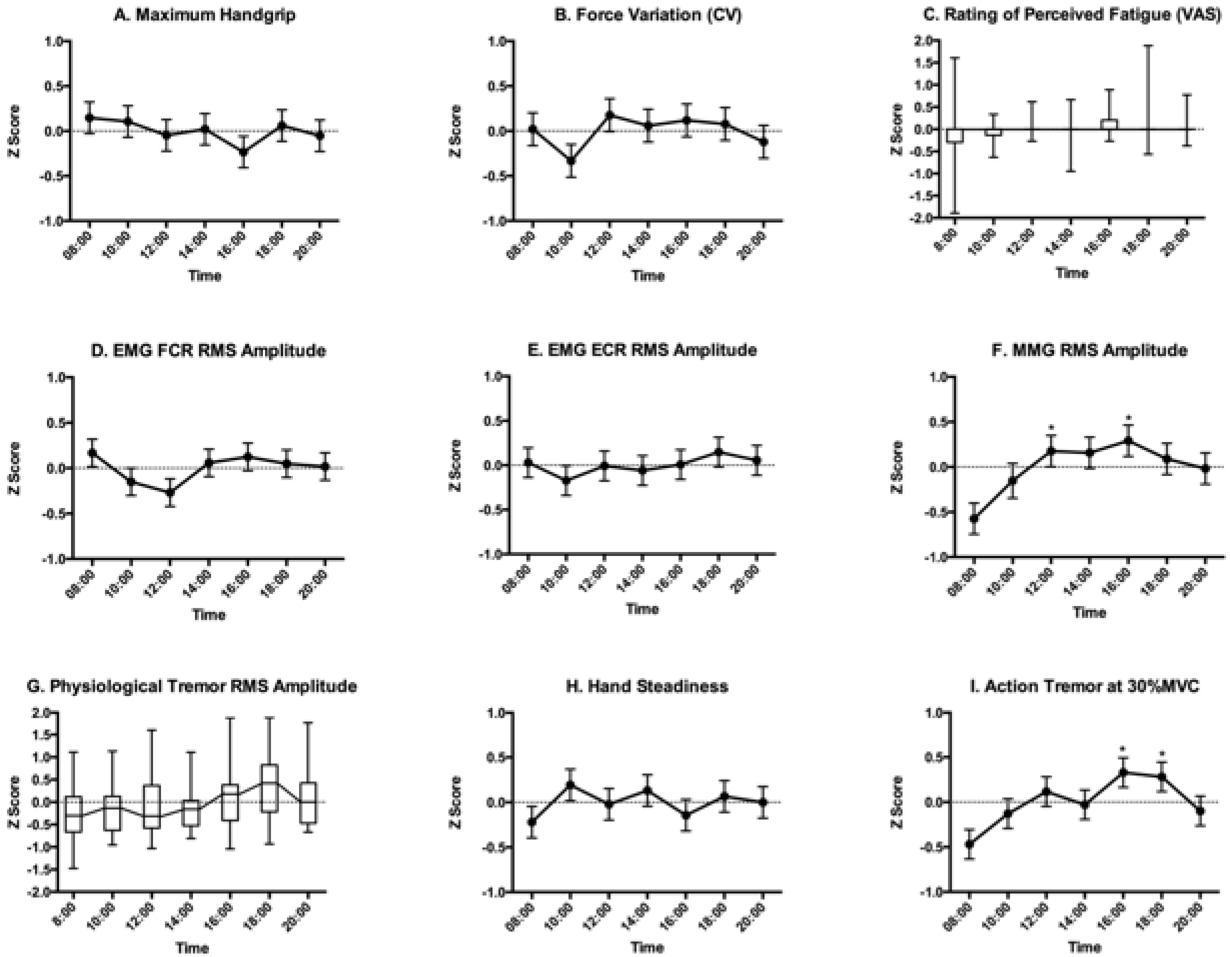


Figure 6.1 Fatigue measures recorded at 2-hour intervals between 08:00 and 20:00.

Force (A-B) and perceived fatigue (C), muscle activity (D-F), and tremor measurements (G-I) plotted with mean and standard error mean (parametric tests) or median, 25th and 75th quartiles, and minimum and maximum values (non-parameteric tests). * = $p < 0.05$ from 08:00.

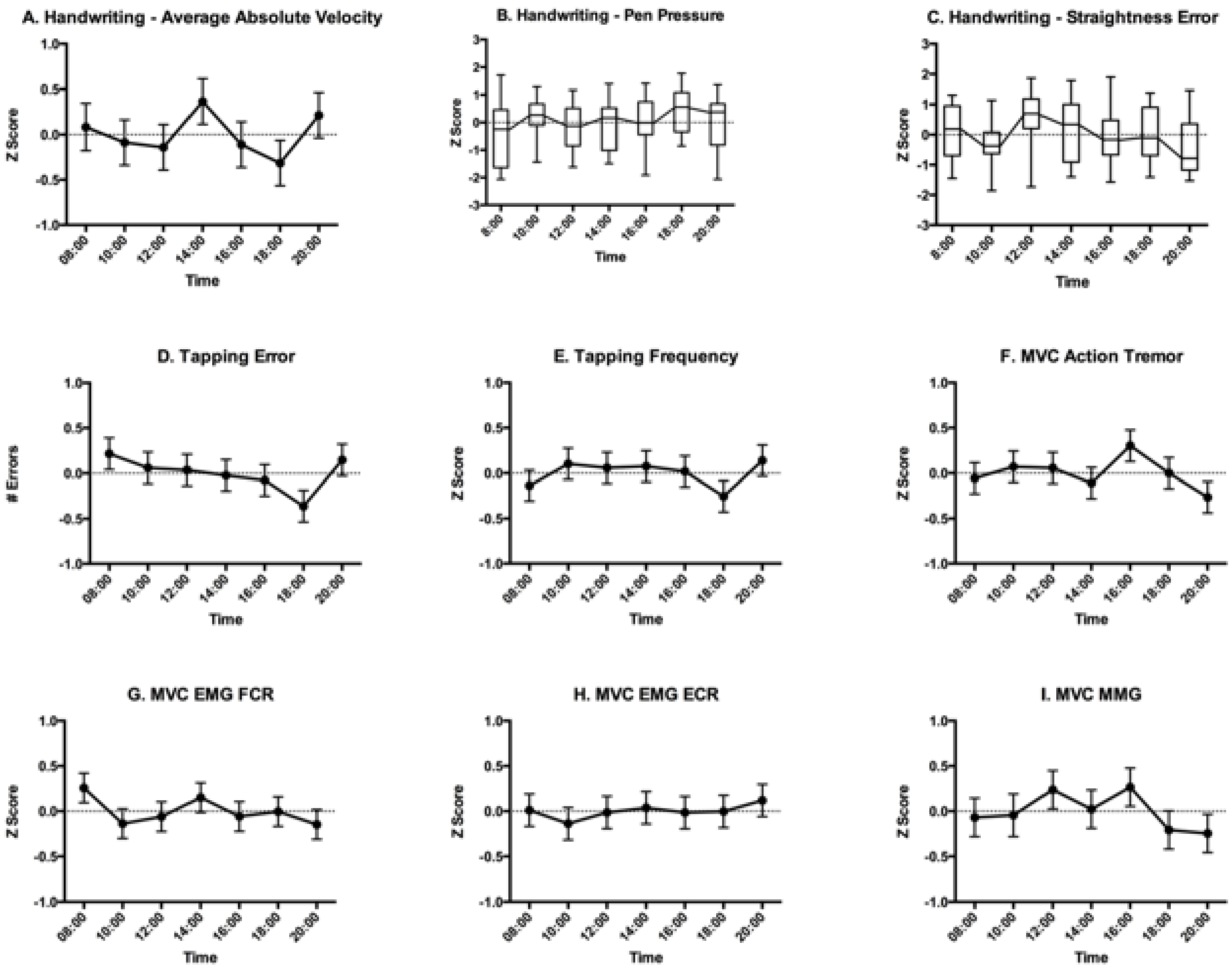


Figure 6.2 Fatigue measures recorded at 2-hour intervals between 08:00 and 20:00.

Handwriting (A-C), tapping (D-E), and measurements collected during a maximum grip force (F-I) plotted with mean and standard error mean (parametric tests), or median, 25th and 75th quartiles, and minimum and maximum values (non-parametric tests).

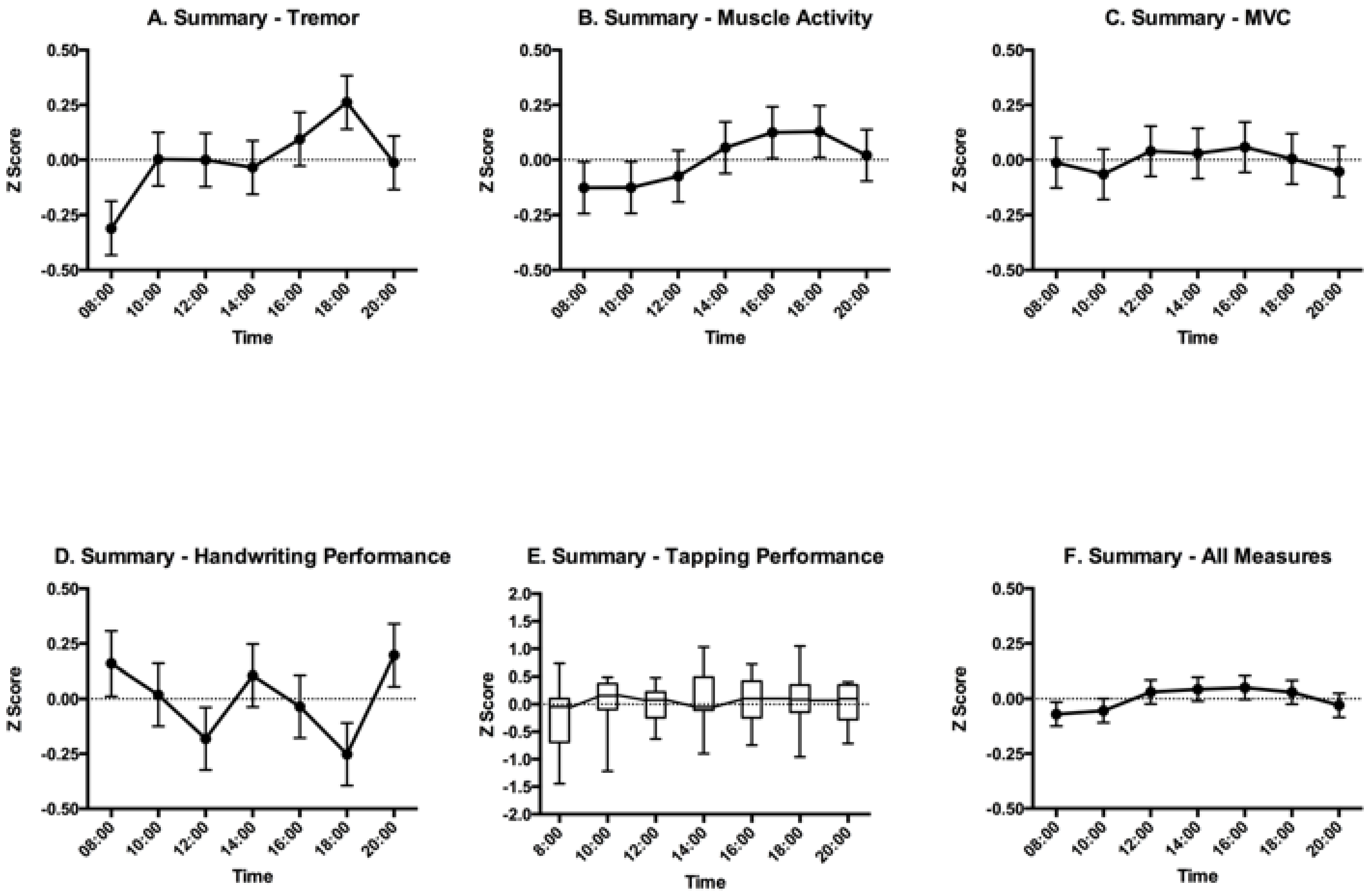


Figure 6.3 Summary fatigue measures recorded at 2-hour intervals between 08:00 and 20:00.

Z-scores averaged by individual and time for measures grouped by common traits and for all measures. Values plotted with mean and standard error mean (parametric tests), or median, 25th and 75th quartiles, and minimum and maximum values (non-parametric tests). Handwriting and tapping metrics adjusted to reflect above-average performance (z>0) and below-average performance (z<0). Summary of all measures are based on raw z-scores for all fatigue measures.

Table 6.1 Single Cosinor Analysis of Fatigue Measures

Measure	Mesor (Z-Value)	Amplitude (Z-Value)	Acrophase (Hr:Min)	Zero-Amplitude Test	% Rhythm
Maximum Hand Grip	0.040	0.134	07:12	F(2,4) = 1.887; p = 0.265	10.6
Force Variation (CV)	0.016	0.152	06:48	F(2,4) = 1.615; p = 0.306	2.8
Rating of Perceived Fatigue	0.000	0.000	-	F(2,4) = 0.000; p = 1.000	0.0
EMG FCR RMS	-0.004	0.182	15:56	F(2,4) = 6.034; p = 0.063	53.4
EMG ECR RMS	0.000	0.193	07:24	F(2,4) =3.367; p = 0.139	34.8
MMG FDS RMS	-0.159	0.457	18:28	F(2,4) = 30.228; p = 0.006 **	83.1
Physiological Tremor RMS	-0.044	0.302	18:44	F(2,4) = 5.921; p = 0.065	55.8
Hand Steadiness	0.003	0.101	04:08	F(2,4) = 0.743; p = 0.534	0.0
Action Tremor	-0.121	0.381	18:56	F(2,4) = 10.715; p = 0.026 **	63.0
Handwriting – Abs Avg Vel	0.039	0.270	17:40	F(2,4) = 4.435; p = 0.097	37.9
Handwriting – Pen Pressure	0.163	0.227	23:48	F(2,4) = 1.302; p = 0.367	1.0
Handwriting – Str Error	0.142	0.534	14:48	F(2,4) = 3.455; p = 0.135	28.7
Tapping – Error	0.057	0.196	07:24	F(2,4) = 2.556; p = 0.193	12.7
Tapping – Frequency	0.015	0.144	05:24	F(2,4) = 2.585; p = 0.190	20.3
MVC – Action Tremor	-0.066	0.180	16:12	F(2,4) = 1.763; p = 0.282	0.0
MVC – EMG FCR RMS	0.015	0.144	21:00	F(2,4) = 2.234; p = 0.223	16.4
MVC – EMG ECR RMS	0.015	0.067	01:16	F(2,4) = 1.553; p = 0.317	0.1
MVC – MMG FDS RMS	-0.107	0.280	15:48	F(2,4) = 6.116; p = 0.062	33.8
Summary – Tremor	-0.049	0.188	19:52	F(2,4) = 3.691; p = 0.124	33.1
Summary – Muscle Activity	0.0002	0.144	16:12	F(2,4) = 134.433; p = 0.001 **	97.4
Summary – MVC	0.011	0.054	11:32	F(2,4) = 6.155; p = 0.061	55.9
Summary – Handwriting	0.058	0.153	05:36	F(2,4) = 1.256; p = 0.378	0.0
Summary – Tapping	0.049	0.086	07:20	F(2,4) = 3.476; p = 0.134	29.7
Summary – All Measures	-0.029	0.083	18:12	F(2,4) = 55.684; p = 0.003 **	89.9

** = Statistically significant zero-amplitude test at $\alpha = 0.05$. Mesor = Midline Estimating Statistic of Rhythm; % Rhythm = Proportion of Overall Variance Accounted for by Fitted Model; CV = Coefficient of Variation; EMG = Electromyography; MMG = Mechanomyography; FDS = Flexor Digitorum Superficialis; FCR = Flexor Carpi Radialis; ECR = Extensor Carpi Radialis; RMS = Root Mean Square Amplitude; Abs Avg Vel = Absolute Average Velocity; Str Error = Straightness Error; MVC = Maximum Voluntary Contraction.

Summary z scores revealed no statistical differences in overall handwriting ($p = 0.220$, $\eta_p^2 = 0.087$), muscle activity ($p = 0.510$, $\eta_p^2 = 0.056$), maximum capabilities ($p = 0.985$, $\eta_p^2 = 0.011$), tremor ($p = 0.079$, $\eta_p^2 = 0.116$), tapping [χ^2 (6) = 2.038, $p = 0.916$] and all measures ($p = 0.540$, $\eta_p^2 = 0.053$).

Mean values at each time period was analyzed for its rhythmicity by cosinor analysis (Table 6.1). Zero-amplitude testing determined that MMG RMS amplitude ($p = 0.006$), action tremor amplitude ($p = 0.026$), overall muscle activity ($p = 0.001$), and summary of all measures ($p = 0.003$) demonstrated a rhythmicity over the 12-hour period. The acrophases for these measures ranged between 16:12 and 18:56 hrs.

5. Discussion

Only two measures revealed a statistically significant time-of-day effect: mechanomyography of a flexor forearm muscle and action tremor at 30% MVC. These two measures exhibited rhythmicity based on cosinor analysis where the respective fitted cosine model accounted for 83.1% and 63% of the overall variance. MMG and action tremor measures were also highly responsive and reliable (Study 3), and may be better suited to reveal underlying circadian effects, whereas a less repeatable measure might have high within-subject variance. Therefore there is evidence that a degree of caution might be required when interpreting daylong fatigue with these two measures, whereas the other measures may not be susceptible to, or detect, significant diurnal effects. Although the remaining measures did not reveal statistically significant time effects, most measures were characterized with similar patterns to those found in previous literature. Overall muscle activity and the aggregate of fatigue measures, in particular, demonstrated significant rhythmic behaviour.

In both MMG and action tremor responses, the observed nadir of the oscillatory function occurred at 08:00 hrs and acrophases at 18:28 and 18:56 hrs, respectively. MMG and action tremor measurement values were below the daily average during the morning (08:00 – 10:00 hrs), were above average during the afternoon (12:00 – 18:00 hrs), and decreased to the daily average, or below average, in mid-evening (20:00 hrs). Although there is sparse information on the diurnal changes associated with MMG and action tremor, diurnal rhythms of physiological tremor, particularly under constant routine conditions, have been previously reported. According to Eagles and colleagues (1955), an increase in tremor amplitude occurred during the afternoon and early evening, decreasing to a lower level of tremor in the evening. The reduction in tremor may be attributed to increased muscular relaxation as a response to mental exhaustion or tiredness (Eagles et al., 1955). Action tremor responses in this study generally agreed with this diurnal pattern. While physiological tremor and the aggregate tremor summary scores did not demonstrate significant time effects, their general trend was similar to action tremor. Acrophases for physiological tremor and aggregate tremor was 18:44 and 19:52 hrs, respectively, but there were no statistically significant rhythmical effects. On the other hand, postural tremor measured as steadiness, appeared to follow observations identified by Tyrer and Bond (1974) and Van Hilten et al., (1991). Tyrer and Bond (1974) measured tremor with the forearm and wrist supported and the hand and fingers held horizontally. The authors observed peak tremor activity at mid-morning (11:00 hrs) and a trough at 14:00 hrs. Van Hilten and colleagues (1991) found similar trends, with increased peak power, representing amplitude and duration of tremor, mid-morning (10:00 hrs) and minimal tremor power at 08:30 hrs. In our study, observable hand steadiness trends was at its highest amplitude in the morning, decreased towards 16:00 hrs, and increased towards evening hours.

Insight into the differences between the different tremor measurements, both in trend and statistical significance, might be drawn from the type of tremor exhibited. Physiological tremor is a resting tremor that occurs when a body segment is not voluntarily activated and is supported against gravity (Deuschl et al., 1998). Proposed etiologies include a central 8- to 12- Hz oscillatory mechanism derived from the inferior olive (Lamarre, 1979; De Zeeuw et al., 1998), central oscillations originating at the thalamus (Jeanmonod et al., 1996), stretch-reflex servo-loop (Lippold, 1970; Hagbarth & Young, 1979), and cardioballistic oscillations (Elble & Koller, 1990; Morrison & Newell, 2000). Postural tremor is a sub-category of action tremor and occurs when there is voluntary muscle activity to maintain a particular posture in a position against gravity (Deuschl et al., 1998). Tyrer and Bond (1974) speculated that diurnal variation in postural tremor might be linked to changes in circulating catecholamines, which was previously described to peak between 08:00 and 11:00 hrs and decrease between 11:00 and 14:00 hrs. However, the authors indicated that other factors might account for the observed variation, including arousal levels and nutrition, as the lowest tremor activity was recorded 1 hour after food consumption. Compared to physiological resting tremor, action tremor during an isometric contraction minimizes signal contamination from other sources (McAuley et al., 1997). This was further elaborated in study 3, where action tremor was preferred over physiological and postural tremor for its test-retest reliability and responsiveness. Therefore, it is conceivable that action tremor may also be highly sensitive to diurnal effects or underlying fatigue effects. The latter circumstance is speculative as participants perceived no fatigue over the 12-hour period (Figure 6.1). Another possibility for the observed differences between action and physiological tremor involve the mechanisms and sites of fatigue reflected in both measures. Action tremor, in addition to mechanisms described in physiological tremor, might additionally involve Renshaw cell inhibition (Elble & Randall, 1976; Williams & Baker, 2009), motor unit recruitment and firing (Bilodeau et al., 2009; Endo & Kawahara, 2011), and changes in metabolite concentration (Lakie et al., 2004). Interestingly, there were similarities between diurnal patterns observed in muscle activity and action tremor, which might further support the involvement of peripheral mechanisms in action tremor response. Force variation might be considered a form of action tremor, but rather than body segment accelerations, force output signals are evaluated. Fluctuations in a force signal might be a consequence of neural rhythmicity both central and peripheral in origin, including firing and recruitment motor unit behavior and decreased corticomuscular coupling between cortical output centers of the brain and muscle activation level (Christakos et al., 2009; Contessa et al., 2009; Yang et al., 2009). Diurnal patterns of force variation were also similar to those of electromyography, with a nadir at 10:00 or 12:00 hrs and decreasing signal activity in the evening.

Trends of electromyography FCR and ECR at 30% MVC indicate increasing amplitude toward the afternoon and decreasing amplitude in the evening (20:00 hrs). EMG FCR specifically exhibited this pattern with an acrophase at 15:56 hrs, with a cosinor model fit accounting for 53.4% of the variance. A related measure of muscle activity is mechanomyography. MMG detects intrinsic mechanical properties of active muscle fibres (Søgaard et al., 2003) by measuring skin surface oscillations due to radial thickening and lateral movement of active motor units (Vedsted et al., 2006). One possible mechanism of the observed increases in muscle activity (i.e., MMG and EMG amplitudes; Figure 6.3 – Summary Muscle Activity), particularly in the afternoon, may be changes in muscle/body temperature. Previous literature has shown the effect of increasing muscle temperature, as a result of an active warm-up, including improved neural transmission and enhancement of the rate of ATPase activity that increases the rate of cross-bridge cycling (Stewart et al., 2003; Mohr et al., 2004). These effects should expectedly lead to an increase in conduction velocity but at the expense of a reduction in RMS amplitude of surface EMG signals during a maximum voluntary contraction (Stewart et al., 2003). The EMG signals during a test contraction (Figure 6.1) did not appear to follow this trend, increasing in amplitude over the course of the afternoon. During a maximum voluntary handgrip contraction (Figure 6.2), EMG amplitudes did not appear to demonstrate increasing or decreasing trends. Since participants were asked to refrain from physical activity over the 2 days, muscle/body temperature may not have increased substantially to values comparable to Stewart et al., (2003). Physical activity enhances body/muscle temperature, upwards of 3°C after warm-up activities (Mohr et al., 2004; Stewart et al., 2003). However under natural conditions, body temperature increases from a minimum of 36.5°C, three hours before waking, to 37.2°C at 09:00 hrs, a peak of 37.4°C at 20:00 hrs, and a decrease to 36.5°C at 04:00 hrs (Refinetti & Menaker, 1992). Therefore, there is minimal support as to whether the magnitude of muscle activity change, specifically EMG amplitude, was a result of circadian rhythm of body temperature. Alternatively, changes in muscle activity trends may be better explained by the observed changes in maximum handgrip force.

Jasper and colleagues (2009) found that grip strength, under a constant routine methodology, was at a minimum at 06:00 and at a maximum at 18:00 hrs. Over the course of a 40-hour span sleep deprivation protocol the authors described a significant effect of time. Traditional time-of-day protocols over a normal working day, without controlling for exogenous factors, have also demonstrated a possible circadian effect. Wright (1959) observed a diurnal effect in grip strength between 06:00 to 22:00 hrs, in both left and right hands. The author found an increase in grip strength from 06:00 to 09:00/10:00 hrs, a gradual increase until 12:00/13:00 hrs, and a large decrease in strength in the evening. When tests were performed on participants over the course of 24 hours (with sleep), the diurnal pattern changed. A marked increase in grip strength was found between 06:00 and 08:00 hrs, decreased to a nadir at 14:00 hrs, increased to 18:00 hrs, and decreased in the evening. Wright (1959), however, did not perform statistical testing between time periods. Interestingly, both Jasper et al., (2009) and Wright (1959) observed a consistent decrease in grip strength during the evening (18:00 hrs onwards). In contrast, a few traditional time-of-day studies did not show an intrinsic diurnal variation of grip strength. For instance, Ishee and Titlow (1986) did not find significant differences between grip strength at 09:00, 12:00, and 15:00 hrs. In our study, similar to Ishee and Titlow (1986), there were no statistical differences in grip strength between time periods. Trends did indicate a decrease in the evening, which was consistent with Wright (1959) and Jasper et al., (2009). But contrary to findings reported by Jasper et al., (2009), maximum handgrip strength decreased from 08:00 to 16:00 hrs, with a nadir at 16:00 hrs. This diurnal pattern on the other hand was similar to Wright (1959) when measuring diurnal effects over the course of 24 hours with sleep. There is some evidence between the relationship of maximum strength and body temperature. Wright (1959) found a correlation between temperature, estimated orally, and strength, with corresponding acrophases. This relationship may only be apparent when the maximum is highly dynamic consisting of an elevated rate of contraction (Stewart et al., 2003). Stewart and colleagues (2003) assert that if the contraction is isometric or of low velocity, the rate of ATP hydrolysis is greater than required to perform the contraction, leading to a decrease in mechanical efficiency. Thus body temperature may not significantly affect isometric maximum voluntary contractions. These observations corroborate our findings, where maximum handgrip forces were not statistically different at 2-hour interval time points. The decreasing trend in maximum handgrip force may instead be indicative of neuromuscular fatigue over the course of the day. Neuromuscular fatigue might also explain increasing EMG amplitude during the 30% test contraction. But, as previously mentioned, participants were instructed to refrain from physical activity and participant's perceived fatigue did not change over the day.

Handwriting responses appeared to be variable based on individual metrics, but the summary handwriting performance (Figure 6.3D) demonstrated distinctive trends. Performance peaked at 08:00, 14:00, and 20:00 hrs, and was minimal at 12:00 and 18:00 hrs. Therefore, a decreasing pattern in handwriting performance was observed in the morning and afternoon. When fitted with cosine curves, handwriting metrics and overall handwriting performance did not exhibit a circadian rhythm. These results disagreed with Jasper et al., (2009) who found that handwriting movement speed displayed a circadian rhythm, increasing until noon and decreasing during the evening. Jasper and colleagues (2009) also found that pen pressure from stylus to tablet did not show a time effect, which was similar to our study results. However the authors did not report pen pressure trends. The trends from this study did agree with findings observed by Hölzle and colleagues (2014). In that study, the authors measured average velocity, script size, and stroke frequency over 2-hour intervals during 3 shifts (morning – 05:55 to 14:05 hrs, evening – 13:55 to 22:05 hrs, night – 21:55 to 06:05 hrs). During the morning shift, there was a statistically significant increase of velocity at 08:40 hrs compared to 06:40 hrs, but decreased until 12:40 hrs. During the evening shift, velocity decreased from 14:40 to 18:40 hrs and increased at 20:40 hrs. Finally, during the night shift, velocity decreased from 22:40 to 02:40 hrs. Therefore the decreasing trends from 08:40 and 14:40 hrs observed in Hölzle et al. (2014) were similar to trends, both in average absolute velocity and the aggregate handwriting performance, identified in this study. Unlike Jasper et al., (2009) who instructed participants to write text, this study analyzed handwriting kinematics while drawing concentric circles, a highly automated and overlearned sensorimotor skill. When considering a signature (i.e., a handwriting task that is similarly highly automated and an overlearned sensorimotor skill) compared to text of greater complexity (i.e., a single sentence or a three minute composition), Jasper et al., (2009) demonstrated decreasing frequency from 09:00 to 15:00 hrs and an increase from 15:00 to 21:00 hrs. These changes in frequency were consistent with trends found in this study. Increases in writing complexity may lead to changes in speed of production and pen pressure, however there remains considerable debate as to the influence of complexity (Graham & Weintraub, 1996). For instance, Hölzle and colleagues (2014) did not find differences in fine motor performance between drawing circles and writing a single word, therefore they analyzed the mean data across both superimposed circles and text. Although there appeared to be differences between text complexities, based on trends, Jasper et al., (2009) did not find statistical significance and later averaged the three handwriting tasks to evaluate time-of-day differences. A hallmark of the Jasper et al., (2009) study was its use of a constant routine protocol. The Hölzle et al., (2014) study and the present study were time-of-day studies over the normal working day, and as such, expected circadian patterns that was identified by Jasper et al., (2009), may have been masked by exogenous factors. One exogenous factor is the possibility of food consumption and extended break times that might have occurred before 08:00, 14:00, and 20:00 hrs. A number of studies have shown the effect of mid-day meals on cognitive function and performance. One consistent finding is the "post-lunch dip", which signifies a reduction in performance after a mid-day meal (Gibson & Green, 2002). This effect, however, is more pronounced for short, memory-loaded tasks rather than short perceptual tasks (Smith & Miles, 1987), and there is limited evidence for its effect on fine motor activity. There is some evidence that feeding regimens, possibly through mediation of neuropeptide Y in the medial hypothalamus, might entrain normal circadian rhythms (Dallman et al., 1993). Since handwriting performance seemed to increase in the afternoon and participants did not report food intake, it remains inconclusive whether food intake by itself led to the observed responses.

The number of tapping errors appeared to decrease from 08:00 to 18:00 and subsequently returned to morning values at 20:00. Although tapping frequency was fixed at a rate of 90 taps per minute, average tapping frequency was recorded. Tapping frequency increased in the morning, decreased at 18:00, and increased at 20:00. These trends are generally consistent with Monk and Leng (1982) who found that in simple perceptual motor tasks, there was a change in strategy. Over a day, there was an increase in speed but became progressively less accurate (i.e., increased number of errors). Not surprisingly, when considering overall tapping performance, which might reflect speed-accuracy efficiency, z-score values remained close to 0 (i.e., mean daily performance) throughout the 12-hour collection period. Craig and Condon (1985) assessed speed-accuracy trade-off over 15-hours and found that speed increased at the expense of accuracy, meanwhile efficiency remained relatively stable. When participants were given the option to prioritize speed or accuracy, performance was faster but less accurate later in the day. As a result, Smith (1992) suggested that the speed-accuracy trade off was not a result of adopting a particular strategy at a given time. But like handwriting performance, there is uncertainty as to whether the diurnal pattern is due to time of day or merely a circumstance that coincidentally occur at these times.

A major limitation of this study is the use of a traditional time-of-day protocol in lieu of a constant routine schedule. A traditional time-of-day protocol over a normal working day might have led to changes to expected diurnal patterns. For instance, exogenous factors such as physical activity and food consumption might entrain normal circadian rhythms. However, participants were instructed to refrain from physically intensive activity and caffeine consumption, which might reduce external and internal influences that mask true endogenous rhythms, and participant's perceived fatigue of the upper extremities did not change over the day. A strength of this study is the evaluation of a set of 11 novel fatigue measures that reflect central and peripheral mechanisms, which may be considered for laboratory and field use. These 11 measures were assessed over two, 12-hour periods, which encompass hours of a typical working day. However, it remains

6. Conclusion

Endogenously generated diurnal rhythms might affect interpretability of physiological signals that are measured over the course of a day. Measuring and interpreting fatigue responses, in particular, might be challenging if these endogenous rhythms mask fatigue responses. This study aimed to investigate the effects of 12-hour diurnal changes on selected fatigue measures in a traditional time-of-day protocol over a normal working day. Mechanomyography root mean square amplitude (MMG RMS) and action tremor root mean square amplitude (Action Tremor RMS) during a sub-maximal test contraction demonstrated rhythmic behaviour, with significant time effects from 08:00 to mid-afternoon and early evening. Circadian rythmicity was also observed in overall muscle activity and the aggregate of all measures. Although trends of remaining measures were generally consistent with findings reported in previous literature, they did not indicate significant time of day effects or rhythmical circadian behaviour. Therefore, additional analytical considerations might be required when interpreting daylong responses of

MMG and action tremor, whereas the remaining measures were not significantly affected by intrinsic diurnal variability.

Chapter 7

Task Dependent Specificity of Fatigue Measures During Low-Load Exercise

Abstract
Mechanisms underlying fatigue may be task dependent, influenced by factors such as type of contraction, intensity, and muscle group. Consequently the responsiveness of fatigue measures might be contingent on these work or exercise parameters. The aim of this study was to evaluate selected fatigue measures during time varying intermittent isometric and sustained isometric exercises, with breaks and no breaks, and at both hand and shoulder at force ranges relevant to the development of work-related musculoskeletal disorders. Although no single measure was highly responsive in *all* conditions, there were measures that were responsive in *most* conditions, as either a test battery or continuous measurement. These measures reflect both central and/or peripheral mechanisms: action tremor and maximum voluntary contraction. Rating of perceived fatigue was also found to increase with exercise progression in hand conditions.

1. Introduction

Previous research has emphasized the importance of fatigue measurement in ergonomics and workplace evaluation. Prevailing ideas suggest that fatigue is linked to human performance outcomes, including work quality and productivity, and is possibly a precursor to work-related musculoskeletal disorders (MSD). However, since fatigue is a multidimensional construct, which consists of a complex interaction between central and peripheral mechanisms, there are resultantly a considerable number of measures and measurement parameters. Ideally a test battery of fatigue measures, reflecting multiple domains, can be devised to provide a comprehensive picture of fatigue development (Yung et al., 2014).

A recent study identified 57 fatigue measures or measurement parameters for both field and laboratory settings (Study 1). Seven conventional and novel measurement tools were selected for their perceived validity, reliability, and practicality, and their relationship to work productivity and quality in a field setting (Study 2). In addition to these seven measures, a total of 11 fatigue measures were then evaluated for their test-retest reliability and sensitivity in a controlled laboratory experiment (Study 3), and their response to 12-hour endogenously generated diurnal variation (Study 4). Although it appeared that some measures were responsive to physically demanding work over the day and work week (Yung et al., 2014), and at mechanical exposure levels typically carried out in laboratory studies, e.g., mean amplitude of 30% MVC (Study 3), there remains limited evidence for their responsiveness at force levels relevant to the development of musculoskeletal disorders. These physical workload exposures are typically below 15% MVC (Westgaard & Winkel, 1996).

To further complicate the selection of a test battery of fatigue measures, mechanisms underlying fatigue may be influenced by the task, the environment, and physical characteristics of the individual (Enoka & Stuart, 1992; Weir et al., 2006). Of particular interest are task-specific influences. One task-dependent factor is the intensity and duration of activity. As an example, the predominant mechanisms of fatigue during a marathon race might be different from mechanisms associated with a maximal weightlifting activity (Weir et al., 2006). During long distance running, deficits central in origin are often implicated in observed fatigue response, particular at the spinal (e.g., afferent input, motoneuron properties) and/or supraspinal levels (e.g., biochemical changes including serotonin and dopamine). Therefore, prolonged submaximal tasks are often associated with central factors (Gandevia, 1998). On the other hand, higher intensity activity may be characterized by fatigue where intramuscular factors appear to dominate (Westerblad et al., 2010). For example, the reduction in muscle glycogen may play an important role in demanding tasks/activities that require repeated, intense efforts, particularly with the involvement of large muscle groups (Green, 1997). These exercise intensities range from 60 to 85% of maximal aerobic power (Green, 1991). The type and speed of contraction might also influence fatigue development. In an example, neuromuscular fatigue mechanisms were examined based on the type of muscle contraction. Babault and colleagues (2006) observed that fatigue indeed was dependent on muscular contractile condition, where concentric conditions led to pronounced peripheral impairments followed by central fatigue. Isometric conditions, on the other hand, led to an inverted pattern: central fatigue developed first followed by peripheral fatigue. Finally, fatigue may be task dependent, based on the muscle groups involved, including the affect of muscles classified by morphological features, muscle fiber type, muscle mass, function (e.g., flexors, extensors, single or multi-joint), synergistic activity, and degree of direct cortical control (Enoka & Stuart, 1992). Previous research has demonstrated the influence of fibre type and cross-sectional area on EMG parameters (Kupa et al., 1995) and on mean firing rates (Bigland-Ritchie & Woods, 1984). For instance, muscle architectural parameters have been asserted as the best predictors of muscle function, where physiological cross-sectional area (PCSA) is directly proportional to isometric muscle force (Lieber et al., 1992; Liu et al., 2014).

Both the relative muscle size and distribution of fibre types (i.e., the relative area of the muscle occupied by Type I fibres) is strongly associated with muscle fatigability (Mannion et al., 1998). However, although task dependency is an important attribute in fatigue research, the exact contributions from central and peripheral mechanisms remain unknown.

Due to the apparent task dependency nature of fatigue, the sensitivity of measures might be contingent on work or exercise parameters (e.g., cycle time, duty cycle, mean force amplitude, type of contraction, muscle groups involved). This study thus focused on the responsiveness of select fatigue measures by changing the type of contraction (intermittent isometric vs. sustained isometric), the intensity (rest breaks vs. no rest breaks), and body region (muscle groups involved in handgrip vs. shoulder flexion). An intermittent isometric condition was selected to represent a condition where there were changes in muscle length, similar to a concentric contraction. Previous studies on isometric contractions, including intermittent isometric, have demonstrated changes in muscle architecture leading to an alteration in contractile capacity of the muscle-tendon unit (Mademli & Arampatzis, 2005). Intermittent isometric exercise has also been a well-studied activity, providing opportunity for comparisons to previous literature. And additionally, unlike continuous dynamic isotonic contractions, intermittent isometric exercise controls for the possible involvement of an eccentric phase, which might complicate interpretation. Conditions consisted of exerted forces of magnitudes and patterns relevant to the development of MSDs during various fatigue exercises, representing: tasks characterized by time-varying intermittent isometric force at the hand, tasks characterized by an isometric sustained force output at the hand, tasks characterized by continuous time-varying changes in force without test-battery breaks, and time-varying changes in force exerted by the shoulder.

More specifically, this paper will address the following questions:

(1) In each condition, which measure(s) is/are most responsive when measured as a test battery or as a continuous measure? In each condition, which measure(s), as a test battery or as a continuous measure, will show differences over time?
(2) How does the responsiveness of measures compare between task-dependent factors (i.e., type of contraction, exercise intensity based on break allowances, body region)? How does fatigue develop over time?
(3) Is there a measure or battery of measures that is responsive in all exercise conditions? Are continuous and test battery responses comparable?

2. Methods

2.1 Participants

Sixteen healthy university-aged participants (8 males, 8 females; mean age = 20.7 years, SD = 2.2; mean height = 173.9 cm, SD = 6.8; mean weight = 65.6 kg, SD = 9.4) were recruited to participate. All participants had no current injuries or injuries in the previous 6 months to the dominant upper extremity. Participants were also asked to refrain from exercise of the upper extremities, caffeine, and alcohol consumption, 24 hours prior to all test sessions. Prior to the experimental session, informed consent was provided for all experimental procedures and associated risks, as approved by the University Of Waterloo Office Of Research Ethics.

2.2 Test Battery of Fatigue Measures

The test battery consisted of 7 measures that were selected based on findings from the preceding studies. These measures were analyzed for their amplitude, which in most cases, have been found to be most responsive to fatigue during prolonged low-level dynamic contractions (e.g., de Looze et al., 2009; Bosch et al., 2007; Leyk et al., 2006). A typical test battery required 145 seconds, on average, to perform.

Accelerometer and electrode placement sites were marked with an indelible felt tip pen at the conclusion of each test session, to ensure consistent placement between test sessions. All measures were collected at a sampling frequency of 2048 Hz and data was post-processed with LabChart 7 (ADInstruments, Colorado Springs, CO, USA) and analyzed with MATLAB 7.2 (Mathworks, Inc., Natick, MA, USA). Measures were performed in the following order:

2.2.1 Visual Analog Scale (VAS) – Perceived Fatigue

Previous studies have demonstrated the utility of a visual analog scale as an index of musculoskeletal fatigue (e.g., Leung et al., 2004). In Leung et al., (2004), there was a moderate correlation (0.73), comparable with other applications of VAS, between increasing load and fatigue scores yielded by a visual analog scale. Self-reported perception of fatigue was obtained with a 10-cm visual analog digital scale. Anchor points represented “no fatigue” and “maximum fatigue”. Participants were asked to place the sliding tab along the 10-cm line with the assistance of a body diagram (Corlett & Bishop, 1976) for their hand/forearm and shoulder of the dominant hand. Ratings of perceived fatigue were later expressed as a value between 0 and 100.

2.2.2 Physiological Tremor

A ±3 g tri-axial accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA sensitivity=300 mV/g, noise density=250 μg/rtHz, 4mm x 4mm x 1.45mm) was placed on the dorsum of the hand, on the distal part of the third metacarpal bone. Participants were instructed to adopt a seated posture, with their elbow and forearm supported on the armrest and their hand fully relaxed for a period of 10 seconds. Participants were asked to avoid looking at the hand due to possible visual-dependent peaks in hand tremor (McAuley et al., 1997). Signals were bandpass filtered (Butterworth, 2nd Order, 1 and 20 Hz for hand, elbow, and shoulder, 1 and 30 Hz for finger) and analyzed in the time domain. Instantaneous root mean square amplitude was calculated at 1-second windows and averaged for the middle 8-seconds.

2.2.3 Postural Tremor

Tri-axial accelerometers (ADXL327, Analog Devices, Inc., Norwood, MA, USA) were mounted on bony landmarks of: the tip of the index finger, the dorsum of the hand, the dorsum of the wrist (above the capitate bone), the lateral epicondyle of the humerus, and the acromioclavicular joint of the shoulder. These placements were similar to those used by Carignan and colleagues (2012). Participants were instructed to point with an extended finger (at the metacarpophalangeal joint) towards a target. At the hand, the thumb was adducted and fingers 3, 4, and 5 were flexed, forming a loose fist (Morrison & Newsell, 2000). Postural tremor of the finger, hand, wrist, forearm, and shoulder were respectively measured with the hand supported (finger tremor), the wrist supported (hand tremor), the elbow supported (forearm tremor), and the shoulder flexed (shoulder tremor). When targeting, the unsupported segment(s) were outstretched, with an extended finger, pronation of the forearm, and extended elbow, and 90-degree flexion of the shoulder. In all trials, participants were asked to lean against the backrest to minimize body sway. Signals were digitally bandpass filtered between 1 and 30 Hz (Butterworth, 2nd Order). Instantaneous RMS amplitude was averaged for the middle 8-seconds of the 10-second data collection. Frequencies of interest for all segments of the upper limb typically lie between 1 and 30 Hz and there is little power in the frequencies of postural tremor above this value (Morrison & Newell, 2000; Carignan et al., 2012).

2.2.4 Action Tremor

Accelerometers mounted on the dorsum of the hand, finger, elbow, and acromioclavicular joint also served to measure action tremor during a handgrip contraction at 10% MVC or shoulder flexion at 10% MVC. The acceleration signals were Butterworth bandpass filtered (2nd Order) between 1 and 30 Hz. The instantaneous RMS amplitudes were calculated and averaged for the middle 8-seconds of the 10-second collection duration. Participants used visual feedback (LabView, National Instruments Corporation, Austin, TX, USA), to perform test contractions.

2.2.5 Surface Electromyography (EMG)

Electromyography was recorded using bipolar surface electrodes (Ag-AgCl electrodes, Ambu Blue Sensor N, Denmark) with an inter-electrode distance of 20 mm, placed on the belly of the extensor carpi radialis, flexor carpi radialis, upper trapezius, and anterior deltoid. These muscles were selected as both flexors and extensors co-contract during a maximal power grip, anterior deltoid is involved during shoulder flexion and upper trapezius serves as a shoulder stabilizer. Electrode placement sites were based on the recommendations in Delagi et al., (1975), Cram and Kasman (1998), Zipp (1982), and Soderberg (1982). Hair was removed by razor and skin abraded with ethanol and prepared with NuPrep Gel (Weaver and Company, CO, USA). EMG signals were collected with an eight-channel data system (Bortec, Calgary, AB), with a common mode rejection ratio of >115 dB and a band-pass filter between 10 and 1000 Hz. Signals were amplified and sampled at 2048 Hz. Muscle belly sites were marked with an indelible felt tip pen to ensure consistent placement between exercise conditions. The instantaneous root mean square (RMS) amplitude were calculated and normalized to the MVC at 1-second epochs and averaged for the middle 8-second window of the 10-second test contraction at 10% MVC.

2.2.6 Mechanomyography (MMG)

A low profile (4mm x 4mm x 1.45mm) tri-axial ± 3 g accelerometers (ADXL335, Analog Devices, Inc., Norwood, MA, USA; sensitivity = 300 mV/g, noise density = 250 μg/rtHz) measured mechanical responses of flexor digitorum superficialis and anterior deltoid. MMG accelerometer placements were selected to minimize clutter of equipment while reflecting general flexor activity. The accelerometer were placed on the muscle belly with double-sided tape and loosely secured with medical transpore tape. Participants used visual feedback to perform a 10% test contraction to measure MMG. MMG signals were digitally bandpass filtered at 5-100 Hz (Butterworth, 2nd order). Similar to EMG, the instantaneous root mean square (RMS) amplitude were calculated and normalized to the MVC and averaged for the middle 8-seconds of the test contraction.

2.2.7 Maximum Voluntary Contraction & Test Contraction at 10%MVC

Participants were asked to exert a maximum handgrip force and test contraction with a handgrip dynamometer (Medical Research Ltd., Leeds, UK). The handgrip dynamometer was mounted vertically from a custom fabricated apparatus to minimize fixation rigidity that is associated with high frequency attenuation (McAuley et al., 1997). The dynamometer was placed within comfortable reach of the participant. Participants were asked to comfortably rest their elbows while exerting handgrip forces.

A maximum shoulder contraction was elicited by shoulder flexion with a strap system connected to a load cell. The load cell was attached to a rigid column and the strap was cuffed above the elbow joint of the participant's dominant arm. Participants were asked to flex their shoulder with their thumb pointing forward. The strap system allowed participants to fully relax (i.e., minimal muscle activity) in the absence of mechanical force output.

Force signals was linear enveloped with a Butterworth 2nd order dual lowpass filter at 10 Hz. Force variation was measured by calculating the average coefficient of variation at 1 second epochs of the middle 8-seconds of the 10 second test contraction. Test contraction amplitude was determined from the 3 maximum voluntary contractions performed at the beginning of all test sessions. The middle 3-seconds of the 5 second MVC was windowed and values were averaged.

2.2.8 Sensory Detection Threshold

Semmes-Weinstein monofilaments have been shown to provide a repeatable stimulus for objective cutaneous sensory testing and were included as a test battery measure. Sensory detection threshold was measured at the upper distal extremity, on the palmar surface of the hand, similar to methods described in Schreuders et al., (2008). Measurements were also taken on the dorsal side of the hand, the flexor compartments of the forearm, the anterior deltoid, and upper trapezius. Locations were marked with an indelible felt tip pen to ensure consistent testing. These locations were based on the Weinstein Enhanced Sensory Test (WEST) for hand and body screening (Skirven et al., 2011). The hand was supported and screened to prevent participant observation of monofilament application. Starting with the 2.83 monofilament, the filament was applied to various areas around the hand and forearm, varying location and time of application. Similarly, stimuli were applied in random order to the belly of the anterior deltoid muscle. For thin filaments, three touches were considered as a single test. Tests were performed with progressively thicker filaments, with participants indicating whether they perceived a touch. Due to the time required for testing, sensory detection threshold tests were performed at baseline and at the end of the test session. The hand, forearm, anterior deltoid, and upper trapezius locations and monofilament marking numbers were recorded.

2.3 Continuous Fatigue Measurement

EMG, MMG, action tremor, and force variability were continuously monitored during the exercise conditions. Continuous measures were analyzed on a contraction-to-contraction basis for time varying profiles (i.e., plateau of each square wave or contraction phase of the dynamic protocol) or every 6-seconds in 3-second windows (i.e., sustained isometric contraction). The detailed analytical procedures for each continuous measure were described in section 2.2.

2.4 Visual Feedback System

Participants performed test contractions and the fatiguing protocol by force control with the assistance of a visual feedback system (LabView, National Instruments Corporation, Austin, TX). Visual feedback has been shown to be comparable to proprioceptive feedback (i.e., position control) in long-term response (Søgaard et al., 2003). However, visual feedback may involve a complex control loop, which may increase the amount of variation in motor unit recruitment pattern (Søgaard et al., 2003). Auditory feedback was also provided to assist participants in performing contractions at a fixed duty cycle and cycle time.

When performing postural tremor tests, a visual feedback system (Leap Motion Inc., San Francisco, California) provided a target for participants to engage. Using two monochromatic IR cameras and three infrared LEDs, the Leap Motion system tracks hand and finger motion. At a pre-determined target location, participants were asked to point at this target for a 10-second duration (Figure 7.1).

Figure 7.1 Postural Tremor Tests of the Hand

Participant points with an extended finger towards a target, provided by visual feedback (left visual display monitor). The wrist and forearm was supported with an arm rest and data recorded for 10 seconds.

2.5 Exercise Conditions

All participants performed four fatiguing conditions. An intermittent isometric handgrip protocol, representative of tasks characterized by time-varying changes in force (i.e., mean force amplitude at 15% MVC, duty cycle 50%, cycle time 6 seconds), served as a reference condition (REF). The mean amplitude of 15% MVC is within force ranges documented in previous fatigue studies (e.g., Nussbaum et al., 2001, Yung et al., 2012). This reference condition was used to compare differences in fatigue measure responsiveness between task parameters and between body segments or parts. The intermittent isometric handgrip was compared to a sustained isometric handgrip contraction at 10% MVC (SUS), which represents force levels most relevant to sedentary or light production work (Westgaard & Winkel, 1996). Even at an isometric contraction at 10% MVC, forearm blood flow has been reported to be insufficient (Byström & Kilbom, 1990). At the hand/arm, participants performed the reference condition with no test batteries *during* exercise, i.e., a no break condition (NB). For the NB protocol, test batteries were performed at baseline, and at cessation. Additionally, one fatiguing condition focused on the manifestation of fatigue at the shoulder (SH). In this condition, participants performed an intermittent shoulder flexion isometric exercise at a duty cycle of 50%, cycle time of 6 seconds, and mean amplitude of 15% MVC. These conditions are summarized in Table 7.1.

Table 7.1 Exercise Condition Parameters

Exercise Condition	Type of Contraction	Body Segment	Mean Force Amplitude	Cycle Time	Duty Cycle	Test Battery Collection Intervals
Reference (REF)	Intermittent Isometric	Hand/Arm	15% MVC	6 Sec	50%	10 Minutes
Sustained (SUS)	Sustained Isometric	Hand/Arm	10% MVC	-	100%	10 Minutes
No Break (NB)	Intermittent Isometric	Hand/Arm	15% MVC	6 Sec	50%	Pre/Post
Shoulder (SH)	Intermittent Isometric	Shoulder	15% MVC	6 Sec	50%	10 Minutes

Exercise protocols were randomized and performed on separate test sessions with at least 1 day apart, to minimize potential residual effects between conditions. Although a period of 7 days has been introduced to minimize carry-over effects in previous studies (e.g., Yung et al., 2012), Ebenbichler and colleagues (2002) showed little differences in EMG between fatiguing conditions (i.e., repetitive lifting and lowering of 13 kg box for 4.5 minutes) within a day (2 hours apart) and between days (2 weeks apart). However, this may be dependent on the intensity of the fatiguing activity. Each participant performed the exercise conditions at a consistent time of day to minimize possible circadian effects.

2.6 Protocol

Prior to *all* test sessions (pre-experiment), participants performed three maximum handgrip contractions and three maximum shoulder flexion contractions, which were used to determine normalized forces for all exercise protocols. Two minutes was provided between each maximum contraction. Additionally, participants were given ample time to familiarize themselves with all exercise protocols and test battery measures.

At the beginning of *each* test session (pre-session), participants performed three maximum contractions for each muscle of interest (i.e., ECR, FCR, anterior deltoid, upper trapezius) with at least 2 minutes in between tests. Maximum isometric exertions were elicited against a series of quasi-static and handgrip contractions, while simultaneously collecting EMG and MMG activity. The average peak of the three maximum contractions for each muscle assisted in normalizing physiological signals (e.g., EMG and MMG) for that condition. Following the maximum voluntary contractions, participants performed a baseline test battery. Time was provided before baseline and before the exercise protocol to minimize fatigue effects as a result of exerting maximum contractions. Participants were then asked to begin the exercise protocol, until volitional fatigue. Alternatively, the protocol was terminated if participants were not able to maintain tracking performance and return to targeted forces (i.e., 50% decrease of force output during fatiguing protocol over consecutive contractions and reduction of MVC to less than 60% MVC), or after 60-minutes of continuous exercise. A block of approximately 60-minutes of continuous activity has been previously used when simulating a full workday (e.g., Dennerlein et al., 2003).

Continuous measures were collected during each 3-second contraction, or every 6 seconds, for a 3-second window (sustained condition). Test batteries were performed at baseline, at 10-minute intervals during exercise, and immediately at the cessation of exercise. Semmes-Weinstein test, measuring sensory detection threshold, was performed at the beginning and end of each test session (Table 7.2).

Table 7.2 Fatigue Measurement Collection Strategies

Type of Measurement	Recording Strategy	Measurements
Continuous	During Exercise	EMG (FCR, ECR, Anterior Deltoid, Trapezius), MMG (FDS or Anterior Deltoid), Action Tremor (Finger, Hand, Wrist, Elbow, Shoulder), Force Variation (Coefficient of Variation)

Test Battery	Discretely at 10-minute intervals	**EMG (FCR, ECR, Anterior Deltoid, Trapezius), MMG (FDS or Anterior Deltoid), Action Tremor (Finger, Hand, Wrist, Elbow, Shoulder), Force Variation (Coefficient of Variation)**, Physiological Tremor (Hand/Shoulder, Finger, Wrist), Postural Hand Tremor (Hand, Finger), Postural Forearm Tremor (Hand, Finger, Wrist), Postural Shoulder Tremor (Hand, Finger, Wrist, Elbow, Shoulder)
Pre/Post	Before & After Testing	Semmes-Weinstein Monofilament Sensory Detection Test

Bolded measures denote common measurements collected as a test battery and continuously.

2.7 Data Management & Statistical Analysis

Fatigue measures and measurement parameters were compared as the slope over the test batteries, compared as the rate of response over the entire exercise period, evaluated as a test battery at 10-minute intervals, and evaluated as a continuous measure in 10-minute blocks. These analytical methods allowed for a comparison between measures (slopes) and determined how these measures change over time (10-minute intervals/blocks).

To calculate rate of response, as both continuous and test battery measurement, data for each participant was normalized to baseline and fitted with linear and non-linear regression while constraining the intercept at baseline values (i.e., normalized to 1). Linear regression was found to maximize the coefficient of determination, on average, in all measures in both continuous and test battery data. The slope of the linear regression was considered as the rate of response (%/3 seconds for continuous, %/test battery for test battery). All expected directions were considered positive values, i.e., a negative slope for MVC is interpreted as a reduction in force capability but its inverse was retained to compare magnitudes of rate of response. Slopes that do not follow the expected direction of change were categorized as a negative rate of response.

A two factor (condition and measure) mixed model repeated measures analysis was performed on rate of response for test battery and continuous data. For test battery data, 27 measurement parameters of interest were considered. Tremor signals along the individual axes were excluded, but resultant tremor signals were retained, to allow for comparisons between hand and shoulder exercises. All slopes were composed of test battery values during exercise, with the exception of continuous intermittent, which is limited to test batteries at the beginning and end of exercise. Linear regression coefficient of determination (r^2) ranged from 0.187 to 1. For continuous measurement, 14 measures of interest were compared. These measures were limited to those measures that can be recorded simultaneous to exercise (e.g., EMG, MMG, force variation, action tremor). Coefficient of determination (r^2) ranged between 0.215 and 0.812. For both continuous and test battery analysis, if a main effect was observed, Tukey-Kramer post hoc tests were performed for all pairwise comparisons. A separate mixed-model analysis and Tukey-Kramer post hoc tests was performed, stratifying by condition, to compare all measures within each condition, in the event of significant interaction effects (condition*measure). For test battery data, a mixed model repeated measures analysis was performed with time (baseline, test batteries after 10 minutes, 20 minutes, 30 minutes, 40 minutes, 50 minutes, cessation, and after 1 minute recovery) as the within-subject factor for each measure in three conditions (REF, ISO, SH). NB was limited to comparisons at baseline, cessation, and recovery. For continuous measurement in 10-minute blocks, separated by a test battery, data was fitted with linear or non-linear regression. The slope of the regression equation that maximizes the coefficient of variation (r^2 ranged between 0.158 and 0.725) across all conditions and all participants were compared with a mixed model repeated measures analysis over the 6 blocks of time (60 minutes of exercise). This analysis was performed with the exception of NB, as exercise was not sectioned in 10-minute intervals. In both test battery and continuous analysis, Tukey-Kramer post hoc tests were performed in the presence of significant main effects.

Finally, principal components analysis (PCA) was executed on sustained isometric, intermittent isometric, and shoulder conditions, to help extract sets of variables (i.e., fatigue measures) that account for most of the variation of the original multivariate data. Although PCA requires independence of data for inferential analysis, if the main objective is descriptive, non-independence, such as time series data, does not pose a substantial limitation (Jolliffe, 2002). Therefore, PCA was executed in order to descriptively analyze salient features and patterns. After data was normalized (z-scores), factors were extracted and rotated with Varimax rotation. The number of principal components was determined by the total explained variance, explaining at least 70% of the total variance, and Scree plots. Eigenvector coefficients greater than a cutoff value of 0.40 were associated with a particular component. To describe each principal component, measures and their directions were interpreted based on strong theory and their responsiveness during a fatiguing protocol. For instance, since an increase in EMG amplitude is a compensatory response to peripheral impairment, a positive EMG amplitude response reflects peripheral fatigue whereas a negative response is indicative of central fatigue. The interpretation of all measures in each component, with particular emphasis on measures that reflect a single domain (i.e., central or peripheral), helped assign the component as "central fatigue indicators", “peripheral fatigue indicators”, “central or peripheral indicators but predominantly central or peripheral”. After PCA loadings were determined and interpreted, projections of original data onto the eigenvectors for each mode were interpreted descriptively to determine the relationship of principal components among observations (i.e., time). Essentially, this is the average, over time, of all measures that compose a principal component. The projections were later averaged, and weighted based on total % variance, to form an aggregate projection to help visualize trends. These methods were similar to Hubley-Kozey et al., (2006) in reconstructing and analyzing patterns. All statistical tests were carried out with an alpha level of 0.05 and residual analysis was performed to examine model assumptions. Analyses were completed using Statistical Analysis Software (9.3, SAS Institute Inc., Cary, NC, USA) with the exception of PCA, which was analyzed with MATLAB 7.2 (Mathworks, Inc,. Natick, MA. USA).

3. Results

Participants performed all conditions until exhaustion or up to 60 minutes. The exercise protocol was also terminated if participants could not achieve targeted forces or desired cycle time and duty cycle. The average endurance time for the REF condition was 57.3 minutes (SD = 9.1), the NB condition was 52.9 minutes (SD = 12.9), ISO was 50.0 minutes (SD = 20.8), and SH condition was 60 minutes (SD = 0; i.e., all participants required the full 60-minute period). These endurance times, however, were not statistically different [χ^2 (3) = 6.353, p = 0.096]. The average muscle activity and forces for each exercise condition are reported in Table 7.3. For brevity, statistically significant outcomes are described and other analyses are presented in Appendix B.

Table 7.3 Actual Muscle Activity and Force Output During Contractions Recorded in the First

	EMG 1 (%)	EMG 2 (%)	MMG (%)	Force (%)
Intermittent Hand	20.0 (9.3)	23.0 (7.9)	30.2 (15.2)	34.6 (7.9)
Sustained Hand	7.1 (5.1)	11.8 (5.1)	12.7 (7.9)	12.3 (2.7)
Continuous Intermittent Hand	23.2 (12.9)	28.4 (13.3)	29.2 (11.2)	36.6 (5.6)
Intermittent Shoulder	14.3 (8.5)	12.2 (23.2)	17.7 (8.2)	36.5 (3.6)

Minute of Exercise. EMG 1 = FCR or Anterior Delt. EMG 2 = ECR or Trapezius

3.1 Comparing Conditions Based on Aggregate Data

Continuous measurements were expressed as a percentage increase, from baseline, every 3 seconds. A two-factor mixed model revealed a significant condition effect (F = 5.96, p = 0.002; Figure 7.2A), a measure effect (F = 4.63, p = 0.04), and a significant condition and measure effect (F = 2.26, p = 0.003). Hand intermittent REF condition was statistically different from NB and

SUS. When considering all conditions, although a significant main effect was identified, after Tukey-Kramer post-hoc adjustment, no significant pairwise comparisons between measures were found (Figure 7.3A). After stratifying by condition, no statistical differences were found in SH and REF. Hand tremor (i.e., action tremor) amplitude was found to have a rate of response of 1.073%/3 seconds and was statistically different from EMG amplitude of the upper trapezius during the sustained condition (Figure 7.4B). The NB hand intermittent condition led to a RMS finger tremor increase of 0.576%/3 seconds. Finger tremor amplitude was statistically quicker than EMG of the flexor carpi radialis ($p = 0.04$) and extensor carpi radialis ($p = 0.009$), tremor amplitude of the shoulder ($p = 0.026$), and force variation ($p = 0.036$) during the NB condition (Figure 7.4C). The two-factor mixed model analysis also allowed for comparisons of measures between conditions. When comparing measures between REF and SUS (intermittent vs. sustained), between REF and NB (breaks vs. no breaks), and between REF and SH (hand vs. shoulder), there were no statistical differences between conditions for the same measure. However, tremor amplitude of the hand along the Y-axis (SUS) was greater than the tremor amplitude of the shoulder (REF), $p = 0.043$. Finger tremor amplitude during NB exercise had a quicker rate compared to EMG of the FCR ($p = 0.029$), MMG of the FDS ($p = 0.028$), hand tremor amplitude along the y-axis ($p = 0.049$), tremor amplitude of the shoulder ($p = 0.014$), and force variation ($p = 0.044$) during the REF condition. There were no differences of measures between REF and SH conditions.

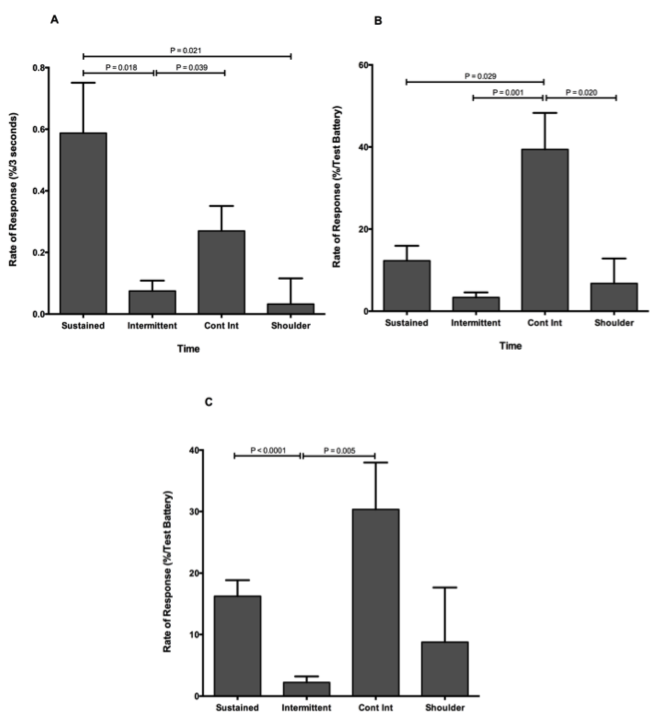


Figure 7.2 Comparing Conditions with Rate of Response Based on All Measures.

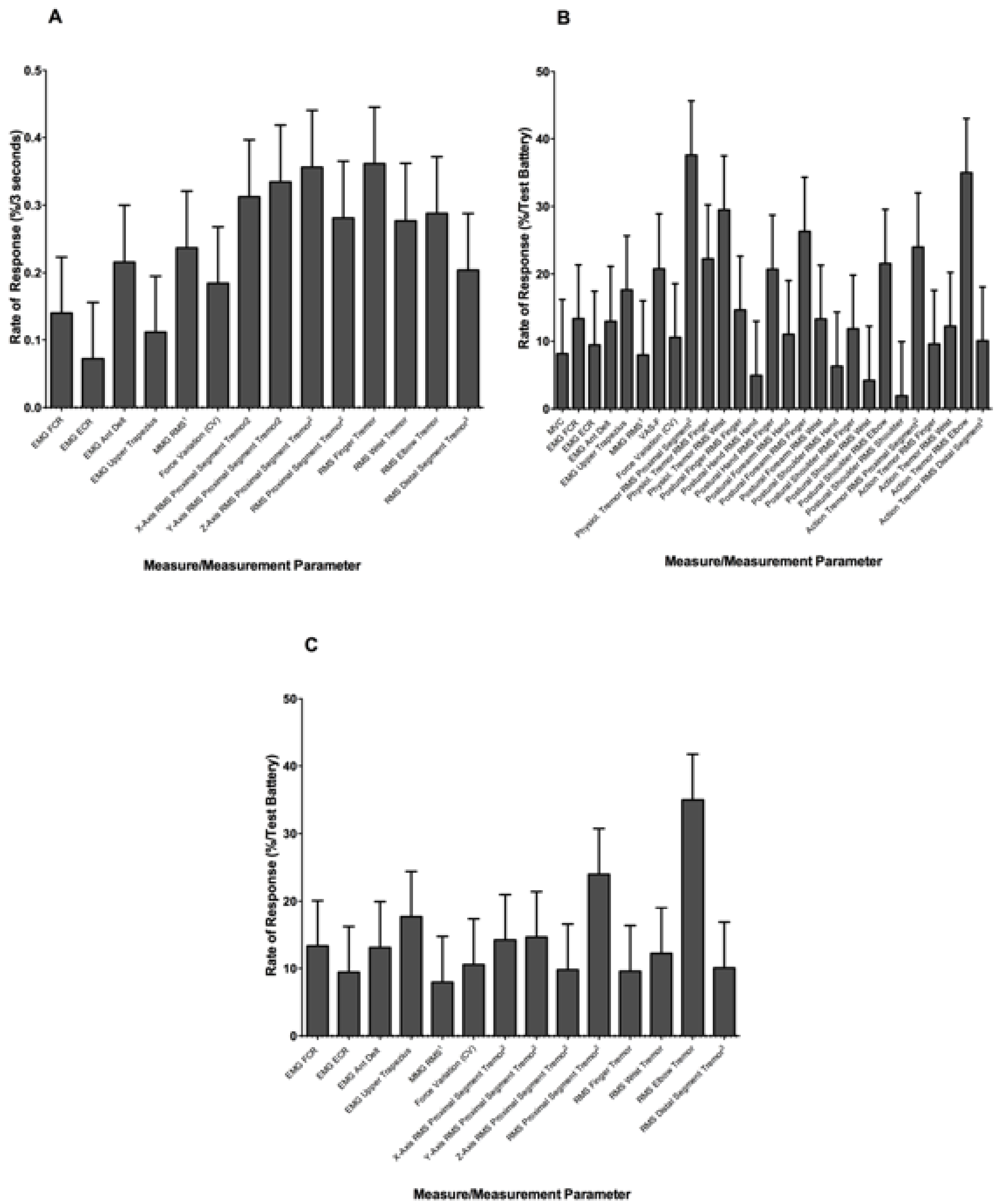


Figure 7.3 Comparing Measures with Rate of Response in All Conditions.

A: Continuous Measurement of 14 measures. B: Test battery of 27 measures/measurement parameters. C: Test battery measurement of 14 measures similar to continuous measurement. [1]Flexor digitorum superficialis for hand exercises or anterior deltoid for shoulder exercise. [2]Hand tremor for hand exercises or Shoulder tremor for shoulder exercise. [3] Shoulder tremor for hand exercises or Hand tremor for shoulder exercise.

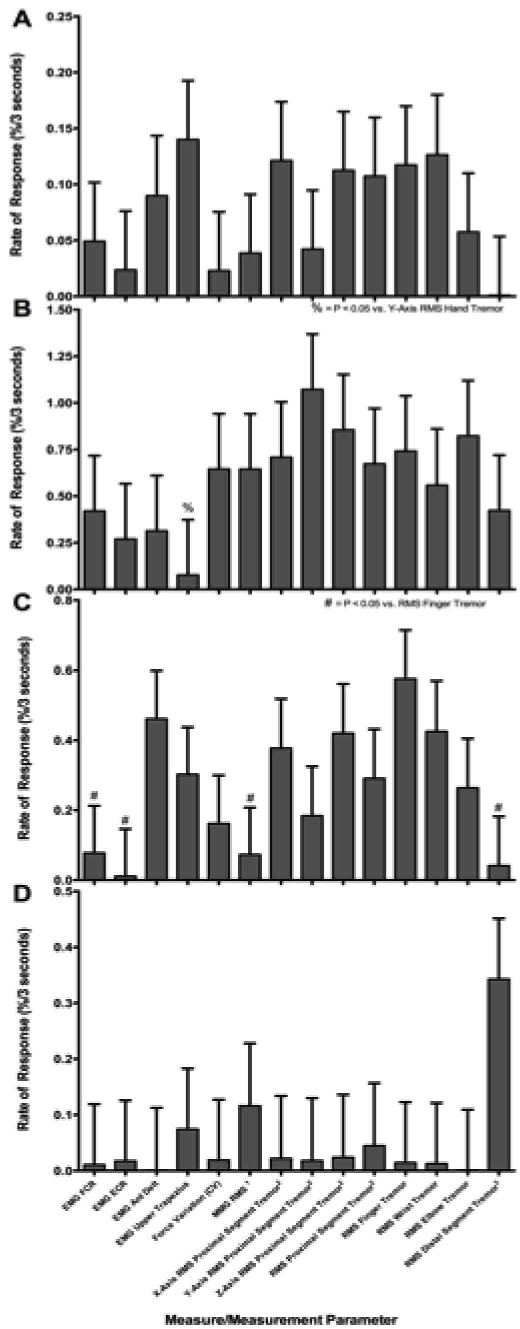


Figure 7.4 Comparing Measures with Continuous Measurement Rate of Response in Each Condition.

A: Hand Intermittent (REF), B: Hand Sustained (SUS), C: Continuous Hand Intermittent (NB), D: Shoulder Intermittent (SH). [1] Flexor digitorum superficialis for hand exercises or anterior deltoid for shoulder exercise [2] Hand tremor for hand exercises or shoulder tremor for shoulder exercise. [3] Shoulder tremor for hand exercises or hand tremor for shoulder exercise

3.2 Rate of Response Over Successive 10-Minute Blocks

Continuous measurements were evaluated by blocks of 10-minute exercise, separated by test batteries that averaged 145 seconds in duration. In the sustained condition, hand tremor in the x, y, and z-axes, and the resultant root mean square amplitude, demonstrated a high rate of response in the first 10-minutes of exercise, a decrease rate of response in the intermediary, and an increase in the final 10-minutes (Figures 7.5A-D). Wrist tremor amplitude, finger tremor amplitude, and elbow tremor amplitude also demonstrated statistically significant effects that were similar to hand tremor (Figures 7.5E-G). Shoulder tremor amplitude during shoulder intermittent exercise demonstrated a similar pattern, a significantly higher rate of response during the first block, decreasing towards the fifth 10-minute block, and a subsequent increase in the last block (Figure 7.5H). There were no statistical effects of 10-minute blocks for any measures during REF and NB conditions.

3.3 Test Battery Rate of Response

The slopes calculated from test battery data were expressed as a percentage per test battery. There was a significant condition effect ($F = 7.13$, $p = 0.001$) and condition*measure interaction ($F = 1.52$, $p = 0.003$). Tukey-Kramer post-hoc adjustment tests were performed for pairwise comparisons. Comparisons of interest are reported. Based on aggregate measurement data, statistically significant differences were found between REF and NB (Figure 7.2B). There were no statistical differences between measures when considering all exercise conditions (Figure 7.3B).

After stratifying by condition, tremor amplitude of the finger during a postural arm test was statistically greater than three other measures (hand tremor during postural hand test, hand tremor during postural shoulder test, and shoulder tremor during postural shoulder test) in the SUS condition (Figure 7.6B). During the SH intermittent condition, rate of response of tremor amplitude of the elbow during a 10% MVC isometric contraction was statistically greater from all other measures with the exception of elbow tremor during a postural shoulder test (Figure 7.6C). There were no measures that distinguished itself from other measures in both NB and REF conditions. To better relate continuous measurement and test battery responses, 14 similar test battery measures were compared in the mixed model analysis. Significant differences between REF and ISO ($p < 0.0001$), and REF and NB were found ($F = 11.31$, $p = 0.005$; Figure 7.2C). However, there were no differences between the 14 measures, with all conditions considered (F =

1.31, p = 0.211; Figure 7.3C). A significant interaction between condition and measure (F = 1.54, p = 0.021),

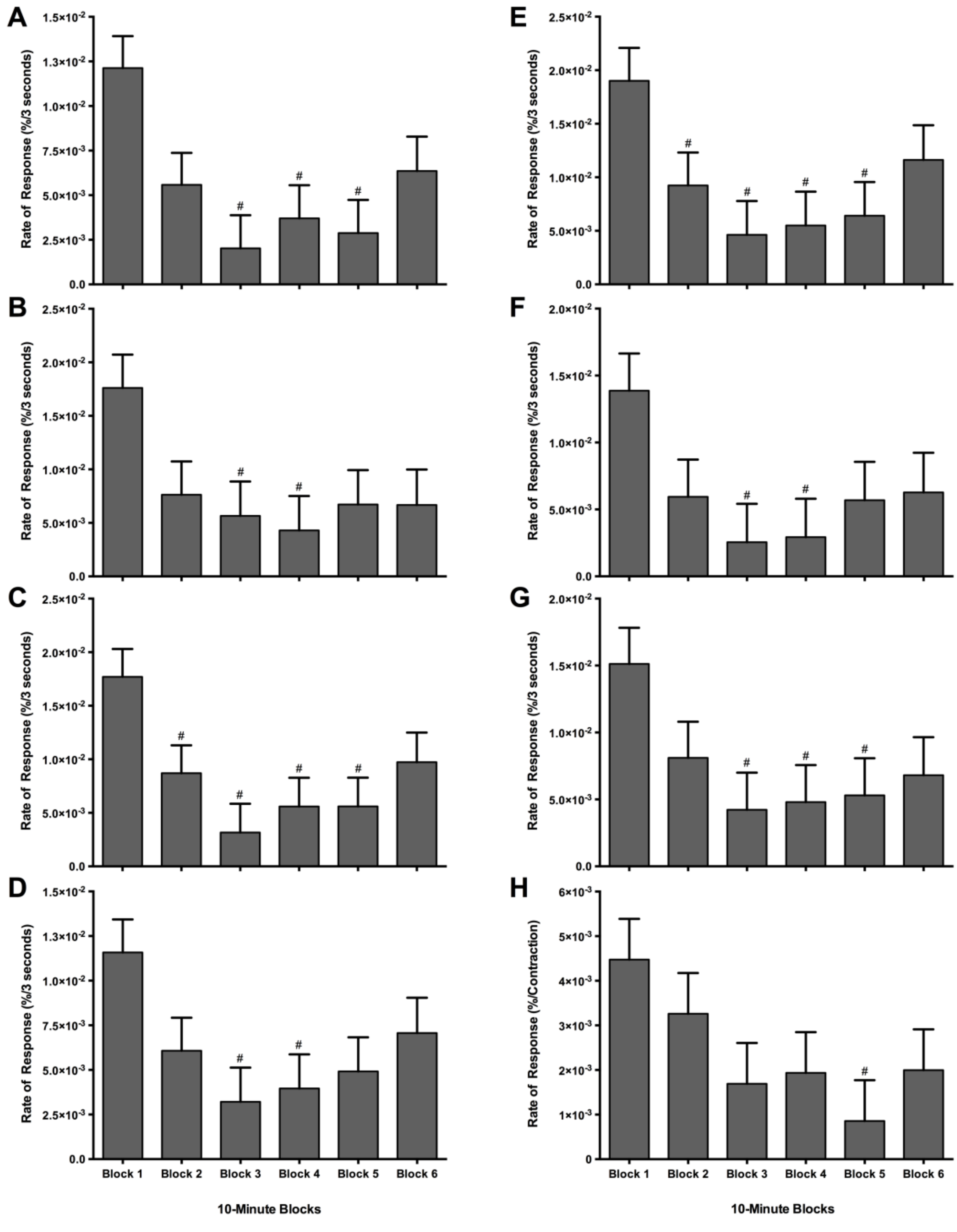


Figure 7.5 Rate of Response (Continuous Measurement) By 10-Minute Block of Exercise

A - D: Sustained Condition X, Y, Z and Resultant RMS amplitude of hand tremor. E - G: Sustained Condition Finger, Wrist, and Elbow Tremor. H: Shoulder Condition Shoulder RMS tremor amplitude. # = P < 0.05 vs. Block 1.

which was later stratified by condition, suggested differences between measures in SUS (Figure 7.6A) and SH (Figure 7.6D). Hand tremor and elbow tremor were different from other measures in SUS and SH exercise, respectively. The 27 test battery measures were compared between conditions: REF vs. SUS, NB, and SH. Tremor amplitude of the finger while maintaining a supported elbow position (postural arm test) was greater in the SUS condition compared to 17 measures in the REF condition. This included finger tremor amplitude during a postural arm test during REF. Tremor amplitude of the hand in a rested physiological tremor test in NB appeared to be more responsive than all 27 measures during REF condition. Finally, fatigue measures during REF and SH was compared. Action tremor amplitude of the elbow during the shoulder condition was statistically greater than all 27 measures during the reference condition. Based on 14 test battery measures, resultant tremor amplitude of the hand during the SUS condition was greater than all measures during the REF condition. Only one of the 14 test battery measures (elbow tremor) during SH was greater than measures during REF. There were no differences between measures when comparing REF and NB conditions.

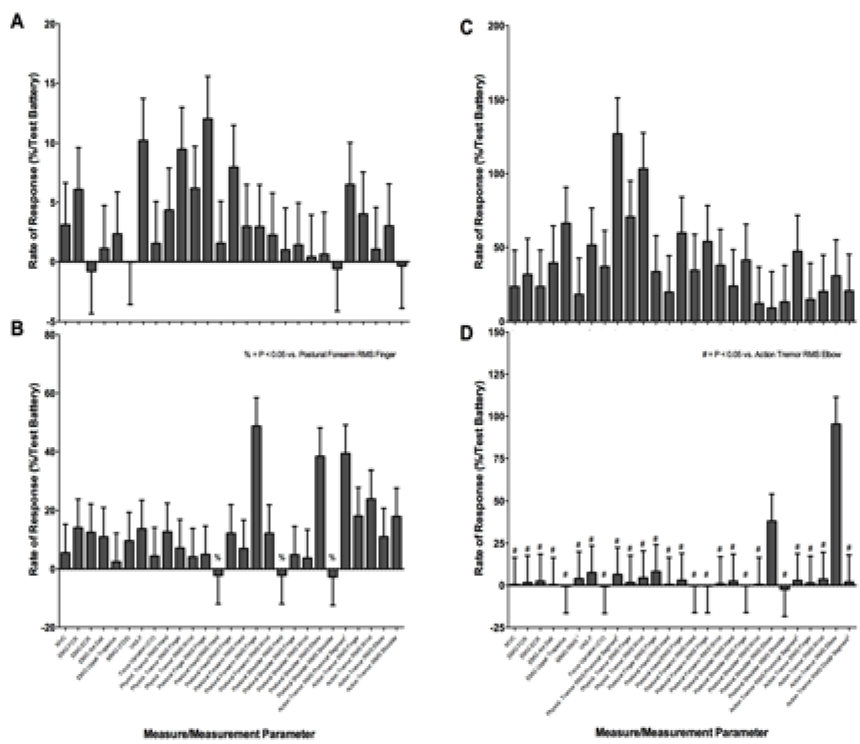


Figure 7.6 Comparing 27 Measures with Test Battery Rate of Response in Each Condition.

A: Hand Intermittent (REF), B: Hand Sustained (SUS), C: Continuous Hand Intermittent (NB), D: Shoulder Intermittent (SH). [1] Flexor digitorum superficialis for hand exercises or anterior deltoid for shoulder exercise [2] Hand tremor for hand exercises or shoulder tremor for shoulder exercise. [3] Shoulder tremor for hand exercises or hand tremor for shoulder exercise

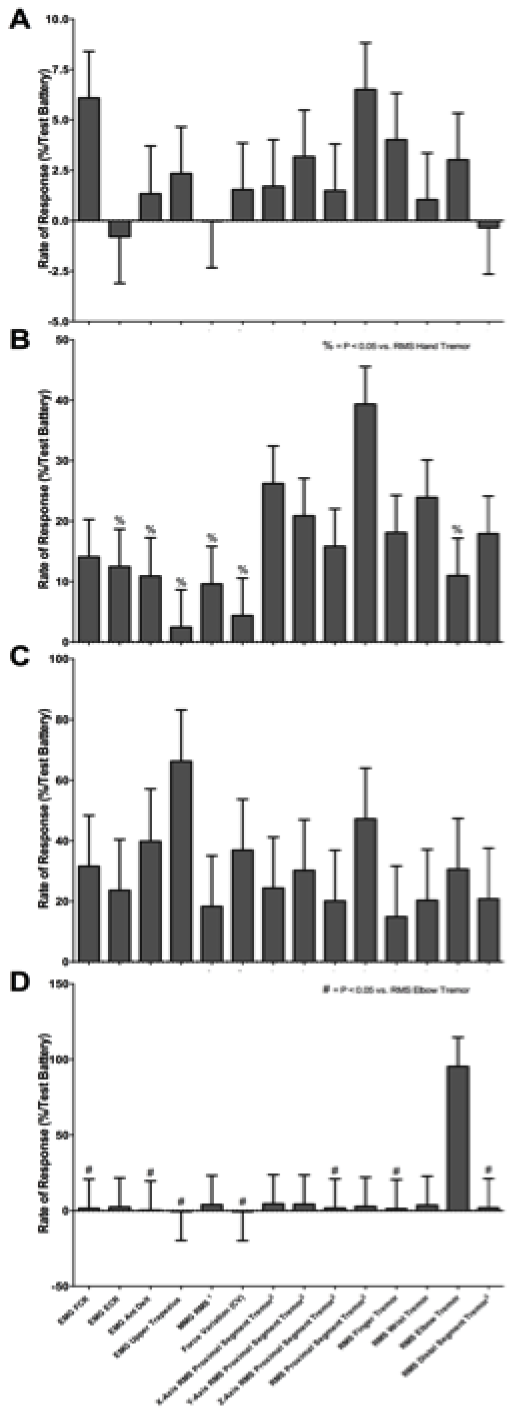


Figure 7.7 Comparing 14 Measures with Test Battery Rate of Response in Each Condition.

A: Hand Intermittent (REF), B: Hand Sustained (SUS), C: Continuous Hand Intermittent (NB), D: Shoulder Intermittent (SH). [1] Flexor digitorum superficialis for hand exercises or anterior deltoid for shoulder exercise [2] Hand tremor for hand exercises or shoulder tremor for shoulder exercise. [3] Shoulder tremor for hand exercises or hand tremor for shoulder exercise.

3.4 Changes in Test Battery Response Over Time Periods

Test battery measures were compared at baseline, at 10-minute intervals, cessation, and 1 minute after exercise. During the REF exercise, EMG amplitude of the FCR demonstrated statistically significant higher %MVC at cessation compared to baseline (Figure 7.8A). Maximum voluntary handgrip contraction decreased from baseline, statistically significant from 20-minutes into exercise until recovery, and from the first 10 minutes, which were statistically different during the last 10-minutes of exercise, at cessation, and at recovery (Figure 7.8B). Ratings of perceived fatigue also increased over the exercise period. From 20 minutes into exercise, participants experienced significant fatigue compared to baseline. Recovery remained elevated compared to baseline perceived fatigue (Figure 7.8C). The NB condition, without test batteries during exercise, allowed for comparisons between baseline, cessation, and 1-minute recovery. Hand tremor amplitude of the resultant signal and x- and y-axes increased at cessation and remained elevated at 1-minute recovery (Figure 7.9A – C). Maximum handgrip strength similarly demonstrated this pattern, a decrease in force output at cessation and attenuated force at recovery (Figure 7.9F). Cessation finger tremor amplitude did not appear to be significantly different from baseline but increased at 1-minute recovery (Figure 7.9D). MMG amplitude increased at cessation but recovery was not different from baseline (Figure 7.9E). Rating of perceived fatigue increased at cessation and decreased during recovery. However, ratings did not return to baseline during the 1-minute recovery period (Figure 7.9 G). Hand tremor amplitude, both the resultant signal and in the x- and y- axes, shoulder tremor, wrist tremor, MMG, maximum voluntary contraction, and rating of perceived fatigue showed significant time effects during the SUS condition. In all tremor measurements and MMG, values increased significantly from baseline, 30 minutes into the sustained 10% MVC contraction and remained elevated until cessation (Figure 7.10A – G). Maximum handgrip force decreased significantly from baseline after 20 minutes into exercise and did not recovery to baseline after 1-minute recovery (Figure 7.10H). Perceived fatigue also increased significantly after 20 minutes and remained elevated 1 minute after exercise (Figure 7.10I).

Since Semmes-Weinstein tests were performed independently from the test battery, sensory detection threshold measures were not explicitly compared to the other fatigue measures. A three factor [exercise condition*testing body site*time (pre/post)] mixed model analysis revealed significant differences between test sites ($p < 0.0001$). However there were no statistical significance in condition or time main effects and no interaction effects. Therefore, sensory detection threshold did not change before and after exercise, in all conditions.

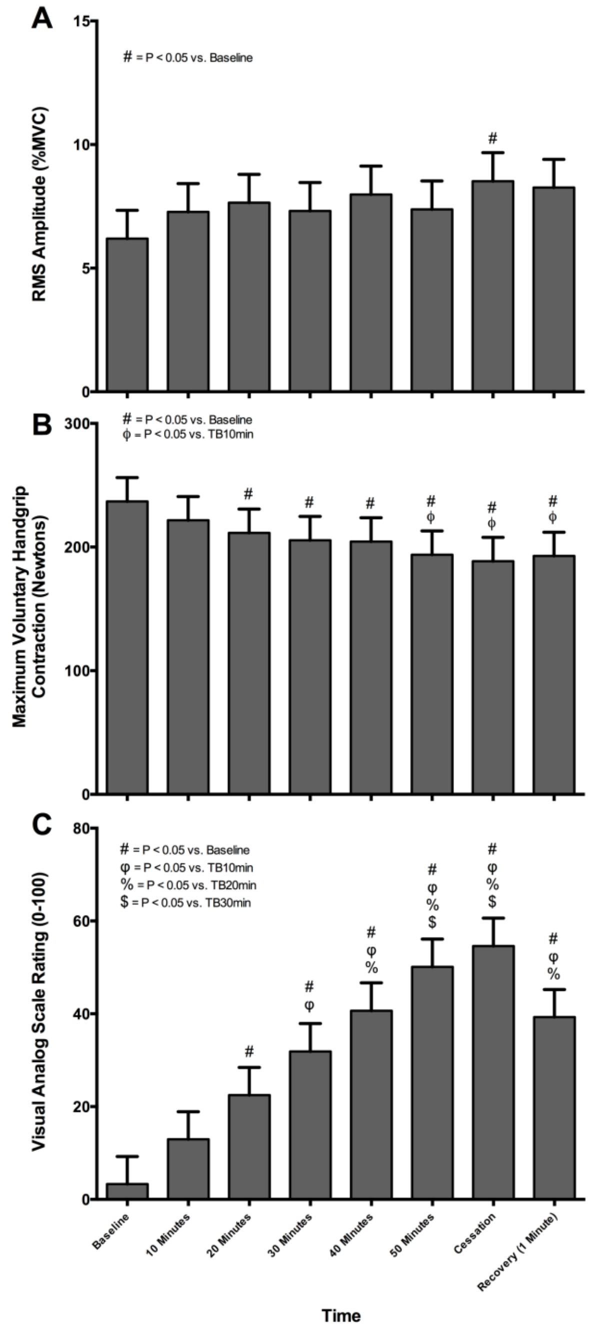


Figure 7.8 Comparing Test Battery Response By Time in Hand Intermittent Exercise.

A: EMG Flexor Carpi Radialis, B: Maximum Voluntary Handgrip Contraction, C: Rating of Perceived Fatigue (VAS)

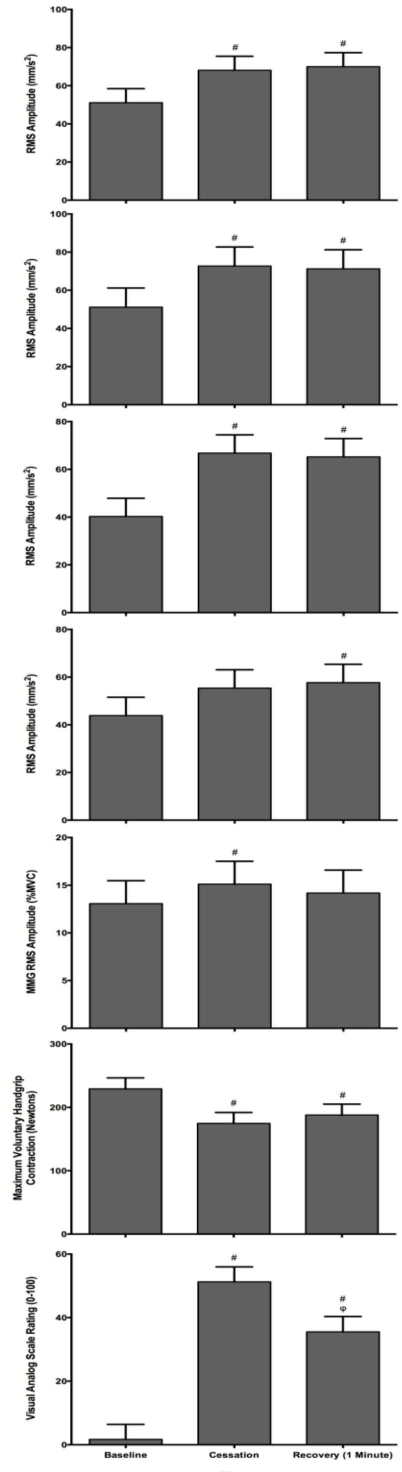


Figure 7.9 Comparing Test Battery Response By Time in Continuous Hand Intermittent Exercise.

A: X axis RMS Amplitude Hand Action Tremor, B: Y axis RMS Amplitude Hand Action Tremor, C: Resultant RMS Amplitude Hand Tremor, D: Finger Action Tremor, E: MMG RMS Amplitude, F: Maximum Voluntary Handgrip Contraction, G: Rating of Perceived Fatigue (VAS). # = $P < 0.05$ vs. Baseline, φ = $P < 0.05$ vs. Cessation.

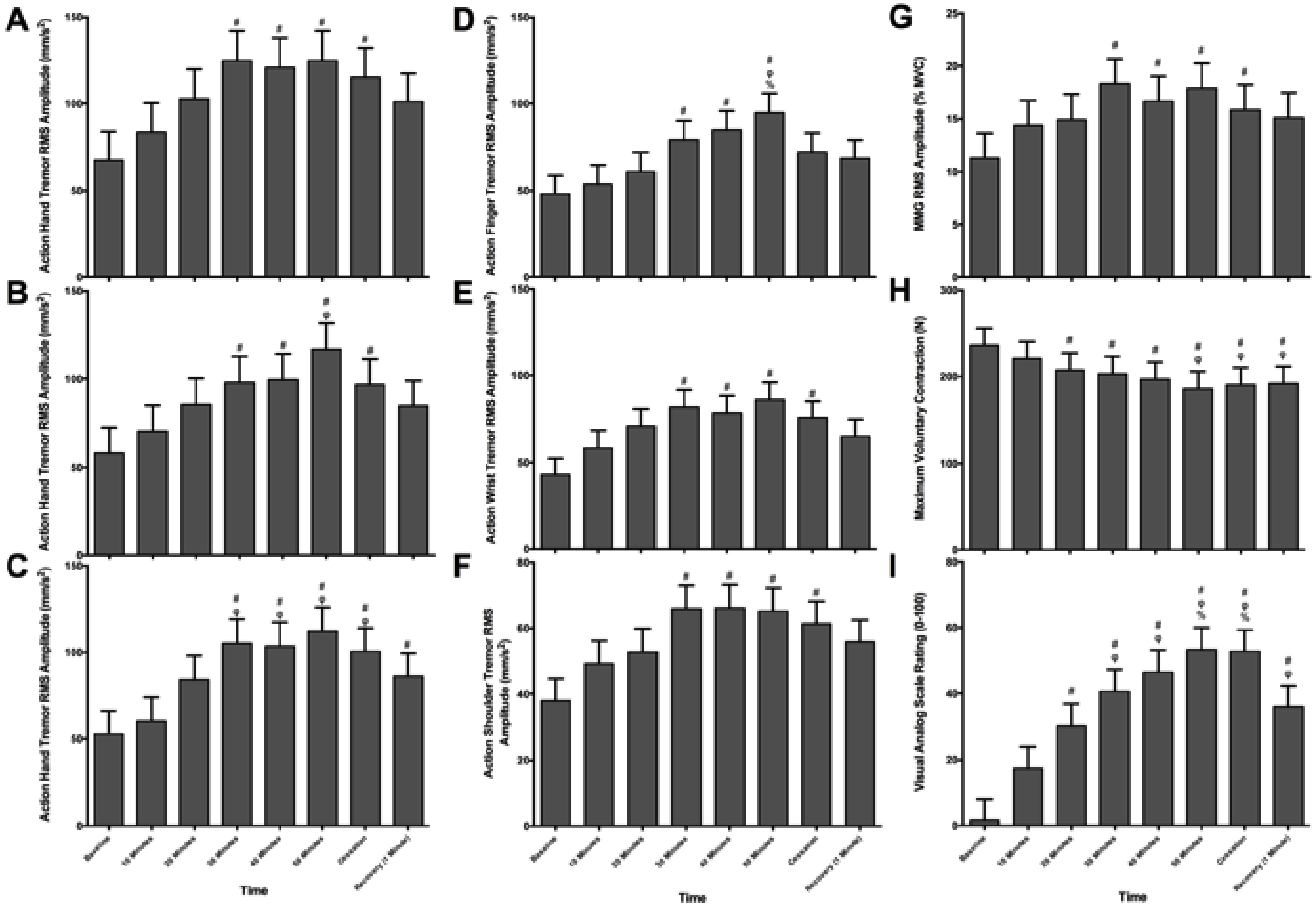


Figure 7.10 Comparing Test Battery Response By Time in Continuous Hand Sustained Exercise.

A - C: X and Y axes and Resultant RMS amplitude of hand tremor, D: Finger Action Tremor, E: Wrist Action Tremor, F: Shoulder Action Tremor, G: MMG RMS Amplitude, H: Maximum Voluntary Handgrip Contraction, I: Rating of Perceived Fatigue (VAS). # = P <0.05 vs. Baseline. φ = P < 0.05 vs. TB10min. % = P < 0.05 vs. TB20min.

3.5 Fatigue Development Over Exercise

Finally, principal component analysis was performed on three conditions with multiple time periods: intermittent isometric, sustained isometric, and shoulder. The principal components were categorized based on the aggregate combination of measures and interpreted on the basis of previous literature and strong theory. If combinations consisted of measures representing both peripheral and central mechanisms but also consisted of measures representing a single domain, the principal component was considered to be *central and peripheral but predominantly central or peripheral*. The reference intermittent condition yielded five components, explaining 97% of the total variance: central indictors, central and peripheral indicators, central and peripheral indicators (predominantly central), peripheral indicators, and central and peripheral indicators, in order of decreasing total variance (Table 7.4). The sustained condition consisted of three principal components, accounting for 73.81% of the total variance, representing: central and peripheral fatigue indicators that are predominantly peripheral measures, central and peripheral indicators that are predominantly central, and central fatigue indicators (Table 7.5). The shoulder condition consisted of six components and were all considered after interpreting Scree plots. The six components represented: peripheral fatigue indicators, central and peripheral (predominantly central), central and peripheral indicators, central fatigue indicators, central and peripheral fatigue indicators, and central fatigue indicators (Table 7.6).

Table 7.4 Intermittent Isometric (REF) PCA ("+" indicates increasing fatigue in the expected direction)

PC 1 (Central)	**PC 2 (Peripheral)**	**PC 3 (Central & Peripheral – Predominantly Central)**
MVC + EMG_ECR_RMS – EMG_Ant Delt_RMS + EMG_Upper Trap_RMS + VAS-F + Rest Tremor_Finger_RMS + Rest Tremor_Wrist_RMS + Postural Finger_Finger_RMS + Postural Arm_Hand_RMS + Postural Arm_Wrist_RMS + Postural Shoulder_Shoulder_RMS –	MVC + EMG_FCR_RMS + EMG_Upper Trap_RMS – VAS-F + Postural Hand_Finger_RMS + Postural Arm_Finger_RMS + Postural Shoulder_Finger_RMS + Action Hand_RMS + Action Finger_RMS +	EMG_Ant Delt_RMS + Force CV – Rest Tremor_Hand_RMS – Postural Hand_Hand_RMS – Postural_Hand_Finger_RMS – Postural Shoulder_Hand_RMS + Postural Shoulder_Finger_RMS + Postural Shoulder_Wrist_RMS + Postural Shoulder_Shoulder_RMS + Action Elbow_RMS –
PC 4 (Peripheral)	**PC 5 (Central & Peripheral)**	
EMG_FCR_RMS + MMG + Postural Shoulder_Elbow_RMS – Action Hand_RMS + Action Finger_RMS + Action Wrist_RMS + Action Elbow_RMS+ Action Shoulder_RMS +	EMG_Ant Delt_RMS + Rest Tremor_Hand + Postural Hand_Hand_RMS + Postural Shoulder_Wrist_RMS – Action Wrist_RMS + Action Shoulder_RMS +	

Table 7.5 Sustained Isometric (SUS) PCA ("+" indicates increasing fatigue in the expected direction)

PC 1 (Central & Peripheral – Predominantly Peripheral)	PC 2 (Central & Peripheral – Predominantly Central)	PC 3 (Central)
MVC + EMG_FCR_RMS + EMG_ECR_RMS + MMG_RMS + VAS-F + Force CV + Rest Tremor_Hand_RMS – Postural Finger_Finger_RMS + Postural Hand_Finger_RMS + Postural Shoulder_Elbow_RMS + Action Hand_RMS + Action Finger_RMS + Action Wrist_RMS + Action Shoulder_RMS +	EMG_FCR_RMS + Rest Tremor_Finger_RMS + Rest Tremor_Wrist_RMS + Postural Finger_Finger_RMS + Postural Hand_Hand_RMS – Postural Arm_Finger_RMS + Postural Arm_Wrist_RMS + Postural Shoulder_Finger_RMS + Postural Shoulder_Wrist_RMS + Action Finger_RMS +	Force CV – Rest Tremor_Wrist_RMS + Postural Hand_Hand_RMS + Postural Hand_Finger_RMS + Postural Arm_Hand_RMS + Postural Arm_Wrist_RMS + Postural Shoulder_Hand_RMS +

Table 7.6 Shoulder (SH) PCA ("+" indicates increasing fatigue in the expected direction)

PC 1 (Peripheral)	PC 2 (Central & Peripheral – Predominantly Central)	PC 3 (Central & Peripheral)
Hand EMG_FCR_RMS + MMG + Force CV + Postural Hand_Hand_RMS + Postural Hand_Finger_RMS + Action Shoulder_RMS + Action Finger_RMS + Action Wrist_RMS + Action Hand_RMS +	MVC – EMG_Ant Delt_RMS + MMG + Force CV + Postural Arm_Finger_RMS + Postural Shoulder_Shoulder_RMS + Postural Shoulder_Finger_RMS + Postural Shoulder_Wrist_RMS + Postural Shoulder_Hand_RMS + Action Wrist_RMS +	EMG_ECR_RMS + EMG_UpperTrap_RMS – MMG + VAS-F + Postural Finger_Finger_RMS + Postural Hand_Hand_RMS + Postural Hand_Finger_RMS + Postural Shoulder_Elbow_RMS –
PC 4 (Central)	**PC 5 (Central & Peripheral))**	**PC6 (Central)**
EMG_AntDelt_RMS – Rest_Finger_RMS + Rest_Wrist_RMS + Postural Arm_Hand_RMS + Postural Arm_Finger_RMS + Postural Arm_Wrist_RMS +	EMG_ECR_RMS + EMG_AntDelt_RMS + Rest_Shoulder_RMS + Postural Arm_Hand_RMS + Postural Shoulder_Elbow_RMS – Action_Elbow_RMS +	EMG_FCR_RMS – Rest_Finger_RMS + Rest_Wrist_RMS + Postural Shoulder_Elbow_RMS –

PCA scores identified time periods that load strongly, or conversely negatively, for a particular component (i.e., high scores for variable "time" indicate that the variable is overwhelmingly explained by that component). Therefore, insight can be gained in determining how fatigue develops, based on central or peripheral mechanisms, over a 60-minute period. Figures 7.11 to 7.13 are graphical representations of the 60-minute protocol (i.e., baseline and test batteries at 10-minute intervals), which are the weighted, based on the % variance for each component projections (top panels), aggregate mean of the principal components (bottom panel) to visualize overall trends. In each condition, as time progresses, time periods are characterized by components that represent central fatigue mechanisms, peripheral fatigue mechanisms, or both.

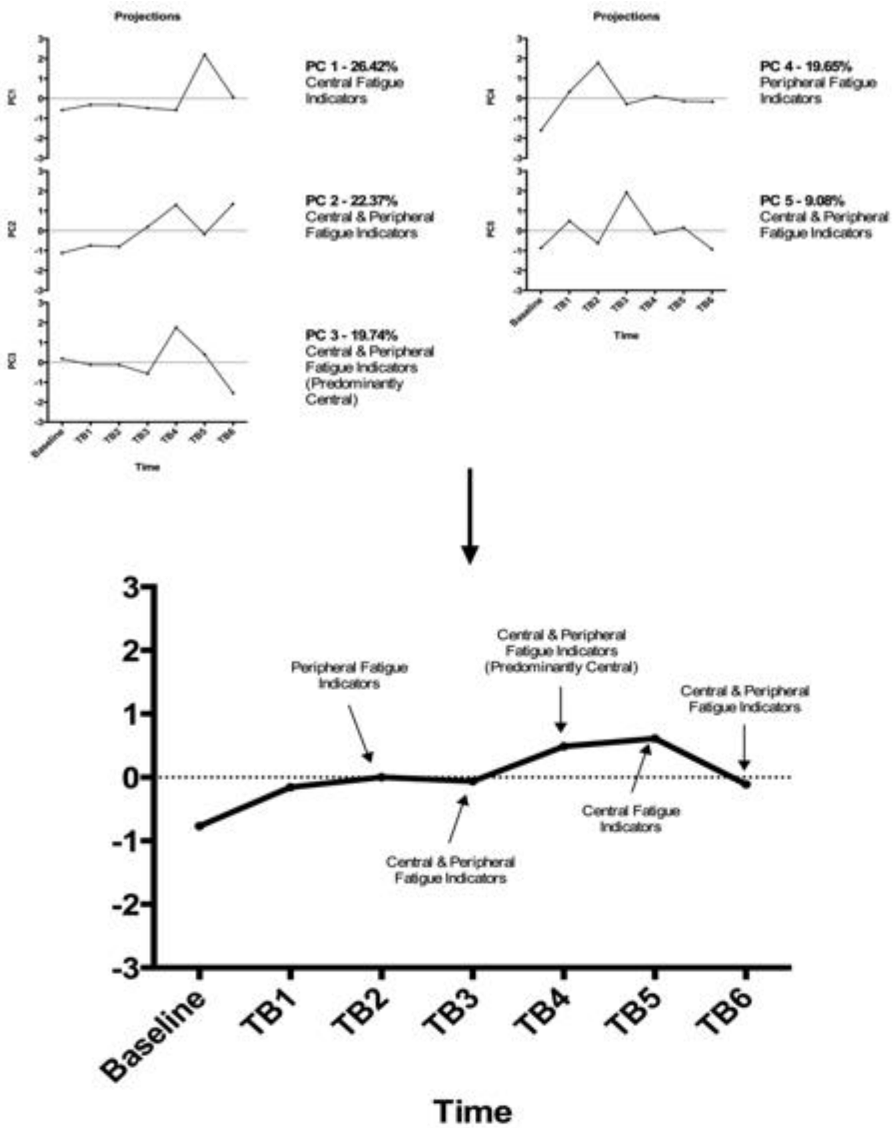


Figure 7.11 Loading of principal components (i.e., peripheral and/or central indicators) by time in an intermittent handgrip contraction (REF).

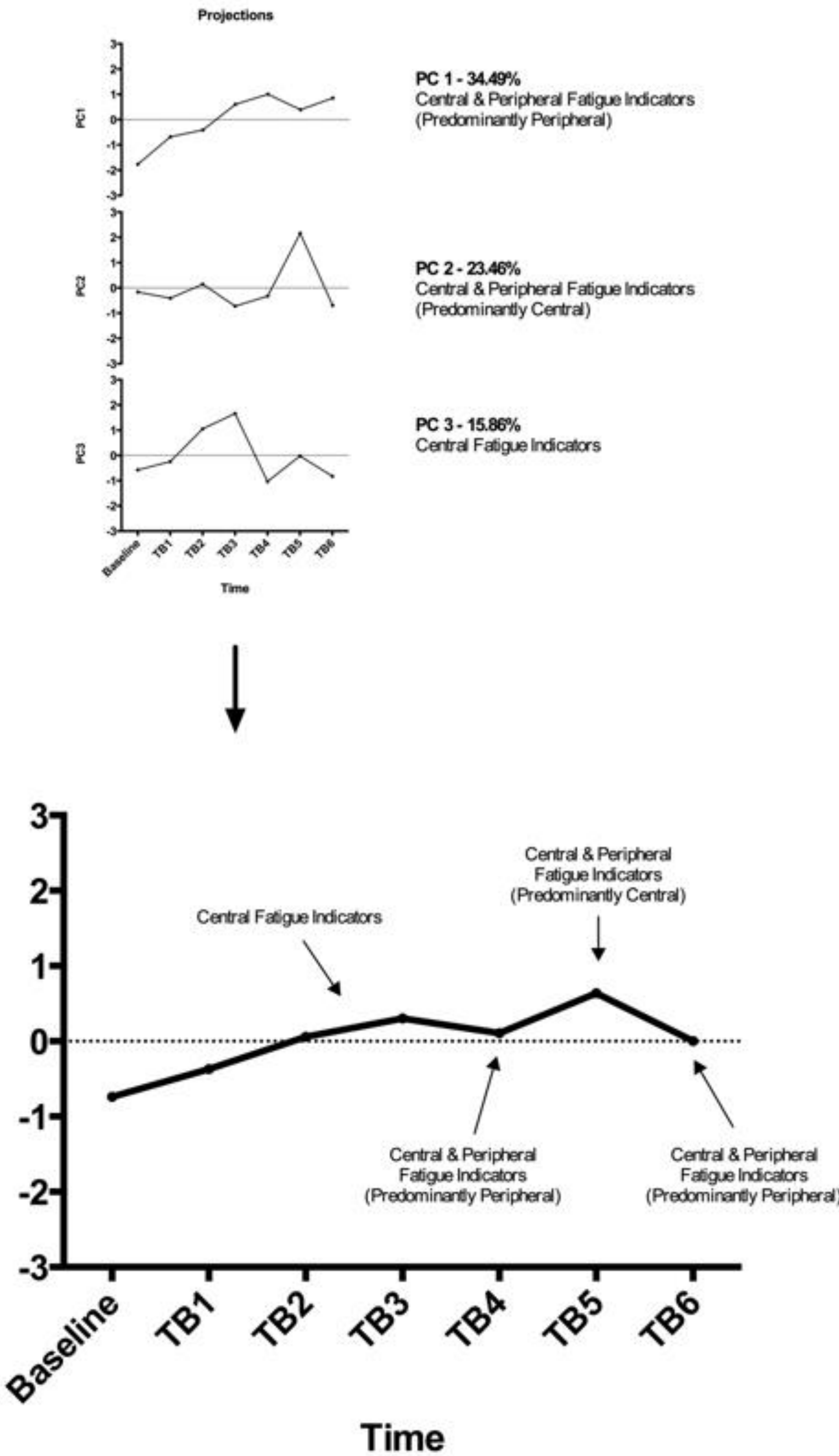


Figure 7.12 Loading of principal components by time in a sustained isometric handgrip contraction (SUS).

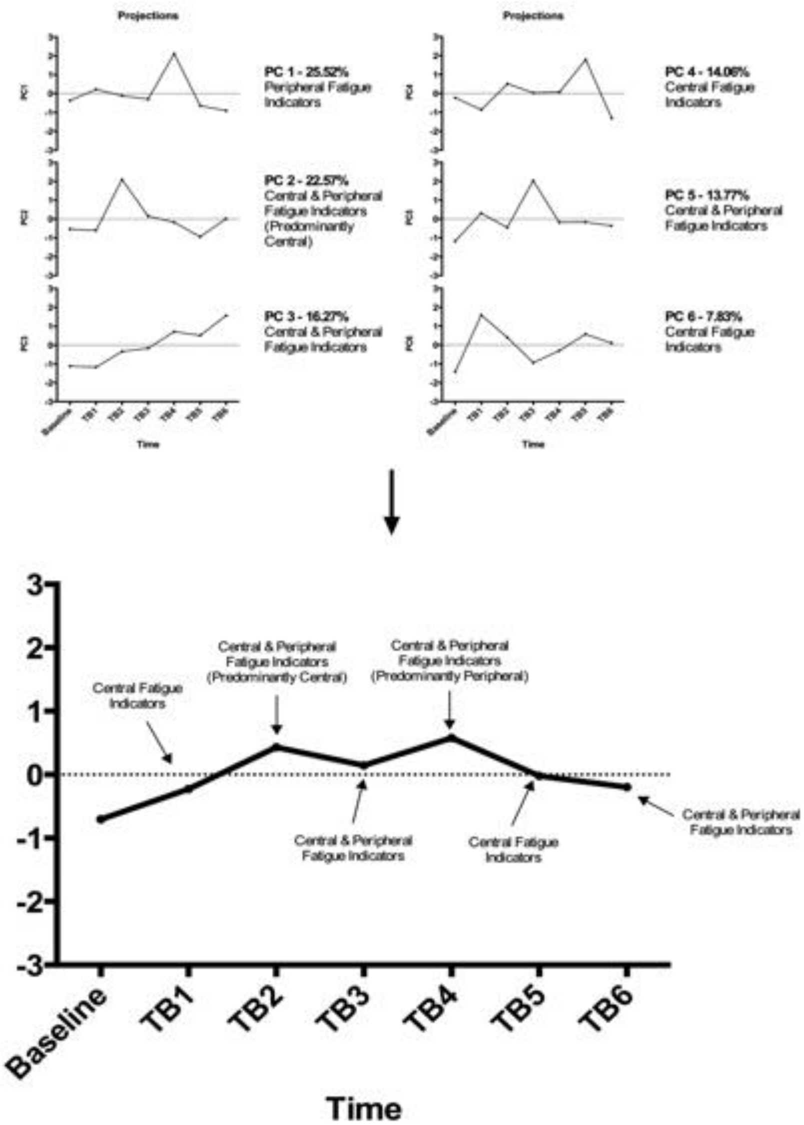


Figure 7.13 Loading of principal components by time in a shoulder intermittent condition (SH).

4. Discussion

4.1 Responsiveness of Measures Based on Task-Dependent Factors

The aggregate rate of response in both test battery and continuous measurement appeared to differentiate exercise conditions (Figure 7.2). This suggests that the rate of fatigue development, based on measures reflecting central, peripheral or both, was dependent on task factors. Collectively in all conditions (Figure 7.3), no single measure/parameter significantly distinguished itself from the remaining measures in either test battery or continuous measurement. Trends from this experiment indicated that physiological tremor of the force-producing segment (i.e., hand during a hand exercise or shoulder during a shoulder exercise) appeared to have the largest test battery response. Based on continuous measurement, there were no significant differences between measures across all conditions. Certain trends nonetheless were consistent with previous literature. For instance, tremor amplitude was highest at distal segments (i.e., finger) and decreased proximally.

4.1.1 Type of Contraction: Intermittent vs. Sustained Isometric Contraction

Based on continuous measurement, intermittent handgrip activity (mean amplitude: 15%, cycle time: 6 seconds, duty cycle: 50%) was shown to have a lower rate of response than a sustained isometric 10% MVC handgrip contraction. Sustained isometric contraction protocols, i.e., minimal changes in muscle geometry, have previously demonstrated a profound decrease in force output compared to time-varying exercise, i.e., changes in muscle geometry (Kay et al., 2000). This may be due to elevations of intramuscular pressure, which might impede microcirculation and lead to accumulation of contraction-inhibiting metabolites (Hagberg, 1981a). Interestingly, in studies where the type of contraction is controlled, time-varying activity appears to minimize fatigue development. Yung et al., (2012) investigated the fatigue effects of time-varying and sustained contractions. In that study, although the authors did not calculate an aggregate fatigue measure/score, they found that sustained and intermittent conditions belong on opposite sides of a spectrum of physiological responses based on the number of statistical differences between conditions.

The SUS condition was found to have responsive measure(s) as a test battery rate of response, test battery over time, as a continuous measurement rate of response, and continuous measure by block of time. As a test battery rate of response based on 27 measures, finger tremor during a postural arm test was quicker than three other measures: hand tremor during a postural hand test, hand tremor during a postural shoulder test, and shoulder tremor during a postural shoulder test. When limited to 14 test battery measures that were comparable to continuous measurement, hand action tremor was greater than six other measures. Finger tremor during a postural arm test and action hand tremor not only were different between measures within the exercise condition, but were also different from measures in the REF condition.

When analysing the effect of time for each test battery measure, there were similarities between SUS and REF. Similar to the REF condition, rating of perceived fatigue and maximum voluntary force exhibited an effect of time. Like REF, perceived fatigue significantly increased after 20 minutes of exercise, remained elevated during exercise, and did not subsequently recover to baseline. Maximum voluntary force decreased in amplitude 10 minutes into exercise and remained depressed at cessation and recovery when compared to baseline. Unlike REF, there were also significant time effects of action tremor of the hand, in x- and y- axes and the resultant signal, wrist tremor amplitude, shoulder tremor amplitude, and MMG. Tremor of the hand appeared to increase over the exercise period between the first 10 and 30 minutes. Coincidentally, wrist tremor, shoulder tremor, and MMG responses similarly increased over time after 30 minutes of exercise and recovered toward baseline values at recovery. Therefore, it appeared that tremor amplitude not only increased at the body segment where force is exerted, but at distal segments as well. Fatigue localized to specific body regions have been previously shown to lead to global effects, including interjoint and intermuscular changes. For instance, forceful hand activity in a neutral position led to activation of select rotator cuff muscles, despite no direct involvement of the shoulder (Alizadehkhaiyat et al., 2011). Even in light manual hand precision tasks, Sporrong et al., (1998) observed a significant increase in shoulder muscle activity. Côté and colleagues (2008) observed centrally mediated changes in intermuscular coordination of distal muscles, remote from the task (e.g., trunk muscle activity during hammering). These global changes however might not directly reflect fatigue but might be compensatory mechanisms to preserve task performance (Fuller et al., 2011) or act to stabilize joints (Sporrong et al., 1998). The significant increase in muscle activity observed during the REF condition, from baseline to cessation, and lack of changes in muscle activity during the SUS condition may provide indications towards the mechanistic origins of fatigue. Kay and colleagues (2000) compared maximal isometric and maximal time-varying protocols, observing a decrease in neural drive during isometric activity but an increase during concentric contractions. The authors hypothesized that muscle shortening or changes in muscle length might initiate different afferent signals, where concentric activity leads to increased efferent command. This study similarly found increases in EMG with intermittent activity but no significant changes during the sustained grip force.

Continuous measurement rate of response revealed that hand tremor along the y-axis (i.e., anterior-posterior) was most responsive when compared to EMG of the upper trapezius during the ISO condition. After comparing against measures in REF, the hand tremor along the y-axis measure was significantly quicker than shoulder tremor amplitude. These results support test battery by time data, with the SUS contraction leading to greater tremor effects than EMG activity, which also appears to result in global changes compared to the reference condition. In addition, these results appear consistent with fatigue development in isometric conditions, if indeed central fatigue develops first and is then followed by peripheral fatigue.

The increase in hand tremor during a sustained exercise was time dependent, demonstrated by a varying rate of response at progressive 10-minute blocks of exercise. Finger tremor rate of response was highest during the first 10 minutes of exercise, decreased towards the third block of 10-minutes, and gradually increased towards the final 10 minutes. This trend was consistent with tremor of the hand, in all three axes and the resultant signal, the wrist, and the elbow. Quite possibly, this change in rate of response of tremor may be reflective of adaptations in neural control strategies that accompany progression of exercise and training. Semmler and Nordstrom (1998) measured tremor amplitude among skill-trained, untrained, and strength-trained participants, finding lower amplitudes with skill training. The authors asserted that in a low force sustained isometric contraction, mechanical oscillation and segmental reflex mechanisms did not play a primary role in tremor generation. Instead, tremor generation may be a consequence of motor unit firing patterns (e.g., rates, synchronization, variability, common modulation) or a central oscillatory effect driven by the central nervous system. According to Semmler and Nordstrom (1998), skill trained individuals exhibited a lower motor unit synchrony; it is thus tempting to suggest that both decreases in tremor amplitude and desynchronization of motor units may be a consequence of changes in recurrent inhibition, mediated by Renshaw cells. However, in another study, during a single bout of continuous isometric force for a 15-minute duration, the strength of synchrony of motor unit pairs did not significantly change (Nordstrom et al., 1990). It thus remains uncertain whether multiple bouts of continuous activity leads to a similar training effect observed by Semmler and Nordstrom (1998). Alternatively, the changes in tremor rate of response may be indicative of the time course of central and peripheral fatigue development. In action tremor measurements, towards the final 10 minutes of exercise, the rate of response increased, and did not appear to be significantly different from the first 10-minute exercise block. Indeed, action tremor appears to increase with fatigue, due to a number of contributing mechanisms, including Renshaw cell inhibition. Recurrent inhibition decreases, allowing for the recruitment of motoneurones, compensating for cellular impairments of fatigue (Pierrot-Deseilligny & Burke, 2005). MMG and MVC measured as a test battery over time, seemingly support this time course of central and peripheral fatigue. Maximum voluntary handgrip contraction, reflecting both central and peripheral mechanisms, decreased after 10 minutes of exercise. MMG, a peripheral measure, conversely, increased from baseline after 30 minutes of exercise.

4.1.2 Exercise Intensity: Breaks vs. No Breaks

The REF rate of response was significantly lower than NB based on both aggregate test battery and continuous measurement. The addition of a test battery may have thus led to some recovery at 10-minute intervals, and reduced work intensity, compared to the NB condition. The test battery might arguably be considered an active rest period, which could contribute to a short peak in metabolite production including local stimuli to trigger vasodilation and an increase in blood volume (Crenshaw et al., 2006).

The NB condition exhibited differences between time, using test battery measurement, and between measures, using rate of response of continuous measurements. As a continuous measurement, the NB condition displayed quicker increases in finger tremor amplitude compared to EMG of the forearm flexor and extensor, shoulder tremor amplitude, and force variation. Finger tremor was also more responsive than EMG ECR, MMG, hand tremor amplitude along the y-axis, shoulder tremor, and force variation in the reference condition. Continuous measurement data support the increases in tremor observed as a test battery measure. Finger tremor in particular appeared to be very responsive, both continuously and as a test battery.

After comparing test battery measures between REF and NB conditions, the resting physiological hand tremor during the no break condition was more responsive than all 27-test battery measures during the reference condition. On the other hand, limiting comparisons to 14-test battery measures did not reveal any differences between measures. Similar to REF, rating of perceived fatigue and maximum voluntary force exhibited time effects. In both conditions, perceived fatigue increased at cessation and did not subsequently recover to baseline. Similarly, maximum voluntary handgrip force remained depressed at cessation and at recovery in both conditions. In comparison to REF, tremor of the finger and hand, and MMG increased at cessation and/or recovery during the no break condition. Therefore, increased work intensity, represented by a no break condition, led to substantial increases in peripheral fatigue. This seems consistent with peripheral fatigue mechanisms that are predominant during higher intensity exercise (Westerblad et al., 2010). Byström and Fransson-Hall (1994) measured the physiological response of intermittent muscle contractions of varying contraction-relaxation periods. Based on potassium and lactate ion concentrations, which might reflect intramuscular changes of fatigue, the authors found that increases in relaxation time led to a reduced potassium loss and reduced venous-arterial difference in lactate concentration. Interestingly in this study, muscle activity did not change, contrary to observations of the intermittent reference condition. The time course of change for these measures might then provide further insight towards the development of peripheral and central fatigue, however measurement was limited to baseline and cessation for the NB intermittent condition.

4.1.3 Involved Body Region: Hand vs. Shoulder

Test battery rate of response for the shoulder condition demonstrated a significant effect of action elbow tremor, when compared to all other test battery measures, in the 27-test battery comparison. In the 14-test battery comparison, action elbow tremor was most responsive relative to 7 other measures. However when comparing time periods (baseline, 6 periods during exercise, cessation, and recovery), elbow tremor during the 10%MVC test contraction did not demonstrate significant time effects. Elbow tremor amplitude during an action tremor test in the shoulder condition was also more responsive than 13 other measures and 2 other measures in the reference condition, for 27-test battery and 14-test battery comparisons, respectively. Based on continuous measurement, it did not appear that any fatigue measure was most responsive. Nonetheless, trends, specifically EMG of the anterior deltoid and upper trapezius, were consistent with those reported in earlier studies. Hagberg (1981b) observed higher EMG activity and self-reported discomfort of the trapezius compared to the anterior deltoid after performed work tasks. Hagberg (1981b) asserted that these observations were similar to clinical studies where deltoid muscle symptoms were rare. However, the continuous measurement rate of response of shoulder tremor changed over time. In SH exercise, tremor amplitude of the shoulder displayed a peak rate of response during the first 10-minute block, a decreasing rate towards the fifth block, and an increase in the last block. There were no differences between measures across the reference and shoulder conditions. Wiker and colleagues (1989) measured both muscle activity and tremor before and after a movement task, inserting a pistol-gripped stylus into holes along horizontal and vertical axes. In that study, authors found that tremor was more effective and reliable in detecting and grading fatigue than either EMG amplitude or shifts in mean power frequency. Our findings support Wiker et al., (1989). Tremor measurement, as part of a test battery, was more responsive than muscle activity of the anterior deltoid or upper trapezius.

There were no differences, in either aggregate test battery or continuous measurement rate of response, between SH and REF. Handgrip and shoulder flexion conditions were selected due to differences in morphological and fibre composition between the extrinsic muscles of the forearm and the primary muscles involved in forward flexing the shoulder. Power gripping requires not only flexor muscles, but also activation of wrist extensors to counteract wrist flexion torque due to finger flexion tendons (Hägg & Milerad, 1997; Hoozemans & van Dieën, 2005). Extensor muscles, such as extensor carpi radialis longus, have been found to have a fibre distribution of

59% - 68% slow oxidative Type I fibres (Fugl-Meyer et al., 1982), a physiological cross sectional area of 2.2 cm^2, and a peak force of 304.9 N (Murray et al., 2000). Flexor muscles, including flexor carpi radialis, have been characterized with a higher percentage of fast twitch Type IIa fibres, estimated at 59.1% (Mizuno et al., 1994). Lieber and colleagues (1990) found that the PCSA of the FCR was approximately 1.60 cm^2 with a peak force of 74.0 Newtons. Muscles involved in shoulder flexion include but not limited to the anterior deltoid and upper part of the trapezius, which have been cited as the most heavily taxed during a fatiguing shoulder flexion activity (Wiker et al., 1989). According to Srinivasan et al., (2007), the anterior deltoid is composed of 47% slow oxidative Type I fibres and a higher proportion of fast twitch fibres. Architecturally, it was estimated that the anterior deltoid has a PCSA of 8.2 cm^2, and a peak force of 1142.6N (Langenderfer et al., 2004). The upper part of the trapezius is predominantly composed of type I fibres (57-61%), but a higher frequency of type II fibres compared to lower regions (Lindman et al., 1991). The absence of significant differences between hand and shoulder in this study may not be indicative of the lack of discriminatory power of fatigue measures between these segments, but may suggest that differences of body segment did not have an extraordinary effect on fatigue response.

4.2 Fatigue Development Over Time

In preceding sections, we were able to address the magnitude of the fatigue effect (i.e., central or peripheral) by comparing measures and by comparing time periods for each measure. Principal component analysis, on the other hand, provided a descriptive analysis of the pattern of fatigue development over the exercise period. In all three conditions (REF, SUS, SH), the aggregate fatigue score consistently increased over the exercise period, slightly decreased at the middle of the exercise protocol, increased rapidly towards the end of exercise, and slightly decreased at cessation. Both central and peripheral indicators appeared to be responsive throughout the exercise duration, consistent with previous findings that fatigue is attributable to both interacting central and peripheral factors (Kent-Braun, 1999). The responsiveness of these measures varied by time. Generally, in the REF condition, the first 20 minutes of exercise were primarily loaded by peripheral fatigue indicators and later by central fatigue indicators. The SUS condition, however, led to an inverted trend: a general increase in peripheral fatigue followed by involvement of central fatigue indicators. These trends were generally consistent with Babault et al., (2006), who observed a similar pattern in both isometric and concentric conditions. However, there were a few discrepancies between trends observed in this study and from previous literature. It appeared that in this study, there was interplay between central and peripheral indicators observed throughout the exercise period. These differences between studies may be primarily due to differences in task intensity (i.e., maximal vs. submaximal) and task duration (i.e., exercise until exhaustion vs. fixed period of time). The shoulder condition led to an increase in central fatigue followed by an increase in peripheral fatigue. Central fatigue mechanisms then appeared to contribute towards the final 20 minutes of exercise. This fatigue development pattern does not appear to be consistent with expected concentric contraction protocols, but instead may be a result of methodological limitations. For instance, participants generated forward flexion movements, producing force from neutral shoulder position (i.e., arm to the side). This position was intended to minimize muscle activity due to increases in external shoulder moment, when raising the arm, to support the segment weight of the distal upper extremity and upper arm. However, this set-up might have inadvertently reduced muscle activity when producing the desired forces. Participants on average elicited 14.3% and 12.2% MVC of the anterior deltoid and upper trapezius, when producing 36.5% maximum force from neutral shoulder position. To support this, lower muscle activity intensity might explain the lower aggregate continuous rate of response in the shoulder condition compared to the reference condition. Conversely, shoulder rate of response was higher than the hand condition in aggregate test battery rate of response. This was, however, principally driven by elbow action tremor, which led to a high rate of response but no significant changes over test battery collection periods. Based on results from all conditions, additional research into complex combinations of task-dependent factors may help understand the observed relationships from this study.

Interestingly, when indicators transition between central or peripheral measures in all conditions, the aggregate fatigue scores decreased, but subsequently increased with the involvement of central or peripheral contributions to the development of neuromuscular fatigue. It might be speculated that a decrease in aggregate fatigue may be a result of inhibitory fatigue effects or alternatively a compensatory mechanism that aim to balance central and peripheral contributions. Few studies (e.g., Kent-Braun, 1999) have attempted to quantify the central and peripheral contributions to muscle fatigue, using direct or invasive measures. However, it remains unclear the relative roles of central and peripheral factors in fatigue development, more specifically the interplay between these two sites, and the capability of field-usable measures to capture these effects. Aggregate fatigue scores also decreased towards the final minutes of the 60-minute exercise period. At cessation, fatigue decreased towards the total mean fatigue value (i.e., Z-score of 0) but remain elevated compared to baseline. There are a number of possibilities that might account for this trend. Participants often performed all exercise conditions for the full 60-minute period, indicating the absence of total muscular exhaustion. The decreasing fatigue score might be a continuation of the observed interplay between central and peripheral mechanisms. Second, fatigue development might not follow a linear change. According to the Central Governor Model (Noakes, 2011), feedback from the periphery and psychological inputs (i.e., motivation) to regulate exercise behaviour. Most notably, “end spurt” phenomenon, due to increased central motor drive, has been shown in real-world scenarios as an increase in power output at the end of exercise (e.g., speeding towards the finishing line). However, further investigation should be devoted to understand the observed phenomena.

4.3 A Single Universal Measure? (And Other Measurement Considerations)

An aim of this study was to help determine the utility of select fatigue measures for different exercise conditions at lower force levels. We found that there is no one universal measure that was common, in terms of responsiveness, in all exercise conditions (Table 7.7). This is consistent with the task-dependency nature of fatigue, and since fatigue manifests itself in various forms, measuring a single test is not a feasible approach (Saito, 1999). Additionally, we also found that the comparability of measures, based on rate of response, might differ when collected as a test battery (Figure 7.2B) or continuously with exercise (Figure 7.2A). This may be mainly due to differences in recorded measurements that comprise continuous (e.g., EMG, MMG, action tremors, force variation) and test battery (e.g., in addition to continuous measures: perceived fatigue, physiological/resting measurements, postural measurements, maximum voluntary force) measurement. When 14 test battery measures similar to continuous measurement were compared, REF was significantly different from both SUS and NB conditions (Figure 7.2C). After stratifying by condition, hand tremor amplitude during SUS demonstrated the highest rate of response, which was similar to that of continuous measurement. Nevertheless, there remained observable differences between measures in each condition based on test battery and continuous measurement. For instance, unlike continuous measurement, elbow tremor amplitude remained most responsive as a test battery measure during SH and there were no differences found in NB. Yung et al., (2012) similarly did not find identical statistical patterns between test batteries and continuous measurements, when comparing rate of response of exercise conditions characterized by varying force amplitudes. Therefore it is reasonable to suggest that test batteries might provide alternative information relative to measures collected continuously and simultaneous to exercise, even when comparing similar measurements, and the comparability between test battery and continuous measurement might be task dependent. There are clear advantages of collecting measures as a test battery or simultaneously with exercise/work activity. In field settings, test batteries can be administered during work breaks to avoid disruptions of the work process. Brief standardized measures would also allow for generalization across different work settings (Rosa et al., 1985). Test batteries might also act to control factors (i.e., muscle length, movement velocity, and magnitude of exerted force) that might lead to erroneous interpretation of physiological signals (e.g., MMG, EMG, etc.). Continuous measurement, on the other hand, might provide information that is representative of the workload. In a controlled laboratory setting, typical of a classical fatigue study, continuous measurement might help avoid unintentional active/passive activity breaks induced by test batteries at discrete periods of time. The latter notion is clearly evidenced by significant contrasts between NB (no test battery) and REF (with test battery) conditions. Interestingly, the trends observed using the selected continuous measurements correspond to condition endurance times. For instance, both rate of response was higher and endurance times were shorter during SUS followed by NB, REF, and SH exercises. However, additional research is required to elucidate this possible relationship.

Although no single measure was found to be most responsive in *all* conditions, there were measures responsive in *most* exercise conditions as either a continuous or test battery measure. This was the case with action tremor of different segments. Action tremor, particularly of the hand, was found to be responsive as a test battery and continuous measure, in SUS and NB exercise conditions. Action tremor of the shoulder and elbow were most responsive in shoulder intermittent exercise. Conceivably, action tremor of the segment proximal to the exerting force appeared to be responsive and lead to significant changes over the exercise period. Action tremor during an isometric contraction minimizes signal contamination from sources that might affect physiological and postural tremor measures (McAuley et al., 1997). As observed in Study 3, action tremor was highly repeatable and responsive at an intermittent handgrip exercise at higher forces, with test batteries taken at 1-minute intervals, but may be susceptible to diurnal variations (Study 4). Action tremor measurements might also demonstrate underlying neural adaptations over the exercise period. Interestingly, when comparing rate of response of continuous measurement over 10-minute blocks and test batteries at 10-minute intervals, there appeared to be a discordant trend. As the rate of response decreased, the magnitude of tremor in a test battery increased. Certainly the decreasing rate of response during exercise is not a decrease in tremor but a slowing of an increase rate of response. Possibly, this further exemplifies the differences between a test battery measurement and continuous measurement. A test battery might elicit responses attributed to the cumulative fatigue effect preceding the test battery. Continuous measurement, on the contrary, is indicative of physiological processes concurrent to exercise or work activity.

Both central and peripheral mechanisms, to a certain degree, may contribute to tremor generation (Lakie, 2010). A maximum voluntary contraction, which is also dependent on processes in both central and peripheral domains (Vøllestad, 1997), was similarly responsive. Changes in maximum voluntary contractions were observed as a test battery over time in REF, NB, and SUS conditions. Therefore fatigue measures, reflecting changes to both central and peripheral processes, may be useful in measuring tasks and exercises of varying parameters. Ratings of perceived fatigue, measured with a visual analog scale, similarly displayed significant differences between time periods in REF, NB, and SUS exercise. Self-reported fatigue, which is likely mediated by central mechanisms where the corollary provides a copy of motor commands to the somatosensory cortex, is positively related to fatigue and reduced work capacity (Sato & Coury, 2009).

This study was limited to investigating fatigue measures based on the type of contraction (i.e., intermittent vs. sustained), the intensity based on rest allowance (i.e., break vs. no break), and muscle groups involved (i.e., hand vs. shoulder), at a low force level relevant to the development of work-related musculoskeletal disorders and sedentary or light production work. Task-dependency of fatigue, however, might involve a multitude of other aspects, including the total activity/exercise duration and intensity based on force amplitude. Participants were asked to perform each condition until exhaustion or up to 60 minutes. In most cases, participants were able to fulfill the 60-minute duration. Therefore, the responsiveness of the measures may not be generalizable to prolonged activity exceeding 60 minutes or until complete volitional fatigue. In Study 3, action tremor, MMG amplitude, postural tremor/steadiness, and rating of perceived fatigue were found to be highly responsive and significantly different from the least responsive measures. In that study, test battery responses were observed during a fatiguing hand intermittent contraction at a mean amplitude of 30% MVC with identical duty cycle and cycle time parameters. In this study, no measure appeared to significantly differentiate itself as a test battery during hand intermittent exercise. Trends indicate a quick rate of response of action hand tremor (6.5%/Test Battery), postural tremor (1.6% - 12.0%/Test Battery), and rating of perceived fatigue (10.2%/Test Battery). MMG, on the contrary, demonstrated a negative average rate of response but was close to zero. MMG, which reflect impairments in cross-bridge cycling (Shinohara & Søgaard, 2006), appears to be most sensitive during higher force amplitudes, consistent with earlier notions of peripheral mechanisms dominating high intensity activity. Although there were no statistical differences between rates of responses, maximum handgrip force, rating of perceived fatigue, and EMG appeared to change over time. These comparisons should be approached with caution. Firstly, test batteries were composed of different measures between the two studies, with a greater number of tremor measurements in this study. And secondly, test batteries were collected at 10-minute intervals, whereas Study 3 involved test batteries at 1-minute intervals. Further studies focusing on different average intensity levels might clarify fatigue measurement responsiveness in this work/exercise parameter. Another limitation is the direct comparability of the exercise conditions. Although duty cycle and cycle time exercise parameters were kept consistent in all conditions, the mean force amplitude varied by 5% MVF in sustained and intermittent contractions. A 15% MVF mean force level for intermittent contractions was selected on the basis of previous work-studies (Yung, 2011), and was also considered the acceptable work limit for intermittent contractions (Byström & Fransson-Hall, 1994). Likewise, a 10% MVF was selected on the basis of its acceptability for a sustained and prolonged isometric contraction (Byström & Fransson-Hall, 1994). Nevertheless, both force levels are within lower intensities that are relevant to occupational tasks (Westgaard & Winkel, 1996).

5. Conclusion

Fatigue is a complex multidimensional construct consisting of an interaction between central and peripheral mechanisms. The task dependency nature of fatigue exacerbates the challenge of selecting measures that are sensitive to work or exercise of varying parameters (e.g., type of contraction, etc.) at forces relevant to work and the development of work-related musculoskeletal disorders. This study investigated the responsiveness of select fatigue measures, collected continuously or as part of a test battery, in exercise conditions representing changes to contraction type (intermittent isometric vs. sustained isometric), changes to work intensity based on rest allowances (break vs. no break), and changes to muscle group (hand vs. shoulder). Although we did not find a measure that was responsive in *all* exercise conditions, there were measures that were responsive in *most* conditions, as either a test battery or continuous measurement. These measures by nature reflect central and peripheral mechanisms: action tremor and maximum voluntary contraction. Rating of perceived fatigue, a centrally mediated measure was also found to increase with exercise progression in hand conditions. This study also contributed further insight towards fatigue detection as a continuous measurement or as a test battery, demonstrating that both provide alternative but complementary information about workload and fatigue accumulation.

Table 7.4 Summary of Results

Collection Method	Exercise Protocol	Measurement	Response [Mean(SEM)]	Significant Pairs (P<0.05)
Test Battery Slope (27 Measures)	Hand Sustained (ISO)	Finger Tremor (Postural Arm)	48.7%/TB (9.77)	• Finger Tremor (Postural Arm) vs. Hand Tremor (Postural Hand), Hand Tremor (Postural Shoulder), Shoulder Tremor (Postural Shoulder)
	Shoulder Intermittent (SH)	Elbow Tremor (Action)	95.3%/TB (16.03)	• Elbow Tremor (Action) vs. All but Elbow Tremor (Postural Shoulder)
Test Battery Slope (14 Measures Similar to Continuous)	Hand Sustained (ISO)	Hand Tremor (Action)	39.4%/TB (6.2)	• Hand Tremor (Action) vs. EMG Amplitude of ECR, Ant Delt, and Upper Trapezius, MMG Amplitude of FDS, Force Variation, Elbow Tremor (Action)
	Shoulder Intermittent (SH)	Elbow Tremor (Action)	95.3%/TB (19.2)	• Elbow Tremor (Action) vs. EMG Amplitude of FCR, Ant Delt, Upper Trapezius, Force Variation, Shoulder Tremor Zrms, Finger Tremor (Action), Hand Tremor (Action)
Test Battery By Time	Hand Intermittent (REF)	EMG Amplitude of FCR	Baseline: 6.2 %MVC (1.1) Cessation: 8.5 %MVC (1.2)	• Baseline vs. Cessation
		Maximum Voluntary Handgrip Contraction	Baseline: 236.9N (19.2) TB10min: 221.6N (19.2) TB20min: 211.5N (19.2) TB30min: 205.5N (19.3) TB40min: 204.4N (19.3) TB50min: 193.8N (19.3) Cessation: 188.6N (19.3) Recovery: 192.8N (19.2)	• Baseline vs. TB20min, TB30min, TB40min, TB50min, Cessation, Recovery • TB10min vs. TB50min, Cessation, Recovery
		Rating of Perceived Fatigue (VAS 0-100)	Baseline: 3.3 (5.9) TB10min: 13.0 (5.9) TB20min: 22.5 (5.9) TB30min: 31.9 (6.0) TB40min: 40.7 (6.0) TB50min: 50.1 (6.0) Cessation: 54.6 (6.0) Recovery: 39.3 (5.9)	• Baseline vs. TB20min, TB30min, TB40min, TB50min, Cessation, Recovery • TB10min vs. TB30min, TB40min, TB50min, Cessation, Recovery • TB20min vs. TB40min, TB50min, Cessation, Recovery • TB30min vs. TB50min, Cessation
	Continuous Hand	Finger Tremor (Action)	Baseline: 43.9 mm/s^2 (7.7)	• Baseline vs. Recovery

Intermittent (NB)		Recovery: 57.7 mm/s^2 (7.7)	
	Hand Tremor (Action)	Baseline: 40.3 mm/s^2 (7.7) Cessation: 66.8 mm/s^2 (7.7) Recovery: 65.2 mm/s^2 (7.7)	• Baseline vs. Cessation, Recovery
	Hand Tremor Xrms (Action)	Baseline: 51.1 mm/s^2 (7.3) Cessation: 68.1 mm/s^2 (7.3) Recovery: 70.0 mm/s^2 (7.3)	• Baseline vs. Cessation, Recovery
	Hand Tremor Yrms (Action)	Baseline: 51.1 mm/s^2 (10.0) Cessation: 72.7 mm/s^2 (10.0) Recovery: 71.2 mm/s^2 (10.0)	• Baseline vs. Cessation, Recovery
	MMG Amplitude of FDS	Baseline: 13.1 %MVC (2.4) Cessation: 15.1 %MVC (2.4)	• Baseline vs. Cessation
	Maximum Voluntary Handgrip Contraction	Baseline: 229.2N (17.3) Cessation: 174.7N (17.3) Recovery: 187.9N (17.3)	• Baseline vs. Cessation, Recovery
	Rating of Perceived Fatigue (VAS 0-100)	Baseline: 1.7 (4.7) Cessation: 51.3 (4.7) Recovery: 35.5 (4.8)	• Baseline vs. Cessation, Recovery • Cessation vs. Recovery
Hand Sustained (ISO)	Hand Tremor Xrms (Action)	Baseline: 67.5 mm/s^2 (16.4) TB30min: 124.9 mm/s^2 (17.2) TB40min: 120.9 mm/s^2 (17.2) TB50min: 124.9 mm/s^2 (17.2) Cessation: 115.4 mm/s^2 (16.6)	• Baseline vs. TB30min, TB40min, TB50min, Cessation
	Hand Tremor Yrms (Action)	Baseline: 58.1 mm/s^2 (14.2) TB10min: 70.4 mm/s^2 (14.6) TB30min: 98.0 mm/s^2 (14.8) TB40min: 99.5 mm/s^2 (14.8) TB50min: 116.9 mm/s^2 (14.8) Cessation: 96.8 mm/s^2 (14.4)	• Baseline vs. TB30min, TB40min, TB50min, Cessation • TB10min vs. TB50min
	Hand Tremor (Action)	Baseline: 52.9 mm/s^2 (13.3) TB10min: 60.3 mm/s^2 (13.7) TB30min: 105.3 mm/s^2 (13.9) TB40min: 103.5 mm/s^2 (13.9)	• Baseline vs. TB30min, TB40min, TB50min, Cessation, Recovery • TB10min vs. TB30min, TB40min, TB50min, Cessation

			TB50min: 112.2 mm/s^2 (13.9) Cessation: 100.6 mm/s^2 (13.5) Recovery: 86.0 mm/s^2 (13.3)	
		Wrist Tremor (Action)	Baseline: 42.9 mm/s^2 (9.5) TB30min: 81.7 mm/s^2 (10.1) TB40min: 78.4 mm/s^2 (10.1) TB50min: 85.9 mm/s^2 (10.1) Cessation: 75.3 mm/s^2 (9.6)	• Baseline vs. TB30min, TB40min, TB50min, Cessation
		Shoulder Tremor (Action)	Baseline: 38.0 mm/s^2 (6.6) TB30min: 65.9 mm/s^2 (7.1) TB40min: 66.2 mm/s^2 (7.1) TB50min: 65.2 mm/s^2 (7.1) Cessation: 61.4 mm/s^2 (6.8)	• Baseline vs. TB30min, TB40min, TB50min, Cessation
		MMG Amplitude of FDS	Baseline: 11.3 %MVC (2.3) TB30min: 18.3 %MVC (2.4) TB40min: 16.7 %MVC (2.4) TB50min: 17.9 %MVC (2.4) Cessation: 15.8 %MVC (2.3)	• Baseline vs. TB30min, TB40min, TB50min, Cessation
		Maximum Voluntary Handgrip Contraction	Baseline: 236.1N (19.6) TB10min: 220.5N (19.8) TB20min: 207.4N (19.9) TB30min: 203.2N (19.9) TB40min: 196.6N (19.9) TB50min: 186.0N (19.9) Cessation: 190.3N (19.7) Recovery: 191.8N (19.6)	• Baseline vs. TB20min, TB30min, TB40min, TB50min, Cessation, Recovery • TB10min vs. TB50min, Cessation, Recovery
		Rating of Perceived Fatigue (VAS 0-100)	Baseline: 1.7 (6.3) TB10min: 17.3 (6.5) TB20min: 30.2 (6.7) TB30min: 40.7 (6.7) TB40min: 46.5 (6.7) TB50min: 53.3 (6.7) Cessation: 52.8 (6.4) Recovery: 36.0 (6.3)	• Baseline vs. TB20min, TB30min, TB40min, TB50min, Cessation, Recovery • TB10min vs. TB30min, TB40min, TB50min, Cessation, Recovery • TB20min vs. TB50min, Cessation
Continuous Slope (14	Hand Sustained (ISO)	Hand Tremor Yrms	1.1%/3Sec (0.3)	• Hand Tremor Yrms vs. EMG Amplitude of Upper

Measures)		(Action)		Trapezius
	Continuous Hand Intermittent (NB)	Finger Tremor (Action)	0.6%/3Sec(0.1)	• Finger Tremor vs. EMG Amplitude of FCR and ECR, Shoulder Tremor (Action), Force Variation
Continuous By 10-Minute Blocks	Hand Sustained (ISO)	Hand Tremor Xrms (Action)	1^{st}10min: 0.012%/3Sec (0.002) 3^{rd}10min: 0.002%/3Sec (0.002) 4^{th}10min: 0.004%/3Sec (0.002) 5^{th}10min: 0.003%/3Sec (0.002)	• 1^{st}10min vs. 3^{rd}10min, 4^{th}10min, 5^{th}10min
		Hand Tremor Yrms (Action)	1^{st}10min: 0.018%/3sec (0.003) 3^{rd}10min: 0.006%/3sec (0.003) 4^{th}10min: 0.004%/3sec (0.003)	• 1^{st}10min vs. 3^{rd}10min, 4^{th}10min
		Hand Tremor Zrms (Action)	1^{st}10min: 0.018%/3Sec (0.003) 2^{nd}10min: 0.009%/3Sec (0.003) 3^{rd}10min: 0.003%/3Sec (0.003) 4^{th}10min: 0.006%/3Sec (0.003) 5^{th}10min: 0.006%/3Sec (0.003)	• 1^{st}10min vs. 2^{nd}10min, 3^{rd}10min, 4^{th}10min, 5^{th}10min
		Hand Tremor (Action)	1^{st}10min: 0.012%/3Sec (0.002) 3^{rd}10min: 0.003%/3Sec (0.002) 4^{th}10min: 0.004%/3Sec (0.002)	• 1^{st}10min vs. 3^{rd}10min, 4^{th}10min
		Wrist Tremor (Action)	1^{st}10min: 0.014%/3Sec (0.003) 3^{rd}10min: 0.003%/3Sec (0.003) 4^{th}10min: 0.003%/3Sec (0.003)	• 1^{st}10min vs. 3^{rd}10min, 4^{th}10min
		Finger Tremor (Action)	1^{st}10min: 0.019%/3Sec (0.003) 2^{nd}10min: 0.009%/3Sec (0.003) 3^{rd}10min: 0.005%/3Sec (0.003) 4^{th}10min: 0.006%/3Sec (0.003) 5^{th}10min: 0.006%/3Sec (0.003)	• 1^{st}10min vs. 2^{nd}10min, 3^{rd}10min, 4^{th}10min, 5^{th}10min
		Elbow Tremor (Action)	1^{st}10min: 0.015%/3Sec (0.003) 3^{rd}10min: 0.004%/3Sec (0.003) 4^{th}10min: 0.005%/3Sec (0.003) 5^{th}10min: 0.005%/3Sec (0.003)	• 1^{st}10min vs. 3^{rd}10min, 4^{th}10min, 5^{th}10min
	Shoulder Intermittent (SH)	Shoulder Tremor (Action)	1^{st}10min: 0.004%/3Sec (0.001) 5^{th}10min: 0.001%/3Sec (0.001)	• 1^{st}10min vs. 5^{th}10min

Chapter 8

Fatigue Responses During Simulated Light Precision Work: An 8-Hour Study

Abstract

Many contemporary occupations can be characterized by having long periods of low loads. However, these lower force levels, which are relevant to development of work-related musculoskeletal disorders, are usually not the subject of fatigue studies. In studies that measured fatigue in light manual work, there are inconsistencies within measurement responses. A complementary set of fatigue measures, reflecting neuromuscular and cognitive mechanisms, were measured over the course of an 8-hour light precision micropipetting task. Nine measurement parameters were found to be responsive over the 8-hour period, including: ratings of perceived fatigue, postural tremor, blink frequency, and critical flicker fusion frequency threshold. Scheduled work breaks generally provided amelioration of physical fatigue but had no effect on error rates and inconsistent effects on cognitive fatigue indices. Error rates might be a consequence of fatigue, both cognitive and neuromuscular, but might also reflect changes in arousal level. Overall, a complex interplay between peripheral and central mechanisms was observed in different body segments of the upper limb, which indicates that at a local level, the development of fatigue may be dependent on task parameters.

1. Introduction

There has been a growing interest in the development of fatigue in work tasks (de Looze et al., 2009; Kajimoto, 2007). Fatigue, as a design and evaluation tool, might improve work productivity and product quality, which are both important issues with societal and firm competitiveness consequences. In occupational work, however, there is limited information on the temporal development of fatigue during a work shift and across multiple workdays. A particular challenge is the selection of measures to detect neuromuscular fatigue in realistic work. To circumvent this challenge, a complementary set of fatigue measures might provide some insight towards fatigue development over time. This notion was reinforced by an exploratory study in physically demanding work (Yung et al., 2014), which demonstrated the responsiveness of different sets of measures, reflecting different mechanisms, at different periods of time (i.e., during a workday or between multiple workdays). In light or sedentary work, it appears that detecting fatigue might also benefit from a complementary set of fatigue measures. For instance, Bosch et al., (2007) observed no signs of fatigue (i.e., based on EMG parameters) within a work shift and between the first workday and last day of the week in light manual work, but found increases in perceived discomfort. The authors asserted that EMG might not have captured physiological processes, including cellular changes and mechanical properties of excitation-contraction coupling, that might contribute to neuromuscular fatigue. Arguably, differences between measures, where certain measures demonstrate a lack of fatigue development, may also be due to opportunities in realistic work to vary muscle forces, posture, and work pace, with scheduled and discretionary breaks (Bosch et al., 2011).

Even in simulated light work tasks under controlled laboratory settings, there also appears to be inconsistencies between fatigue measures. Dennerlein and colleagues (2003) measured fatigue over a simulated 8-hour working day based on a repetitive ulnar deviation task at self-selected acceptable workloads. Although the psychophysically accepted workloads caused negligible soreness, pain, or discomfort in the forearm, the authors observed low frequency fatigue measured by electrostimulation. Bennie et al., (2002), in an identical study, found conflicting electromyography (EMG) evidence during repetitive ulnar deviations over an 8-hour day. Despite a shift to lower frequencies in electromyography (EMG) power spectra, which is consistent with fatigue, the authors found a decrease in signal amplitude. In another example, Bosch and colleagues (2011) simulated light industrial assembly work for a 2-hour duration at two work paces. In both work pace conditions, the authors did not find any signs of muscle fatigue based on standard EMG indicators. However, perceived fatigue and pressure pain threshold appeared to change over time.

In Study 5, it was apparent that the mechanisms underlying fatigue might be task dependent, influenced by the type of contraction, the work intensity, and the muscle groups involved. In that study, no single measure was most responsive in all measures, but measures that reflect both central and peripheral mechanisms were responsive in most conditions. Fatigue may not only be task dependent but there also appears to be some temporal dependency. The mechanisms and sites of fatigue may change as the task proceeds with time (Enoka & Stuart, 1992). For instance, early in a submaximal task, peripheral regulation of performance capacity is predominant, substantiated by increases, rather than decreases, in central governor activity, i.e., the level of motor unit activation (MacIntosh & Shahi, 2011). As time progresses, reflex inputs from small-diameter muscle afferents may play a prominent role in exercise limitation. Indeed, large central activation deficits and a disproportionate increase in perceived effort have been observed despite a moderate change in peripheral fatigue (Martin et al., 2010). After the cessation of activity, peripheral mechanisms (e.g., DHPR and RyR uncoupling, failure in sarcoplasmic reticulum Ca^{2+} handling) may contribute to low-frequency fatigue, persistent fatigue, and neuromuscular weakness. Controlled laboratory studies have demonstrated fatigue after bouts of heavy exercise, and weakness between exercise repetitions (e.g., Green et al., 2004). These studies have provided insight into the mechanisms responsible for fatigue and persistent fatigue, employing direct assessment of muscle function, including electrical stimulation, muscle biopsy, venous blood samples, etc.

The overall aim of this study was to investigate the responsiveness of a complementary set of fatigue measures, over a period of 8 hours, of simulated light precision work. The complementary set of measures, which are all field usable, reflect both central and peripheral mechanisms of neuromuscular fatigue, and cognitive and perceptual fatigue. More specifically, this study addressed the following objectives:

(1) Identify which measures revealed underlying physiological changes in a psychosphysically acceptable frequency-adjusted light precision task.
(2) Document the responses of each measure over a simulated 8-hour workday and determine the effect of scheduled morning and afternoon breaks (15 minutes each) and a lunch break (30 minutes).
(3) Track work performance (i.e., targeting, precision, technique errors) over the course of the workday. Relate these changes in work performance to fatigue responses.

2. Fatigue Measurement

The test battery consisted of measures reflecting central and peripheral neuromuscular mechanisms, cognitive, and perceptual fatigue. Cognitive or mental or central fatigue, henceforth referred to as cognitive fatigue, involves decrements in human information processing due to mental workload. It may be conceptualized as an executive failure to sustain attention in order to maintain or optimize performance. A decrease in performance occurs during acute but sustained mental effort, resulting in lower and variable performance (Holtzer et al., 2010). Physical fatigue involves the inability to maintain physical performance, and can be attributed to metabolic disturbances, failure of neuromuscular transmission, changes affecting the myosin-actin complex, etc. Physical fatigue might also be attributed to changes in function of the central nervous system and impairments might occur in supraspinal areas, spinal areas, and in the muscle afferent system (Behm, 2004). Therefore, it might be misleading to term *cognitive* fatigue as *central* fatigue, as central mechanisms might contribute to physical fatigue without changes in cognitive workload. According to Megaw (1995), visual fatigue manifests as a decline in visual performance and/or an increase in visual discomfort. Visual fatigue is a consequence of prolonged visual activity rather than mental workload, which causes changes in arousal level. Visual fatigue might be confused with cognitive fatigue, as there are cases where a decrement in arousal may lead to changes in oculomotor behavior despite no visual discomfort (Megaw, 1995). It is important to note that there is considerable overlap and interaction between the three categories of fatigue. For instance, Mehta & Agnew (2012) have shown that physical capacity was adversely affected by mental demand.

2.1 Perceived Fatigue

Perception of fatigue was obtained using a 10-cm visual analog digital scale. The anchor points represented "no fatigue" and "maximum fatigue". Ratings of perceived fatigue was later expressed as a value between 0 and 100. Participants were instructed to rate their perceived fatigue of their dominant upper extremity used to micropipette.

2.2 Maximum Voluntary Contraction

Participants exerted a maximum lateral pinch force and a maximum handgrip force with a handgrip dynamometer (Medical Research Ltd., Leeds, UK). Participants performed their maximum lateral pinch force and maximum handgrip force in a standing posture with their elbows at 90 degrees and to the side of their body. A maximum contraction was also elicited during shoulder flexion with a strap system connected to a load cell. The force signal was linear enveloped with a Butterworth 2nd order dual lowpass filter at 10 Hz and normalized to baseline measures. Each ramped maximum contraction was performed for 5 seconds, and later windowed and averaged with the middle 3-seconds of the MVC.

2.3 Surface Electromyography

Electromyography was recorded by bipolar surface electrodes (Ag-AgCl electrodes, Ambu Blue Sensor N, Denmark) with an inter-electrode distance of 20 mm. Hair was removed by razor and skin abraded with ethanol and prepared with NuPrep Gel (Weaver and Company, CO, USA). EMG signals were collected with an eight-channel data system (Bortec, Calgary, AB), with a common mode rejection ratio of >115 dB and a bandpass filter between 10 and 1000 Hz. Signals were amplified and sampled at 2048 Hz. Muscle activity of the upper trapezius, anterior deltoid, flexor carpi radialis (FCR), and extensor carpi radialis (ECR) were recorded. These muscles were selected to reflect general flexor and extensor activity of the hand and shoulder flexion activity (anterior deltoid), and a shoulder stabilizer (upper trapezius). Electrode placement sites were based on the recommendations in Delagi et al., (1975), Cram and Kasman (1998), Zipp (1982), and Soderberg (1982), and Yung and Wells (2013). EMG was analyzed as a test battery measure and as a continuous measure, simultaneous to pipetting work. As a test battery, the instantaneous root mean square (RMS) amplitude was calculated and normalized to the MVC and averaged for the middle 8-second window of the 10-second test contraction (e.g., hand grip and shoulder flexion). Participants used visual feedback to perform the test contractions, both at 10% MVC, to measure changes in muscle activity. A 10% MVC test contraction is within muscular activity ranges for both shoulder and forearm muscles during pipetting as indicated by Lintula and Nevala (2006). As a continuous measure, EMG data was analyzed for the first 5 minutes of the session and at 30-minute intervals for a window of 5-minutes. Amplitude probability distribution function (APDF) was performed and the 10^{th}, 50^{th}, and 90^{th} deciles were identified, representing static, median, and peak muscular load, respectively (Jonsson, 1982). Changes to the APDF curve (i.e., quantified by %MVC at 10^{th}, 50^{th}, and 90^{th} deciles) were documented over the course of the test session.

2.4 Mechanomyography

A low profile (4mm x 4mm x 1.45mm) tri-axial ± 3 g accelerometer (ADXL335, Analog Devices, Inc., Norwood, MA, USA; sensitivity = 300 mV/g, noise density = 250 μg/rtHz) measured mechanical responses of the flexor pollicis longus. The accelerometer was placed on the muscle belly with double-sided tape and loosely secured with transpore tape. MMG signals were digitally bandpass filtered between 5 and 100 Hz (Butterworth, 2^{nd} order). Similar to EMG, the instantaneous root mean square (RMS) amplitude was calculated, normalized to the MVC, and averaged for the middle 10-seconds of the test contraction. Participants used visual feedback to perform a handgrip and shoulder flexion test contraction at 10% MVC.

2.5 Physiological Tremor

Tri-axial ±3 g accelerometers (ADXL327, Analog Devices, Inc., Norwood, MA, USA; sensitivity = 420 mV/g, noise density = 250 μg/rtHz, filter capacitor = 0.01μF) were mounted on the thumb, hand, wrist, elbow, and acromioclavicular and were used to measure physiological resting tremor of the hand and shoulder. To measure physiological hand tremor, participants were instructed to support their elbows and forearms with the armrest of the chair, with the hand relaxed. Participants were asked to relax their fingers while supporting their wrist, forearm, and elbow when measuring physiological hand/thumb tremor. Similarly, physiological tremor of shoulder was measured with the participant's dominant arm relaxed and unsupported to their side. Tremor was Butterworth bandpass filtered (2^{nd} order) between 1 and 30 Hz for the thumb accelerometer and 1 and 20 Hz for all other accelerometer placements. The instantaneous RMS amplitude was calculated and averaged for the middle 8-seconds of the 10-second collection duration.

2.6 Postural Tremor

An identical tri-axial accelerometer (ADXL327, Analog Devices, Inc., Norwood, MA, USA) was mounted onto the tip of the thumb. For postural tremor of the fingers, participants pointed with an extended thumb (at the metacarpophalangeal joint) towards a target, with the elbows and wrists comfortably supported. At the hand, the thumb and index fingers were extended and fingers 3, 4, and 5 were flexed, forming a loose fist in a neutral hand position. Postural tremor of the hand/forearm and shoulder were also be measured by collecting tremor during a pointing task, respectively with the elbow supported and with the shoulder flexed. Accelerometers on the dorsum of the hand reflected tremor of the hand and forearm, and accelerometers attached to the anterior deltoid reflected tremor of the shoulder. Participants similarly targeted with the unsupported segment(s) outstretched, i.e., an extended thumb, pronation of the forearm, an extended elbow, and 90° flexion of the shoulder. Signals were digitally bandpass filtered between 1 and 30 Hz (thumb) or 1 and 20 Hz (all remaining accelerometers) with a Butterworth, 2^{nd} Order filter. Instantaneous RMS amplitude was calculated by averaging the middle 8-seconds of a 10-second data collection. Frequencies of interest for all segments of the upper limb typically lie between 1 and 30 Hz and there is little power in the frequencies of postural tremor above this value (Morrison & Newell, 2000; Carignan et al., 2012).

2.7 Action Tremor

The tri-axial accelerometer (ADXL327, Analog Devices, Inc., Norwood, MA, USA) mounted on the tip of the thumb, dorsum of the dominant hand, and shoulder will serve to measure action tremor during lateral pinch grip, handgrip contraction, and shoulder flexion, respectively. The placements of these accelerometers were similar to those of Morrison and Newell (2000) for the upper arm and distal upper extremity when measuring limb segment tremor. The acceleration signals were Butterworth bandpass filtered (2^{nd} order) between 1 and 30 Hz (thumb) or 1 and 20 Hz (hand and shoulder). The instantaneous RMS amplitude was calculated and averaged for the middle 8-seconds of the 10-second collection duration. Participants used visual feedback (LabView, National Instruments Corporation, Austin, TX) to perform a test contraction to measure action tremor. The test contraction was 10% of the participant's maximum force, which is within the mean muscle activity for the simulated pipetting work task (Lintula & Nevala, 2006).

2.8 Postural Sway

Impairment of the postural system was documented by measuring postural sway, using centre-of-pressure measures from a force platform. Participants were asked to stand on a Nintendo Wii balance board, with their feet at pelvis width, looking straight ahead, and their arms at their sides in a comfortable position. Participants will maintain this position, as still as possible, for 60 seconds (Carpenter et al., 2001). Data was sampled at 64 Hz and extracted with custom software (LabView, National Instruments Corporation, Austin, TX) for offline processing. Force data was digitally filtered with a dual pass 4th Order Low Pass Butterworth filter with a 6 Hz cutoff (Ma, 2012 – thesis). The root mean square of the center of pressure displacement amplitude in the A-P direction was calculated, as this analysis parameter has been shown to be sensitive to both postural and lower limb fatigue (Dickin & Doan, 2008; Lafond et al., 2009).

2.9 Critical Flicker Fusion Frequency

The flicker reactive value of the eye measured by critical flicker fusion frequency tests (CFF) evaluated the sensitivity of the participant's visual acuity that may change as a result of perceptual fatigue (Yuan et al., 2011). The test consists of participants staring at a light source, increasing or decreasing in frequency, which forms the basis of "the methods of limits" (Curran & Wattis, 1998). The state, at which an intermittent light becomes less distinct and fuses, is known as the ascending critical fusion threshold. Alternatively, the alteration of perceptual state from a continuous supra-threshold light to an intermittent one is referred to as the descending critical flicker frequency threshold. The critical flicker fusion threshold is therefore the average of ascending and descending thresholds (Curran & Wattis, 1998). A CFF device was custom designed and consisted of a white LED stimulus, an optical viewing distance between 6 and 7 inches, and a focal point of 12 meters (LabChurch, 2014). Participants were instructed to observe a flickering light that increased in frequency, indicating the frequency at which they can no longer detect flicker. The light then decreased in frequency at which the participant reported the threshold when flicker recommenced. The frequency was increased or decreased at a constant rate, at 1 Hz per second, which is a preferable method to minimize the risk of temporal adaptation (Curran & Wattis, 1998). Ascending and descending threshold protocols were performed 3 times each and the average was calculated as the flicker fusion threshold, to the nearest 0.1 Hz. Due to the time required for testing, CFF tests were performed at baseline, before and after lunch break, during morning and afternoon breaks, and at the end of the day.

2.10 Oculomotor Behaviour

Blink frequency and duration were continuously monitored as participants performed the light precision task, and as a test battery during the 60-second postural sway test. A commercially available Muse headband (Interaxon, Toronto, CAN), consisting of dry surface electroencephalogram electrodes, measured these oculomotor behaviour parameters. The participant's forehead was cleaned with an ethanol swab and the headband was mounted on the forehead prior to collection of oculomotor behaviour. The headband was removed at non-recording periods. As part of a test battery measure, participants were asked to gaze at an imaginary target on the wall for the 60-second duration. Oculomotor signals were processed similarly to methods described by Skotte and colleagues (2007) for electrooculorgraphy (EOG). EOG signals will be digitally filtered with a high-pass filter (0.1 Hz cut-off frequency, fourth order Butterworth) to remove amplifier DC offset, and low-pass filtered (dual pass, fourth order Butterworth, 10 Hz cut-off frequency) to remove EMG information from the recording. Blink events were determined using threshold criterion based on standard deviations from the mean eyeblink voltage at baseline recorded during the training session. Signals that exceed two standard deviations above and two standard deviations below the mean eyeblink voltage were treated as artefacts and excluded from further analysis. In one study, on average, in non-fatigued individuals, blinks occur 15-20 per minute with an interval of 2-10 seconds between blinks, blink duration of 100 - 400 milliseconds, and amplitude of 380 mV (Dey et al., 2012). Frequency (per minute) and duration of blinks were recorded (LabChart 7, ADInstruments, Colorado Springs, CO, USA).

2.11 Performance Measures

Once the maximal acceptable frequency was determined, participants were asked to maintain the fixed pace for the 8-hour experimental session. A monitor displayed a randomly chosen number between 1 and 12 and an auditory cue signaled the beginning of a pipetting cycle. After completing a full 12-tube rack, the numbers were re-randomized, and the process was repeated. Participants were instructed to transfer the liquid to the numbered micro-centrifuge that corresponded to the displayed number. This served as a performance measure (i.e., targeting). Thumb forces were recorded with a force-sensing resistor (FlexiForce A301 Sensor, Tekscan, Inc., MA, USA) mounted on pipette's plunger. The recorded thumb forces provided a measure of a completed cycle. Quality and precision of pipetting was also assessed over the course of the 8-hour day (Table 8.1). Participants were instructed to aspire liquid from the test tube into the micro-centrifuge without transferring glycerin, and to transfer liquid to the appropriate numbered micro-centrifuge. Finally, participants were asked to perform the pipetting task with no errors in technique (i.e., no air bubbles, equal volume aspired and dispensed, no spillage of liquid, proper ejection of the tip into the disposal beaker). Each completed micro-centrifuge tube rack was analyzed and errors were recorded and time stamped. Errors were later organized by each hourly block of pipetting time. Errors were classified based on Reason's (1984) taxonomy of errors. Briefly, slips are skill-based errors. Slips occur when committing an error while having the correct mental model. Thus it occurs in tasks that involve a considerable degree of automaticity and errors occur due to attention failures. Lapses are also skill-based errors but usually involve failures of memory. Lapses occur when an action is omitted due to a failure in the storage stage of an action sequence. Mistakes are rule-based errors and occur when the operator has the incorrect mental model. These are planning failures that take place in unfamiliar situation. Mistakes are further categorized as rule-based or knowledge-based mistakes. Rule-based mistakes occur when applying a rule used successfully in the past to an incorrect situation, conversely applying a wrong rule to the current situation. Knowledge-based mistakes, on the other hand, are planning errors when stored rules are not applicable to the current situation. An incorrect decision is executed due to limited time and cognitive resources.

Table 8.1 Performance Metrics Categorization, Classification, and Operational Description.

Type of Error	Error Classification	Description
Precision	Slips	Aspiring and dispensing glycerin into a microcentrifuge tube. Clear glycerin layer evident on the bottom of colour-dyed water solution. Requires consistent immersion depth.
Targeting	Mistakes	Dispensing solution into incorrectly numbered tube, mismatched from the visual display.
Technique – Air Bubble	Slips (Aspiration) Lapses (Checking)	An air bubble observed within the colour-dyed water solution. Air bubbles are typically found on the side of the tube. Requires consistent immersion depth, angle, speed, and consistent pickup and dispense rhythm.
Technique – Volume	Slips	Solution neither fully aspired nor dispensed to the desired volume (500 μL). Requires consistent trigger pressure to the dispensing stop and complete blowout, proper immersion depth, and expelling technique.
Technique – Spillage	Slips	Solution dribbling from pipette tip or dispensing imprecision. Requires consistent pickup and dispense rhythm and proper expelling technique.

Technique – Ejection	Mistakes (Perception) Lapses (Memory)	Ejection of pipette tip into the incorrect beaker or accidental ejection. Requires consistent pickup and dispense rhythm and trigger pressure.

2.12 Test Battery vs. Continuous Measurement

Previously, test battery and continuous measurements were compared to assess whether test batteries approximate physiological responses during activity representative of different physical workloads and task parameters. In realistic work, it may be infeasible to obtain continuous measurement. Test batteries, on the other hand, can be administered during work breaks to avoid disruptions to the work activity. Additionally, test batteries provide a standardized measure, which control for factors that might lead to erroneous interpretation of physiological signals (i.e., test contraction at a consistent magnitude of force). Due to these collection concerns, this study employed test batteries as a measurement of fatigue, collected over the 8-hour simulated light precision work task. Continuous measurement at 30-minute intervals, for a short duration window, was collected to support test battery observations (Table 8.2).

Table 8.2 Fatigue Measurement Recording Strategy

Measurement Strategy	Fatigue Measure
Test Battery (Hourly)	• Rating of Perceived Fatigue (Visual Analog Scale) • Physiological Resting Tremor (Hand and Shoulder) • Postural Tremor (Finger, Hand, Arm, Shoulder) • EMG (10%MVC of Pinch, Handgrip, Shoulder Flexion) • MMG (10%MVC of Pinch, Handgrip, Shoulder Flexion) • Action Tremor (10%MVC of Pinch, Handgrip, Shoulder Flexion) • MVC (Pinch, Handgrip, Shoulder Flexion) • Blink Frequency & Duration (Muse Headband) • Postural Sway (Wii Board)
During Breaks	• Test Battery + Critical Flicker Fusion Frequency Threshold
Continuous (Every 30 minutes, 5-minute window)	• EMG (Amplitude Probability Distribution Function) • Performance (Precision, Targeting, Technique)

3. Methods

3.1 Participants

As a requirement to participate, volunteers had prior micro-pipetting experience, were proficient in forward pipetting technique, with at least 60 hours of pipetting experience in the previous 12 months. All participants had no current or injuries in the previous 6 months to the dominant upper extremity and the lower back, and no previous episodes of epileptic seizures, nausea, or eye discomfort and dryness. Participants were asked to refrain from exercise of the upper extremities, caffeine, and alcohol consumption, within 24 hours prior to the experimental session. Prior to the training session, informed consent was provided for all experimental procedures and associated risks, as approved by the University of Waterloo Office of Research Ethics.

3.2 Simulated Precision Task: Micropipetting & Set-Up

Work in real life is usually performed for fixed periods of time, not until exhaustion. Therefore, micropipetting was selected, as it is a light precision task that can be completed over an extensive period without undue strain and exhaustion. Pipetting has been extensively studied and has been simulated to model repetitive and standardized work of the upper extremities (Park & Buchholz, 2013; Srinivasan et al., 2015), and also affords the capability to measure performance errors based on common pipetting metrics. Pipetting work requires concentration, accuracy, and precision, and is physically demanding on the hands (particularly the thumb), shoulders, neck, and back (Fredriksson, 1995; David & Buckle, 1997). For instance, David and Buckle (1997) observed increased levels of elbow and hand complaints among regular pipette users compared to a control group. The onset of complaints increased with the number, rate, and duration of pipetting tasks. Not surprisingly, pipetting is a major source for aches, pains, and musculoskeletal injuries among laboratory workers, particularly while using manual pipettes. Although mechanical pipettes were introduced 30 years ago in place of aspiration by mouth or bulb, changes to the design of manual pipettes have remained stagnant over the decades. Electronic pipettes have been introduced to reduce muscular strain of the hand (Lintula & Nevala, 2006) but like mechanical designs, operators must continue to suspend the pipette above the work area (Costello, 2005). The most common type of manual pipette is plunger operated, which is held with a combination of a power- and precision- grip (Fredriksson, 1995) or a dagger grip (David & Buckle, 1997), with the distal phalanx of the thumb held flexed on the plunger.

In general, pipetting typically consists of tipping, aspirating, dispensing, and tip ejection actions (Park & Buchholz, 2013). Forward pipetting is the most frequently used technique in laboratory work, and has been extensively studied in previous literature (e.g., Lu et al., 2008; Lichty et al., 2011; Park & Buchholz, 2013). For single forward pipetting (Figure 8.1A), the tip is first placed on the discharge end of the pipette. Second, to aspirate liquid, the plunger is depressed until the initial resistance (the first measuring stroke), the tip is inserted into the liquid, and the plunger is slowly released by the user’s thumb through a spring-loaded mechanism. Third, when dispensing the liquid, the plunger is depressed until the initial resistance and subsequently pressed fully to discharge the entire volume and residual liquid (blowout). Finally, the pipette tip is removed by engaging the ejector (Lu et al., 2008). During repetitive pipetting, aspiration requires depression until the second stop (i.e., blowout position), with dispensing to one vessel to another at the initial resistance (Figure 8.1B). Compared to forward pipetting, repetitive pipetting is advantageous for repeated pipetting of the same volume into multiple receiving vessels.

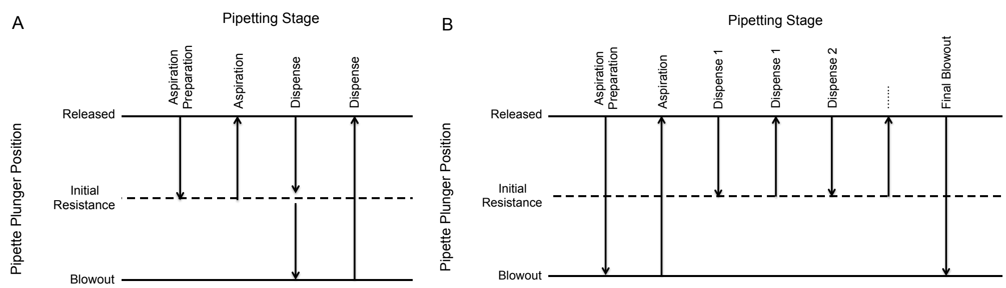


Figure 8.1 Pipetting Techniques – Forward (A) and Repetitive (B)

According to Asundi and colleagues (2005), during dispense and blowout, participants applied a peak force between 23 and 35 Newtons (N), which represents 23% to 34% of maximum strength. However, the magnitude of pipetting and blowout forces is dependent on the type of pipette. For instance, Lu et al., (2008) measured hand and thumb forces in three types of pipettes and found that pipette design dictated exerted forces regardless of pipetting task, body position, and sample volume. In their study, they found thumb force range between 15 N and 28 N during aspiration, 18 N to 31 N during blowout, and 10 N to 42 N during tip ejection. Hand forces were greatest during "pick up tip" (i.e., attaching the tip directly from the storage box to the end of the pipette by engaging the pipette into the tip), requiring 6.5% to 15% of maximum handgrip force (Lu et al., 2008). Similarly, Lintula and Nevala (2006) compared five pipettes based on surface electromyography of four muscles (flexor pollicis longus – FPL, flexor pollicis brevis – FPB, flexor digitorum sublimis – FDS, and trapezius). Although there were no differences between pipettes in the muscular activity of FPB, FDS, and trapezius, there were significant differences in muscular strain of FPL. Muscular activity ranged between 7% and 8% MVC for the trapezius, 3.4% to 4.3% MVC for FDS, 7% to 9% MVC for FPB, and 8.7% to 11.5% MVC for FPL. Exacerbating the risk for fatigue or tendon-related injuries, high-precision pipetting (i.e., transferring small volumes or careful tip placement) led to elevated static thumb muscle loads (Asundi et al., 2005). Plunger-operated pipettes have been extensively used to simulate light precision work in ergonomic intervention studies on arm supports (e.g., Feng et al., 1997), usability of different pipetting systems (e.g., Lintula & Nevala, 2006), and consistency of kinematic motor variability (e.g., Srinivasan et al., 2015).

In this study, one complete cycle consisted of the four fundamental discrete actions: (1) attach the tip on the discharge end of the pipette, (2) aspirate the sample from a large test tube, (3) target, dispense, and overblow the sample into a microcentrifuge tube, and (4) eject the tip into a disposal beaker (Figure 8.2).

Figure 8.2 Pipetting Cycle (Forward Pipetting Technique)

Participants performed the pipetting task with their dominant hand and were allowed to rest their non-pipetting hand/arm on the table or to their side. In rare cases, participants adopted a technique where they used their non-pipetting arm to aid in pipetting (i.e., stabilizing the hand during aspiration and dispensing or picking up tube during dispensing). Participants were instructed to maintain their posture throughout the entire 8-hour protocol. All materials and equipment (e.g., locations of pipette, samples, tips, tip disposal bin) were placed in fixed locations on the work surface (Figure 8.3), similar to Park and Buchholz (2013) and Srinivasan et al., (2015). A 12x2 numbered vial array was placed in front of the participant, 10 cm away from the edge of the table, and occupied with 0.5 mL micro-centrifuge tubes (Eppendorf Canada, Mississauga, Ontario). The safe lock covers were removed from the tubes to avoid visual obstruction of the numbered positions on the rack. The tip storage rack was placed behind the vial array, approximately 30 cm away from the edge of the table. With this arrangement, participants were instructed to retrieve a disposable tip from the storage rack by plunging the micropipette onto each tip. A sample, contained within a glass beaker, was placed to the dominant side of the participant (i.e., side of the pipetting hand), 30 cm away from the edge of the table and 25 cm to the right from the midline of the participant. The sample consisted of 300 mL of colour-dyed water suspended over 300 mL of glycerine USP (density = 1.26 g/cm^3, 100.0% v/v). The sample was intended to increase the level of required precision during aspiration, as participants were asked to avoid transferring the glycerin into the micro-centrifuge tubes (Asundi et al., 2005). In the event that glycerin was transferred from the sample to the receiving vessel, the cycle was recorded as an error (i.e., a product quality deficit). The volume of water was replenished after every hour. The tip disposal bin was placed adjacent to the beaker sample, 30 cm away from the edge of the table and approximately 35 cm to the right from the midline of the participant.

All testing was completed at a work surface height designed for pipette work in a standing posture. Despite the fact that laboratory workers adopt both seating and standing postures, Park and Buchholz (2014) concluded that seated postures should be avoided in pipette work. The authors claim that in all seated work surface heights, muscle activity of the shoulder muscles exceeded recommended values determined by Kroemer (1989) and Rohmert (1973). Pipetting while standing has been employed in other studies, including Lichty and colleagues (2011) who asserted that standing work would minimize the influence of other factors, including chair design and hood design. Although introducing *both* seating and standing posture might mitigate the risk of low back pain and discomfort (Gallagher et al., 2014), changing working posture may introduce random variability. Controlling for work posture and physical exposure might reduce inter-subject variability. Participants, however, were given the opportunity to adopt a seated posture during hourly break times and scheduled 15-minute or lunch breaks. While in a standing posture, the table surface was placed at the level of the pipette tip, when it is held with the hand at elbow height (Park & Buchholz, 2014). Park and Buchholz (2014) found that this work posture arrangement reduced shoulder strain and minimized hand and neck strain.

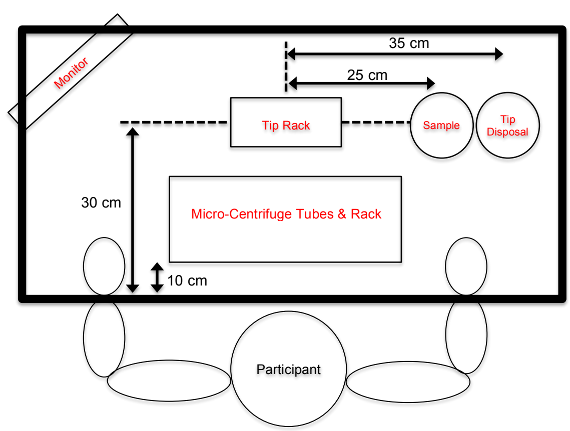


Figure 8.3 Simulated precision task workstation layout

3.3 Psychophysical Approach to Determine Maximal Acceptable Work Cycle Frequency

The psychophysical approach requires the participant to judge their capacity to perform a task safely, based on physiological and biomechanical sensations. This method has been used to determine maximum acceptable weights of lift for a variety of manual tasks (e.g., Snook et al., 1970; Snook & Ciriello, 1991). An extensive set of literature has also demonstrated the use of psychophysics to determine maximum acceptable frequency in drilling tasks (Marley & Fernandez, 1995), lifting (Fox & Smith, 2014), and simulated roof shingling (Choi & Fredericks, 2008). Participants were instructed to perform the simulated precision task (i.e., pipetting) as if it were on an incentive basis without experiencing unusual and undue discomfort in the hands, wrists, forearms, and shoulders. Additionally, participants were also instructed to ensure good quality pipetting based on the aforementioned performance metrics. The frequency set to perform one cycle for the entire 8-hour collection duration was determined by method of adjustment. Instructions (Appendix C) were similar to those described by Ciriello et al., (2002). Although upwards of 1.5 hours during the training session was provided to allow participants adjust the frequency, it was upon the researcher's discretion to provide additional time. A computer program served as an auditory cue to perform a pipetting cycle and participants instructed the research study facilitator to increase or decrease the cycle time. The initial cycle time was randomly determined and participants were blinded to the frequency. The work frequency was determined from the training session and was set as the initial frequency for the test day. However, participants were allowed to adjust the frequency for the first 55 minutes of the test session. Snook and Irvine (1968), as cited in Fox and Smith, (2014), found that participants did not make any further adjustments to frequency after 40 minutes in 90 percent of their test sessions; this was further validated by Wu and Chen (2003). Therefore, the final frequency set within the first 1-hour block of pipetting work will be considered the maximal acceptable frequency for an 8-hour period.

3.4 Protocol

Participants arrived to the laboratory on two consecutive days to perform a training, practice, and familiarity session and an experimental test session. With the exception of two participants, all training sessions started at 10:00. The two exceptions occurred at 8:30 and 14:30. All participants arrived to the lab at 7:30 for the test session.

3.4.1 Day 1: Training Session

Participants were given ample time to practice both test battery measures and the pipetting task. After participants provided informed consent, measuring equipment (i.e., EMG, MMG, and tremor) were mounted and participants were instructed to perform three of each grip, pinch, and shoulder flexion maximum voluntary contractions, and three series of quasi-static functional tests. These maximal grip, pinch, and shoulder flexion voluntary contractions were later averaged to determine the amplitude for the 10% MVC test contractions for Day 2. Participants were then given time to familiarize themselves with the critical flicker fusion frequency device and the Muse headband, and practice quiet standing on the Wii Balance Board. The initial CFF frequencies, set for ascension and descension tests, were calculated by determining ±15 Hz the mean threshold value, based on three CFF tests. While wearing the Muse headband, participants were asked to glare towards a target on the wall. The data served as a baseline to determine blink threshold (i.e., mean and ± 2 standard deviation). After providing instructions and practice time, participants completed a test battery. Time was given to familiarize themselves with the pipetting equipment, the pipetting task, and the psychophysical method. After sufficient preparation, participants randomly selected a number less than 20, which served as the initial cycle time. The pipetting task proceeded, with adjustment to the work pace, for an hour. A test battery was performed after the first hour, identical to testing procedures on Day 2, and resumed for at least 30 minutes. A test battery and CFF measure was collected at the conclusion of the practice pipetting session.

3.4.2 Day 2: Experimental Test Session

A test session was performed for an 8-hour period, between 8:30 and 17:30 (Figure 8.4). To simulate an 8-hour work shift, 15-minute rest periods were provided in the morning (10:30) and afternoon (15:15). Morning and afternoon breaks between 10 and 15 minutes are standard at many workplaces (Taylor, 2005). A 30-minute lunch break, consistent with previous studies in realistic work (e.g., Henning et al., 1997), was provided at 12:45. During these break periods, a test battery and CFF test was collected, and participants were asked to sit and relax and were provided with standardized meals, snacks and drinks. Lunch meals were standardized to meet acceptable macronutrient distribution ranges (Health Canada, 2006). The macronutritional content was recorded for each individual and later averaged (Figure 8.4).

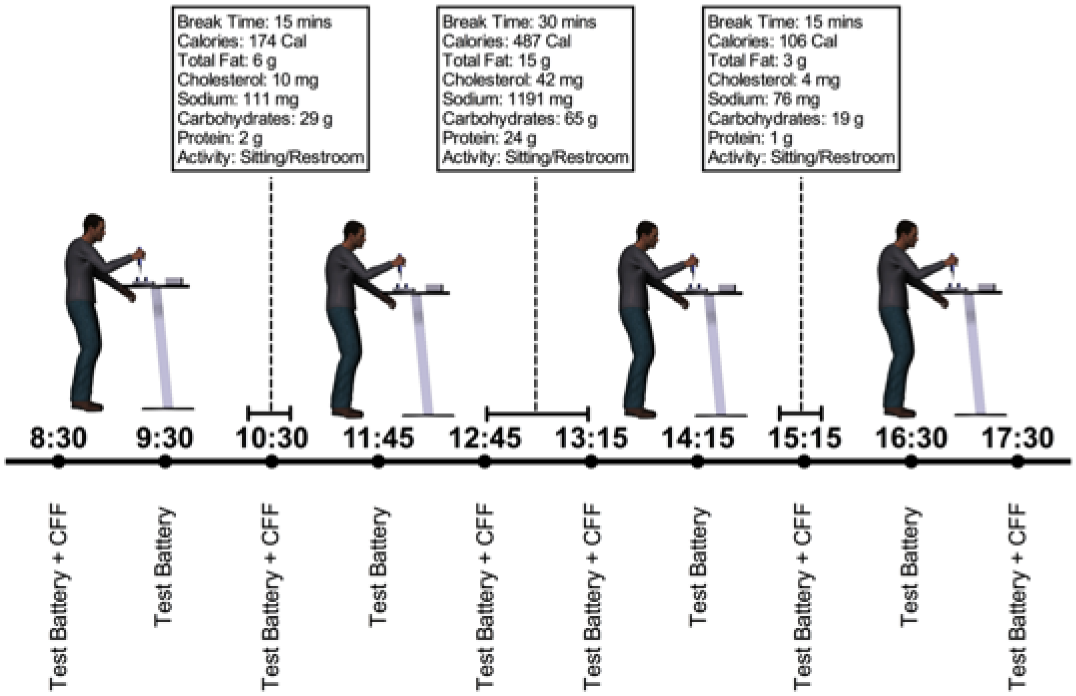


Figure 8.4 Experimental Test Session Data Collection Schedule

Test battery measurements were collected at hourly intervals (i.e., every 55 minutes) and continuous measurements were obtained every 30 minutes, for a 5-minute period. This data collection arrangement was similar to Dennerlein et al., (2003) who simulated a full workday with seven 55-minute segments; with 15-minute work breaks after segments 2 and 6, and a 30-minute lunch break after segment 4. Supporting the use of 1-hour work blocks, Smith and Jiang (1984) demonstrated that 1-hour work duration closely approximates an intermittent work schedule. Activities may thus occur in 1-hour work bouts with opportunities for some recovery between bouts. Continuous pipetting is typical among pipette users (e.g., laboratory technicians). Among pipette users, over half performed continuous pipetting work for greater than 30 minutes, almost a quarter pipetted greater than 60 minutes (David & Buckle, 1997).

3.4 Statistical Analysis

Test battery measures and EMG APDF values were compared over time; ten periods in test battery measurement (i.e., 8:30, 9:30, 10:30, 11:45, 12:45, 13:15, 14:15, 15:15, 16:30, 17:30) and 24 periods in continuous measurement (i.e., every 30-minute interval). Data was then evaluated for normality by plotting data as a histogram, drawing Q-Q plots, and the Shapiro-Wilk test. If data deviated from a Gaussian distribution, nonparametric approaches were considered. Otherwise, a mixed-model repeated measures analysis compared values at the multiple time points, and Tukey-Kramer post-hoc tests calculated statistical differences between these time periods if a significant main effect was observed. Residual analyses were undertaken to examine model assumptions and to detect outliers or influential data points.

All measures were submitted to principal component analysis to descriptively analyze salient features and patterns (MATLAB 7.2, Mathworks, Inc,. Natick, MA. USA). Data was normalized as z-scores so that all variables were measured in the same units, and factors were extracted and rotated with Varimax rotation. Scree plots and the total explained variance helped determine the number of principal components. A total explained variance cutoff of 70% was selected. An eigenvector coefficient threshold of 0.40 was chosen in order to select fatigue measures in each principal component. Principal components were categorized based on the same criteria from study 5, but on a body segment basis (i.e., thumb, hand, shoulder). After PCA loadings were determined and interpreted, projections of the original data onto eigenvectors were interpreted to determine the relationship of principal components among observations (i.e., time). This was equivalent to the mean of all measurement values, at each time point, that comprise the principal component. To help visualize trends of all projections, an aggregate loading vector was generated, based on weighted projections. All statistical analyses were performed using Statistical Analysis Software (Version 9.4, SAS Institute Inc., Cary, NC, USA) at an alpha level of 0.05.

4. Results

Eleven participants (6 females, 5 males; mean age = 21.3 years, mean weight = 68 kg) meeting inclusion criteria volunteered to participate in this study. All participants were right-hand dominant and had an average of 97.3 minutes of micropipetting experience on a weekly basis in the previous 12 months. Participants, on average, pipetted at least twice per week. All participants were university undergraduate or graduate students from biology, biochemistry, pharmacy, chemistry, and physiology.

During the training session, participants required an approximate total of four hours to familiarize and practice test battery measures and the pipetting task. On average, two hours were dedicated to the psychophysical training of the pipetting task. This resulted in the practice of four test batteries (e.g., at baseline with CFF, 0.5 hour, 1 hour, 1.5 hours with CFF). Based on the psychophysical frequency-adjusted training session, the self-selected cycle time was 12.07 seconds (SD = 1.64 seconds, range = 10 to 14 seconds). All participants completed the training session one day before their scheduled test session.

Participants arrived to the laboratory at 7:30am for preparation and completion of the baseline test battery. At 8:30am, participants started their 8-hour pipetting task, with two, 15-minute breaks mid-morning and mid-afternoon, and a 30-minute lunch break. Since test batteries were collected at the beginning and end of the lunch break, 20-minutes were dedicated to lunch and rest.

4.1 Responsiveness of Test Battery Measures Over The Simulated Pipetting Task

A test battery consisted of 13 measures or tests, and critical flicker fusion frequency threshold recorded during breaks. The 13 measures or tests resulted in 45 measurement parameters (i.e., amplitude or frequency). Of the 45 measurement parameters, nine measures revealed statistically different responses over the pipetting task, and for brevity, are further described in detail. The remaining measures are presented in Appendix C and will be briefly discussed in later sections.

A mixed model repeated measures analysis revealed significant change over time in rating of perceived fatigue using a visual analog scale (Figure 8.5). Relative to baseline (mean = 4.18), ratings at 10:30 (mean = 24.89), 12:45 (mean = 25.77), and from 14:15 to 17:30 hrs (means = 26.05, 32.35, 36.42, 40.72, respectively) were significantly higher. When compared to 9:30 hrs (mean = 12.82), late afternoon periods between 15:15 and 17:30 hrs were statistically greater. Later time periods (i.e., 15:15 to 17:30 hrs) demonstrated higher ratings than early afternoon (i.e., after lunch at 13:15 hrs). Finally, the final test battery, at 17:30 hrs, revealed a statistically higher rating value than ratings at 11:45 hrs (mean = 19.63). Postural tremor effects of the finger (hand supported), hand (arm supported), arm (elbow supported), and shoulder (fully flexed) demonstrated changes in tremor amplitude over the pipetting task. During a postural finger test, finger tremor amplitude decreased immediately after lunch (i.e., 13:15 and 14:15 hrs) compared to early/mid morning (mean = 173 mm/s^2 at 9:30 hrs). Finger tremor amplitude was also found to change over the pipetting task during postural hand and arm tests. During a postural hand test, finger amplitude was statistically lower at 13:15 hrs when compared to 9:30 and 10:30 hrs. Similarly, hand tremor amplitude was also significantly lower at 13:15 hrs relative to 10:30 hrs during the postural hand test. During a postural arm test, finger amplitude was lowest at 13:15 hrs compared to 9:30 hrs. However, finger tremor increased towards the end of the day, with significantly higher finger tremor amplitude at 17:30 compared to 13:15 hrs. Wrist tremor amplitude also led to changes over time during a postural arm test. Wrist RMS amplitude increased at 17:30 hrs, and was significantly higher than late morning (11:45 hrs) and after lunch (13:15 hrs). Hand amplitude measured during a postural shoulder test increased over the pipetting task. More specifically, afternoon test batteries (14:15 to 17:30 hrs) were statistically higher than

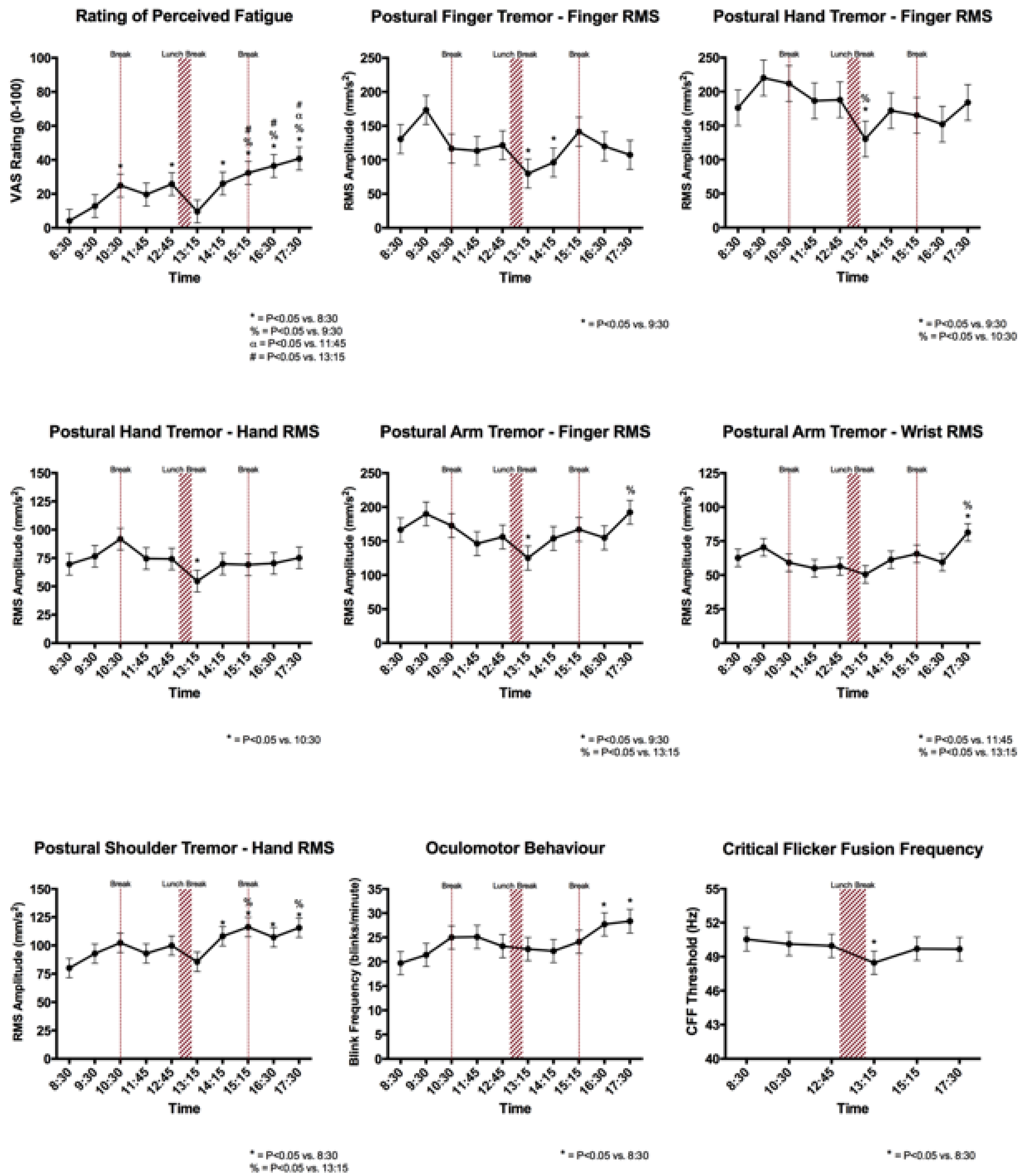


Figure 8.5 Fatigue measures demonstrating significant time-of-day effects during an 8-hour micropipetting task.

baseline at 8:30 hrs and after lunch (13:15 hrs). Oculomotor behaviour, in particular eyeblink frequency, increased significantly at the end of the 8-hour pipetting task. Blink frequency at 16:30 and 17:30 were higher than baseline. Finally, critical flicker fusion frequency, recorded at the beginning and end of the 8-hour session and during breaks, revealed a low threshold value after the lunch break, prior to commencement of work in the afternoon (13:15 hrs).

4.2 Pipetting Performance & Concurrent Muscle Activity

Performance metrics were recorded after completion of a microcentrifuge tube rack. Data was then arranged on an hourly basis, coinciding with blocks of continuous pipetting performed for 55-minutes. Errors were classified and were recorded as a rate (number of errors per number of pipetting opportunities) for each participant. Figure 8.6 shows the mean % error rate per hour at the eight blocks of 55-minutes for the six categories of errors.

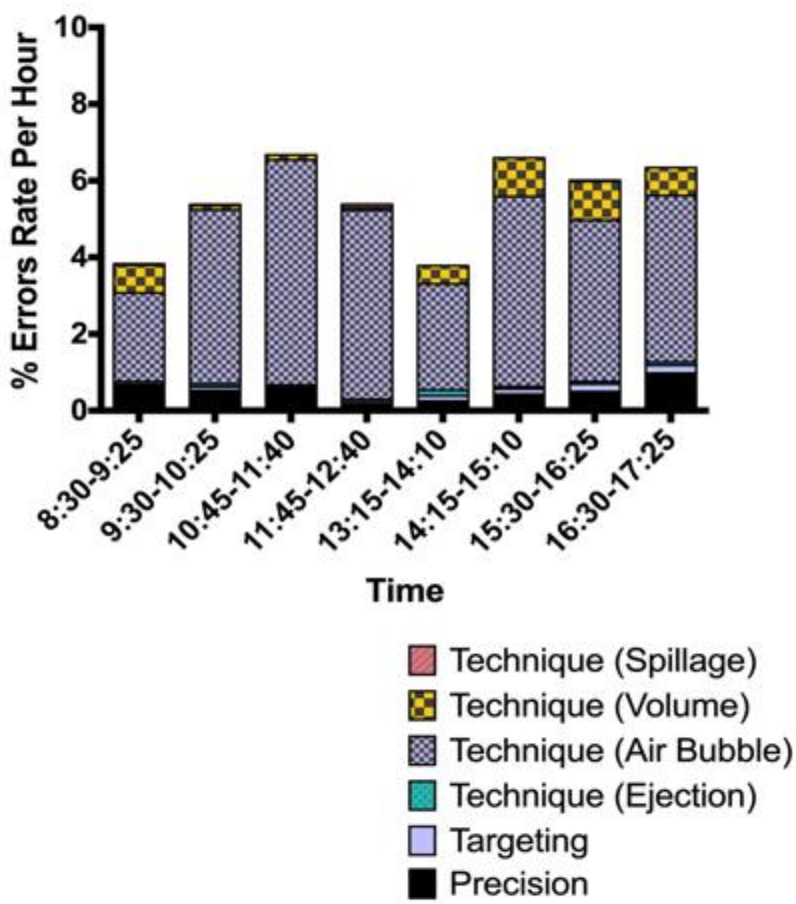


Figure 8.6 Error rate (%/hour) by error classification types. Error rates quantified on an hourly basis over the 8-hour light precision task.

EMG muscle activity recorded at 30-minute intervals, for a 5-minute window, was submitted to APDF analysis. The mean value for each muscle, at each decile, at each 30-minute interval over the workday is shown in Figure 8.7. Over the 8-hour pipetting task, mean loads (P = 0.5) in FCR, ECR, anterior deltoid, and upper trapezius were 2.90%, 4.26%, 4.81%, and 5.78%, respectively. The static contraction level (P = 0.1) in the FCR, ECR, anterior deltoid, and upper trapezius muscle were 1.45%, 1.80%, 0.89%, 2.70%, respectively. Peak loads (P = 0.9) for the FCR was 5.93%. ECR, anterior deltoid, and upper trapezius had peak loads of 8.88%, 10.82%, and 9.45% MVC, respectively. There were no observable changes of the static, mean, and peak loads in FCR, anterior deltoid, and upper trapezius over the 8-hour pipetting task. The extensor carpi radialis experienced a decrease in mean and peak muscle activity from baseline towards the final hour of the pipetting task.

4.3 Fatigue Development Over Time

Principal component analysis extracted six components, accounting for 80.73% of the total variance. Principal components were categorized based on the aggregate combination of measures and interpreted based on previous literature and strong theory. The first component comprised of 17 measurement parameters (Table 8.4) and was categorized as peripheral fatigue of the distal upper extremity (hand/thumb), peripheral fatigue of the shoulder, cognitive fatigue (i.e., decrement in vigilance), and errors. The second component consisted of 16 measurement parameters and primarily represented central fatigue of the shoulder, central and peripheral fatigue of the distal upper extremity, and errors. The third component, accounting for 13.04% of the total variance, was comprised of 11 measurement parameters. These parameters predominantly reflected central and peripheral fatigue of the thumb, postural sway, a decrease in blink duration, and errors. The fourth component reflected central and peripheral fatigue mechanisms of the distal upper extremity, predominantly of the hand. Nine measurement parameters were identified based on the 0.40 eigenvector coefficient critierion that contribute to the fourth component. Finally, the fifth and sixth components account for 9.48% and 9.40% of the total variance, respectively. The fifth component consisted of 8 measurement parameters, whereas the sixth component was comprised of 7 measurement parameters. Peripheral fatigue of the distal upper extremity, predominantly of the thumb, characterized the fifth component. The sixth component reflected peripheral fatigue of the thumb.

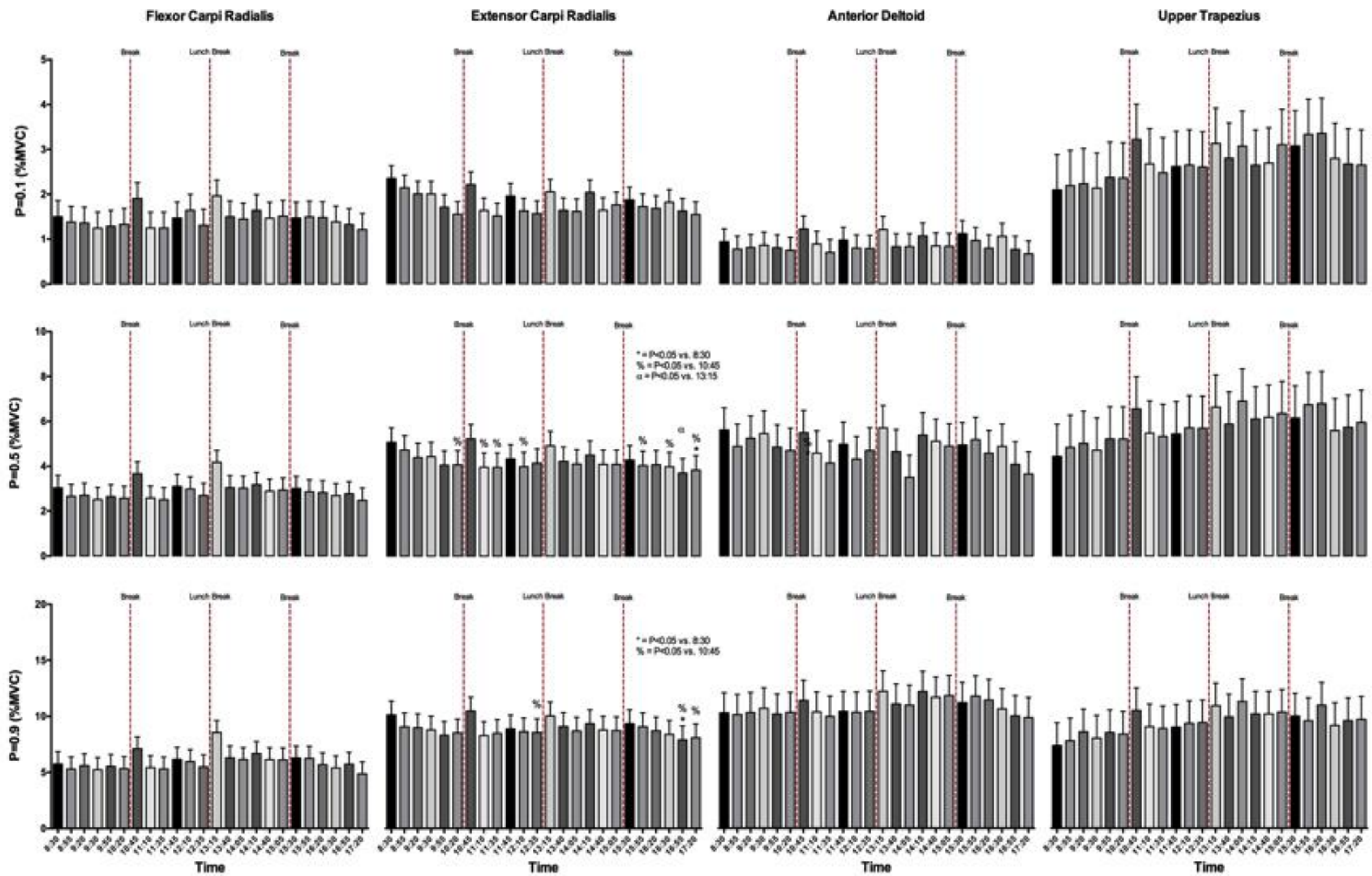


Figure 8.7 Muscle activity (APDF) at static (P = 0.1), mean (P = 0.5), and peak (P = 0.9) loads for four muscles at 30-minute intervals.

Table 8.4 Principal Components for Fatigue Measures Over the Pipetting Task.

PC 1	PC 2	PC 3	PC 4
Action Hand_Finger_RMS +	Action Hand_Hand_RMS +	Action Pinch_Finger_RMS +	Action Hand_Finger_RMS +
Action Pinch_Hand_RMS +	Action Pinch_Hand_RMS +	Blink Duration +	Action Hand_Hand_RMS +
Action Shoulder_Elbow_RMS +	MVC_Shoulder -	Hand EMG_FCR_Freq +	Action Pinch_Hand_RMS +
Blink Frequency +	Postural Arm_Finger_RMS +	MVC_Pinch +	Grip CV +
Hand EMG_ECR_Freq -	Postural Arm_Hand_RMS +	Postural Arm_Finger_RMS +	Hand EMG_ECR_RMS +
Hand EMG_FCR_RMS +	Postural Arm_Wrist_RMS +	Postural Finger_Finger_RMS +	Rest Tremor Hand_Finger_RMS +
Pinch EMG_FCR_Freq +	Postural Finger_Finger_RMS +	Postural Hand_Finger_RMS +	Rest Tremor Hand_Hand_RMS +
Pinch EMG_FCR_RMS +	Postural Shoulder_Elbow_RMS +	Postural Hand_Hand_RMS +	Rest Tremor Shoulder_Hand_RMS +
Postural Finger_Finger_RMS -	Postural Shoulder_Finger_RMS +	Postural Shoulder_Finger_RMS +	MMG_Pinch +
Postural Finger_Hand_RMS -	Postural Shoulder_Hand_RMS +	Postural Sway +	
Postural Shoulder_Elbow_RMS +	Postural Shoulder_Wrist_RMS +	Errors +	
Postural Shoulder_Hand_RMS) +	RPE +		
Rest Tremor Shoulder_Hand_RMS +	Shoulder CV +		
RPE +	Shoulder EMG_UpperTrap_Freq -		
Shoulder EMG_AntDelt_Freq +	Shoulder EMG_UpperTrap_RMS -		
Errors +	Errors +		
MMG_Grip +			

PC 5	PC 6
Blink Frequency –	Action Pinch_Finger_RMS +
Hand EMG_ECR_RMS +	Action Pinch_Hand_RMS
Hand EMG_FCR_Freq +	Action Shoulder_Shoulder_RMS +
MVC_Pinch +	Hand EMG_ECR_Freq –
MVC_Shoulder –	Hand EMG_FCR_RMS +
Shoulder EMG_Ant Delt_RMS +	MVC_Pinch +
MMG_Pinch +	Shoulder EMG_Ant Delt_RMS -
MMG_Grip +	

Original data was projected onto eigenvectors, and a vector of pattern scaling factors (scores) was identified. PCA scores identified time periods that loaded strongly, either positively or negatively, for principal components. For instance, a high score for a particular time interval indicate that the time variable was overwhelmingly explained by that component (i.e., fatigue measure). Therefore, based on central and peripheral mechanisms, insight can be gained into fatigue development over the 8-hour work period. The weighted aggregate, based on the % variance for each component, of the six components was calculated and plotted over time (Figure 8.8). Time periods were then characterized based on the components that represent central or peripheral mechanisms for the thumb, hand, and shoulder.

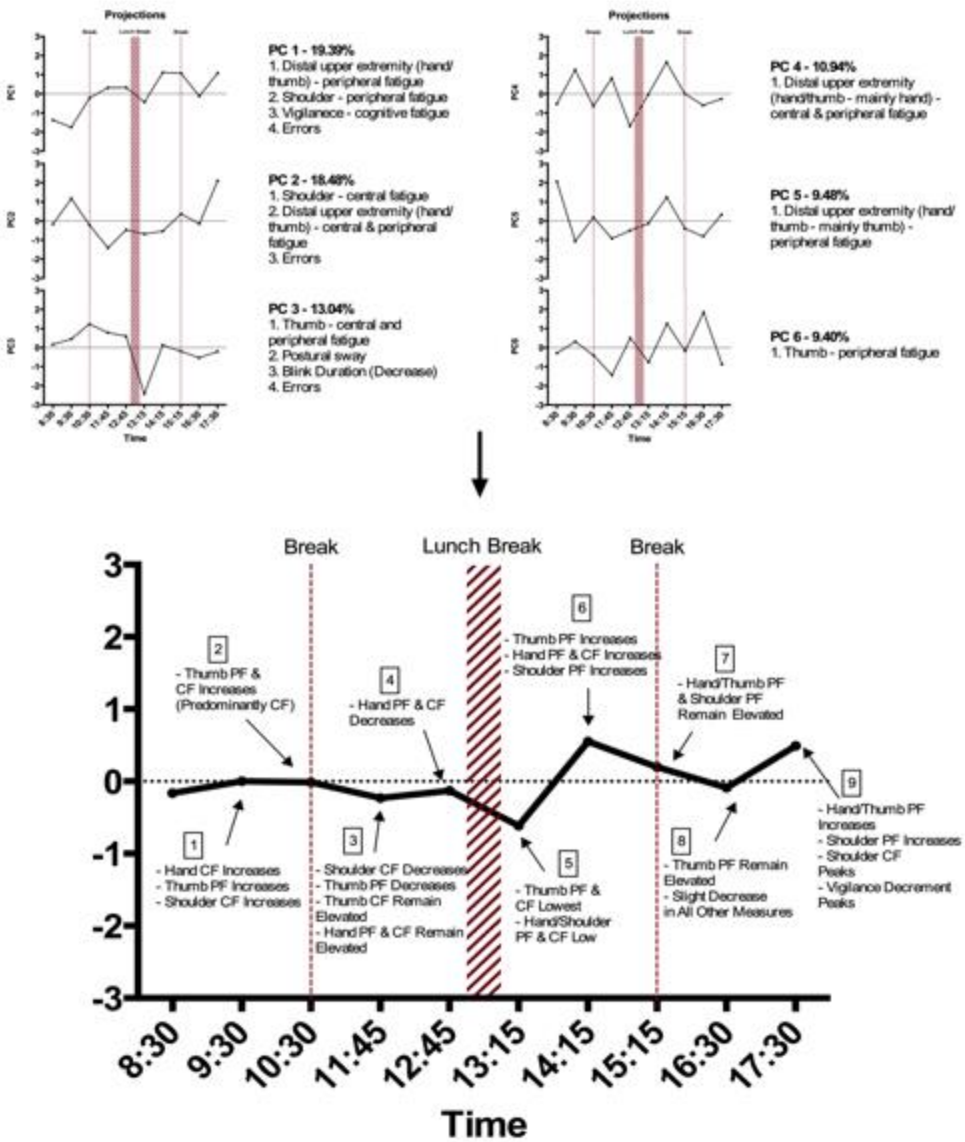


Figure 8.8 Original data projected onto each eigenvector and aggregated (weighted by explained variance) to descriptively show the pattern of fatigue development over the workday.

4.4 Fatigue Development Over Time Corresponding to Errors

Since error rates were collected and recorded for each hourly block, error rates were interpolated to allow for equitable comparisons with fatigue measures (Figure 8.9). These interpolated error rate values were considered for PCA. As previously described, six components accounted for approximately 80% of the total variance. The first three principal components reflected changes to physiological responses as well as error rates (Table 8.4). A weighted aggregate score was calculated and plotted over time for these three principal components and time periods were characterized, based on PCA scores, by components (Figure 8.10).

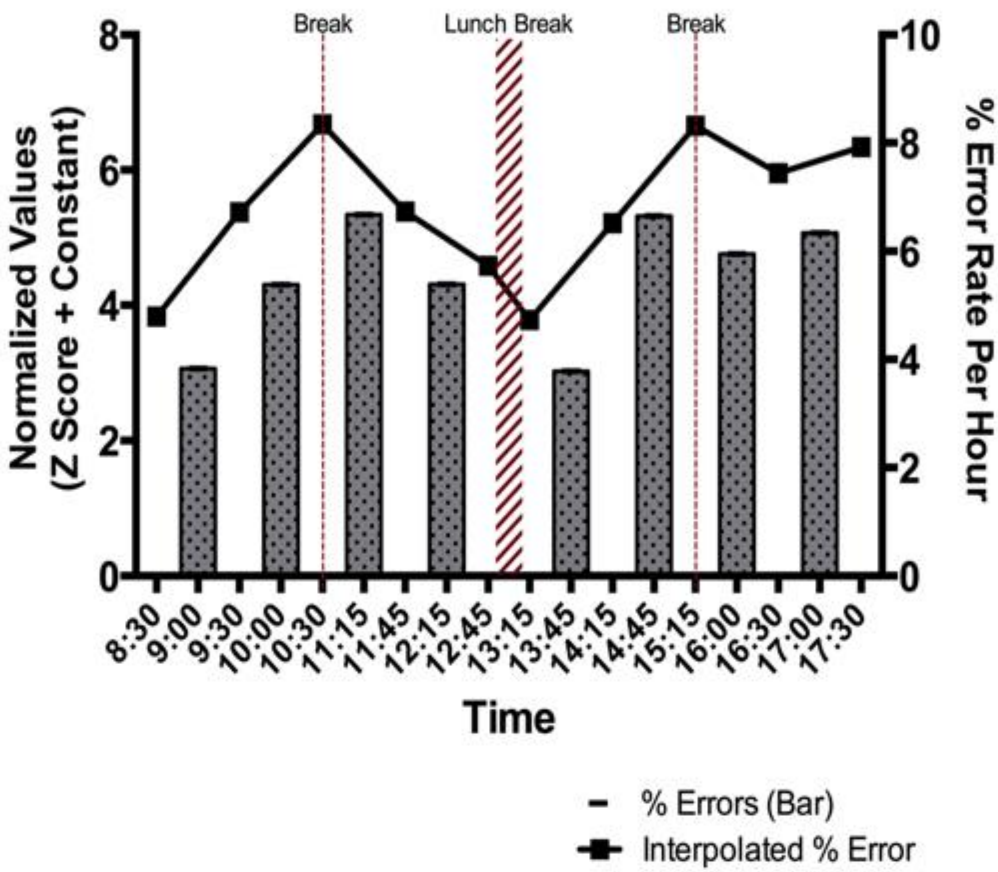


Figure 8.9 Interpolation of error rates to allow equitable comparisons with fatigue measures in PCA.

**A constant was added to the normalized interpolated scores for graphical purposes but was removed in PCA.

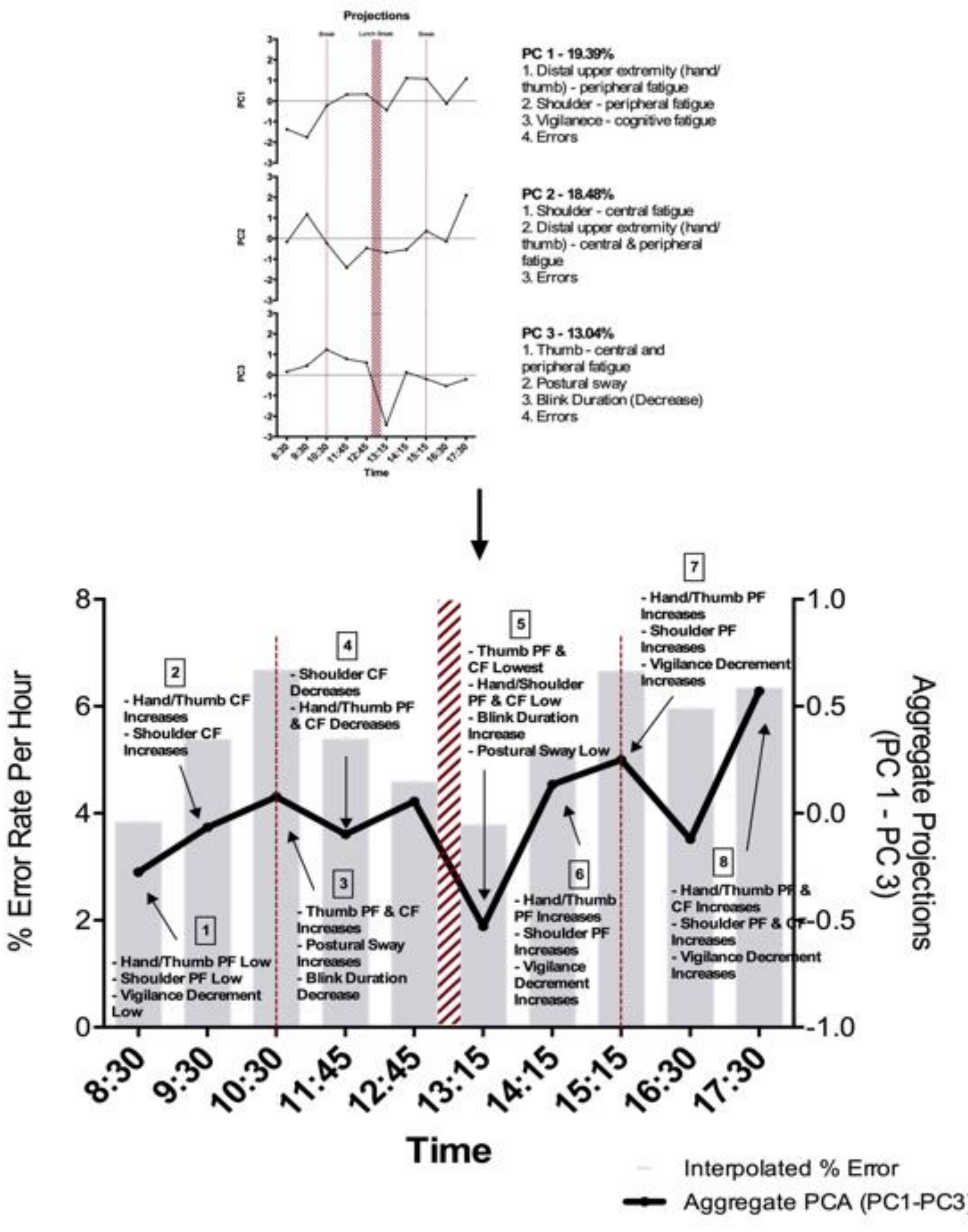


Figure 8.10. Aggregate scores for the first three components that reflect changes in error rates and physiological measures. Aggregate fatigue pattern superimposed on error rates (%/hr).

5. Discussion

The average cycle time determined from the frequency-adjusted psychophysical approach was 12.1 seconds. For comparison, when participants were asked to perform a cycle of pipetting at a pace similar to their usual work, Asundi et al., (2005) found mean cycle times between 4.46 seconds and 6.76 seconds in four task conditions. Conditions differed by precision and solution viscosity. However, direct comparisons may be limited based on the content of actions that constitute a cycle. Asundi and colleagues (2005) characterized a complete cycle as actions between two exertions of force: aspiration (i.e., pressing the micropipette trigger) and dispense/blow out. In our study, a complete cycle began with tip insertion until tip disposal. Better comparisons may be drawn from Lu et al., (2008). In that study, actions consisted of picking up the pipette, pick up tip, aspiration, dispense and blow out, and tip ejection. With an Eppendorf axial micropipette, the mean cycle time was 9.1 seconds and standard deviation ±2.6. However, unlike Asundi et al., (2005) and Lu et al., (2008), there were also added visual and cognitive requirements in our study. This included the time required to process visual feedback information and to accurately target the desired microcentrifuge tube. The duty cycle can be approximated based on thumb force profiles from all participants over selected intervals during the 8-hour period. Thumb forces were applied during aspiration, dispense and blow out, and tip ejection. The average duty cycle was 33%.

5.1 Were There Any Measures Responsive to Underlying Physiological Effects?

Field-based studies are often limited to a select number of fatigue measures. In a review of previous fatigue literature, muscle activity (i.e., surface electromyography), strength capability (i.e., maximum voluntary contractions), and self-reported fatigue or discomfort (e.g., Borg Scale, VAS, surveys/questionnaires) were typical measures in field-based studies. According to continuous EMG measurement, the static, mean, and peak loads in the FCR, anterior deltoid, and upper trapezius muscles remained unchanged during the pipetting task. Therefore, based on APDF analysis of continuous EMG during the pipetting task, there was no evidence of muscle fatigue development in these muscles. EMG recorded during a 10% test contraction correspondingly did not demonstrate changes over time. Maximum voluntary contraction forces during a pinch, grip, and shoulder flexion did not appear to change significantly over the 8-hour pipetting task. In fact, with the exception of maximum handgrip, maximum voluntary forces slightly increased from baseline to the end of the workday. On the basis of maximum strength capability, there was no evidence of neuromuscular fatigue. Perceived fatigue measured from a visual analog scale increased from the beginning of the workday towards the middle of the morning at 10:30 hrs, slightly decreased at 11:45 hrs, increased prior to lunch at 12:45 hrs, and decreased towards baseline values after lunch at 13:15 hrs. Ratings of perceived fatigue increased thereafter, peaking at the end of the workday at 17:30 hrs. The final rating at 17:30 hrs was not only significantly higher than the beginning of the workday, by almost 10 fold, but was also higher than ratings at 9:30, 11:45, and 13:15 hrs. Therefore, contrary to EMG and maximum strength, self-perceived measures indicated the presence of fatigue or fatigue symptoms.

Yet do these results indicate that fatigue was absent, as intended by the psychophysical protocol? Or, since results appear contradictory, are certain measures less or more responsive to the 8-hour pipetting task? If indeed fatigue is a process and will occur from the start of activity, then we are persuaded by the latter concept.

In the present study, nine measurement parameters led to statistically significant changes in response to an 8-hour light precision task. Aside from rating of perceived fatigue using a visual analog scale, the eight other measurement parameters include: finger tremor amplitude during a postural finger test, finger and hand tremor amplitude during a postural hand test, finger and wrist tremor amplitude during a postural shoulder test, oculomotor behaviour, and critical flicker fusion frequency threshold.

Postural tremor tests of the finger, hand, and arm (i.e., while supporting segments proximal to the segment of interest) revealed similar trends with one another. Generally, trends indicated an increase in postural tremor amplitude at the second time period at 9:30 hrs. Postural tremor decreased before the morning break and continued to decrease towards the lunch break. The lowest tremor amplitude occurred after the lunch break and increased towards the end of the workday. Indeed, finger and hand tremor amplitude at 13:15 hrs was significantly lower than morning values during postural finger, hand, and arm tests. Postural arm and shoulder tests also revealed increases in finger, hand, and wrist tremor towards the end of the workday, relative to post-lunch break tremor amplitude values. Therefore, it appeared that hand and finger postural tremor peaked in the morning and decreased after a 30-minute break, whereas arm and shoulder tremor increased significantly at the last time period. Tremor may be an outcome of physical exertions, namely fatigue, or a reflection of an individual's cognitive state, namely sleep deprivation and mental exhaustion. Previous studies have shown an increase in tremor amplitude during and as a result of physically intensive tasks (e.g., Leyk et al., 2006, Lippold, 1981). Tremor, on the other hand, exhibited reduced amplitude as a result of increased muscular relaxation due to sleepiness and sleep deprivation (Eagles et al., 1955). There are similar conflicting ideas towards the origins of tremor. Both central and peripheral mechanisms have been cited, and quite possibly, both domains might contribute. Interestingly, in study 5, we found that physiological resting tremor and postural tremor were consistently grouped among measures that predominantly reflect central fatigue mechanisms.

Eyeblink frequency also increased mid-morning, slightly decreased prior to the lunch break, decreased after lunch, and increased towards the end of the pipetting task. Changes in oculomotor behaviour, including saccades, corrective saccades, fixations, pupil size changes, and blink rates, may be indicators for the state of alertness. Saccadic speed and fixation duration are closely related to cognitive processing and have been shown as reliable indicators of fatigue. Previous studies have also shown that increased blink frequency and blink duration and decreased blink amplitude were associated with fatigue and were strong predictors for decrements in performance, i.e., tracking and accuracy errors (Morris & Miller, 1996). Increases in blink frequency, due to cessation of attention-driven inhibition, may be indicative of decrements in vigilance. Blink frequency and increased blink duration, reflecting deactivation and decreased neuronal firing rates, are associated with reduced alertness due to sleepiness (Schleicher et al., 2008). Reductions in blink amplitude may be due to a lower starting position of the eyelid, or eyelid droop, reflecting changes in attention or arousal (Morris & Miller, 1996).

Finally, critical flicker frequency threshold generally remained constant throughout the 8-hour pipetting task. The average threshold decreased from 50.5 Hz to 49.7 Hz over the course of the workday. The lowest threshold value occurred at 13:15, with a threshold of 48.5 Hz. This change was statistically significant. Historically, as described by Curran and Wattis (1998), the CFF phenomenon was first recorded in 1829 by Plateau in Belgium and by Charpentier in France in 1887. With the absence of experimental evidence, because sensory nerves are able to transmit discrete impulses above 55 Hz, it was generally assumed that the retina was the “limiting factor” in temporal resolving power of intermittent light (Simonson & Brožek, 1952). Recently, there is some evidence to suggest that cortical components plays a role for human perception of flicker/fusion light flashes (Walker et al., 1943), particularly at the left-brain hemisphere (Goldman et al., 1968). Although flicker light initiates neuronal activity from the retina to cortex, the occipital cortex resolves the temporal resolution of CFF (Curran & Wattis, 1998). According to Łuczak and Sobolewski (2005), if CFF is a function of cortical processes, and changes with arousal, it might also be an indicator of physical activity and workload. These findings led to the use of CFF to measure physiological and pathological stress situations, with the first applications made in studies measuring fatigue of the central nervous system (Simonson & Brožek, 1952).

As a psychophysical measure, CFF has been validated and proven reliable (Seitz et al., 2005). Critical flicker fusion frequency threshold has been used extensively to measure perceptual or cognitive fatigue, sleepiness, and fatigue during physical exertions. There remains uncertainty whether CFF reflects perceptual or central cognitive components. On the one hand, if CFF is mediated visually, ocular fatigue might be superimposed onto cognitive fatigue. On the other hand, it has been argued that CFF is more related to the central system than visual components (Simonson & Brožek, 1952). Generally, during strenuous visual inspection work, CFF decreases over the course of the task (Simonson & Brožek, 1952). Murata and colleagues (1991) studied CFF thresholds of visual display terminal workers over a day and between Monday, Tuesday, and Friday. Despite no significant change in CFF threshold within a day, there was a significant decrease in CFF threshold over the workweek. There was also a significantly lower CFF threshold among VDT workers compared to a control group (no VDT work). Baschera and Grandjean (1979) assessed CFF based on mental workload. They found that *low* and *high* degree of difficulty during a repetitive mental task led to a decrease in cerebral activation and a pronounced post-task decrease in CFF. A decrease in frequency threshold has also been linked to sleep deprivation. Yuan et al., (2011) studied shift-working nurses and found significant decreases in CFF threshold. The exhibited fatigue was strongly linked to poor sleep quality. Sedentary work (e.g., laboratory, clerical workers, fine assembly) led to a decrease in CFF and increase in errors, after 8 hours of work. During intensive physical work, the CCF response was less consistent, with increases after static work (e.g., sustained contraction at 50% MVC) and during incremental cycling to exhaustion (Davranche & Pichon, 2005). However, it has also been shown that CFF decreases after lifting, bicycling, and running (Simonson & Brožek, 1952). Generally, an increase in CFF threshold is reflective of an increase in cortical arousal and sensory sensitivity. A decrease in CFF threshold may indicate a reduced efficiency of the sensory system to process information (Davranche & Pichon, 2005).

These results do not suggest that measures such as EMG or maximum voluntary contraction were not responsive measures for light precision work tasks. EMG indicators have shown inconsistencies in realistic and simulated work at similar force levels. In the studies that documented changes to EMG parameters over an 8-hour simulated work period, both traditional amplitude and spectral parameters appeared to be contradictory, but may be a case of misinterpretation. Bennie and colleagues (2002) found a decrease in EMG amplitude during a test contraction while performing ulnar deviations at a frequency of 20 repetitions per minute. The EMG amplitude decreased particularly during the first day of a two-day protocol. Conversely, with an increase in repetition frequency (i.e., 25 repetitions per minute), EMG amplitude remained relatively constant on both test days. EMG frequency, on the other hand, appeared to decrease over the workday, in both work frequencies and on both test days. The authors argued that a decrease in EMG root mean square amplitude might have been due to a number of reasons: a decrease in motor unit activity pattern, a reliance on type I muscle fibres, muscle and/or neural potentiation, and experimental factors. However, the task dependency nature of fatigue is often overlooked, which may influence the subsequent interpretation of measurement responses. Quite possibly, among the potential reasons, a decrease in EMG amplitude may be indicative of diminished motoneuron discharge associated with central fatigue. In this study, continuous ECR muscle activity did appear to decrease relative to baseline, in mean and peak loads. Interestingly, during a test contraction, this study found that ECR muscle activity during a 10% MVC handgrip contraction followed response patterns of the statistically significant measures. FCR root mean square amplitude increased mid-morning and during the afternoon, accompanied with a coincidental shift to lower frequencies. Minimal extraordinary changes, or even increases, in maximum voluntary contraction may be indicative of underlying facilitatory and inhibitory fatigue mechanisms. Bosch et al., (2011) found no significant maximum voluntary force changes before and after a work bout of repetitive pick and place actions, during low and high work pace set according to industrial time standards. Augmented force production has been shown to occur due to neural and post-activation muscle potentiation but there is no clear evidence for such phenomena in Bosch et al., (2011) or in this study. The lack of consistent changes in maximum voluntary contractions may be due to possible endogenous and exogenous factors. Motivation has been cited as a potential factor for the lack of observable strength changes over a prolonged time period. Chang et al., (2009) documented, among construction workers, higher grip forces at the end of the work shift compared to measurements at the beginning, and asserted that motivation was a primary reason for the increased strength. In this study, methodological considerations were in place to help mitigate motivation-related effects, including consistent positive verbal encouragement and instructions on how to exert force (Kroemer & Marras, 1980). In study 2 (Yung et al., 2014), we observed a similar effect in a physically demanding job and attributed the trend to possible diurnal effects. However, subsequent circadian experiments (study 4) revealed no significant effects in a traditional time-of-day protocol.

During the pipetting task, the test battery was not limited to surface EMG, rating of perceived fatigue, maximum voluntary contractions, oculomotor behaviour, critical flicker fusion frequency, and resting and postural tremor measurements. As part of a complementary set of measures, we recorded force variation of the output force signal, muscle mechanomyography, action tremor, and postural sway. However, these measures did not demonstrate predictable changes over the 8-hour pipetting task. Similar to study 2 (Yung et al., 2014) in physically demanding work, force variation using coefficient of variation, did not indicate clear trends. As indicated in Yung et al., (2014), force variability has been shown to increase during a fatiguing isometric contraction but have led to inconsistent responses with increasing fatigue as a test contraction (Søgaard et al., 2003; Svendsen & Madeleine, 2010). There was a lack of clear trends in muscle mechanomyography response. Action tremor of the thumb during a hand or pinch contraction, although not statistically significant, revealed trends similar to postural tremor. Action tremor of the hand during a pinch and hand contraction revealed responses similar to MMG. In earlier studies, both MMG and action tremor have been responsive to fatiguing exercises. In study 3, MMG and action tremor were most responsive to an intermittent isometric handgrip contraction with mean force amplitude of 30% MVC, duty cycle of 50%, and cycle time of 6 seconds. In study 5, action tremor was one of three measures (i.e., maximum voluntary contractions and rating of perceived fatigue) that were responsive in most conditions, which were distinguished by task parameters (i.e., type of contraction, intensity, body segment). Action tremor appeared to be most responsive, over multiple time periods relative to baseline, during no rest break (i.e., high intensity) and sustained isometric handgrip conditions. MMG of the FDS similarly appeared to be significantly responsive at progressive 10-minute intervals in the same two conditions. MMG, a measure that detects intrinsic mechanical properties of active muscle fibres, supports the notion that higher intensity tasks are dominated by intramuscular factors (Westerblad et al., 2010). Since action tremor, which reflects both central and peripheral mechanisms, appeared to share similar responses to MMG, there is evidence to suggest that action tremor is capable of effectively measuring changes peripheral in origin. If both MMG and action tremor are “peripheral measures”, then it may not be surprising that neither measure were responsive during a handgrip test contraction, given the low intensity handgrip force (6.5% to 15% MVC) required to grasp and operate the pipette. Postural sway in the antero-posterior (A-P) direction did not change significantly over the day, but there was a slight decrease in centre of pressure RMS subsequent to the lunch break. The observed postural sway responses were not consistent with previous literature. In theory, the integration and use of information from sensory and motor systems assist in maintaining an upright stance. Carpenter et al., (2010) hypothesized that postural sway is a consequence of the CNS ensuring that it receives a certain quality and quantity of sensory information. An increase in postural sway is therefore a correction of the CNS to account for increases in sensory thresholds or reduced integration capacity (Carpenter et al., 2010). Both *general* (i.e., mobilizing whole body, soliciting energetic metabolism) and *local* (i.e., specific muscle groups, segmental movements) fatiguing exercises contribute to deterioration of sensory input and motor output of the postural system (Paillard, 2012), and therefore may lead to increases in postural sway. A previous study has shown challenges to postural control in the antero-posterior (A-P) direction following fatigue (i.e., a decrease to 70%MVC in flexors and extensors at ankle and knee through isokinetic concentric actions and repeated squat jumps) of the lower extremities; these effects persisted up to 30 minutes post-exercise (Dickin & Doan, 2008). Prolonged standing has also been shown to increase centre of pressure RMS (mm) in the A-P direction during 60-second quiet standing, before and after 30-minutes of prolonged unconstrained standing, particularly among chronic low back pain sufferers (Lafond et al., 2009). However, a number of other studies have shown that postural sway during quiet upright stance is dependent on the type of exercise, the intensity, and visual conditions. Nardone and colleagues (1997) measured quiet upright postural sway, before and after treadmill walking, as participants exercised to intensity above and below estimated anaerobic threshold. The authors found that postural sway increased after exercise reached above the estimated anaerobic threshold. On the other hand, exercise below the estimated anaerobic threshold had no effect on sway variables, and in fact led to a decrease in postural sway. Other than task intensity (e.g., prolonged standing vs. dynamic fatiguing protocol), methodological limitations might account for the observed lack of clear trends in postural sway. In this study, we recorded postural sway during 60-second quiet standing trials. Previous studies have shown differences in centre of pressure measurement parameters when recording postural sway *during* prolonged standing compared to during a quiet standing trial *before and after* prolonged standing (Lafond et al., 2009). According to Lafond and colleagues (2009), quiet standing protocols assist in determining the amount of "noise" in the postural control system and sensory sub-systems. Postural sway recorded during prolonged standing, on the contrary, is less constrained, allowing participants to make voluntary movements as a response to reduce musculoskeletal discomfort. Secondly, in previous studies, postural sway was recorded immediately after the fatiguing exercise or prolonged standing task. In this study, postural sway was recorded as part of an extensive test battery, approximately 2 minutes after the pipetting task. During the course of the intermediary two minutes, participants were seated during tremor tests. Although Dickin and Doan (2008) observed postural sway effects, in the A-P direction, exceeding 30 minutes post activity, these effects were found after performing a dynamic fatiguing protocol. Therefore, the collection strategy, the time between prolonged standing and quiet standing trials, and intensity of the activity might have all contributed to the lack of extraordinary trends.

5.2 Fatigue: "A rose by any other name would smell as sweet"

A consistent trend among all statistically significant measures was a nadir after the 30-minute lunch break, at 13:15 hrs. After 13:15 hrs, fatigue indices generally increased towards the end of the 8-hour pipetting task. In most statistically significant measures, fatigue indices increased mid-morning (i.e., 9:30 or 10:30 hrs), relative to baseline at 8:30 hrs. Bosch and colleagues (2007) measured daylong fatigue responses in two light assembly work tasks. Muscle activity and discomfort measurements were obtained at the beginning of the workday, before and after lunch, and end of the working day. In that study, regular breaks were provided to workers in the morning and afternoon. Discomfort scores increased in both work tasks. One work task (e.g., repetitive picking and placing) showed a decrease, but not significant, change in discomfort during the lunch period. The second work task (e.g., repetitive assembly task) revealed an increase in EMG amplitude and a slight, but not significant, decrease of amplitude after lunch. Dennerlein and colleagues (2003) documented perceived fatigue over 8 hours in a repetitive ulnar deviation task. Although perceived forearm fatigue increased significantly over the day, the levels of perceive fatigue was small. In physically demanding work, rating of perceived fatigue and maximum handgrip strength significantly changed over a workday (Study 2, Yung et al., 2014). In study 2, fatigue measures were recorded at the beginning of the workday, before lunch, and at the end of the workday. Rating of perceived fatigue increased over the course of the day, with a significant time effect between pre- and post- work shift. Relative to pre- workshift measures, maximum handgrip strength increased prior to lunch break. There was a significant decrease in handgrip force between lunch and post- workshift. In this study, although maximum voluntary contraction did not change over the course of the pipetting task, rating of perceived fatigue increased before lunch and further increased at the end of the 8-hour task.

The combination of complementary fatigue measures can provide insight towards patterns of fatigue development over the pipetting task. Principal component analysis revealed six components, accounting for 80.73% of the total variance. Patterns indicate increasing upper extremity fatigue, primarily central in nature, prior to the first 15-minute work break. Thumb-related fatigue increased as well, first demonstrating increases in peripheral fatigue, and later predominantly central fatigue. Subsequent to the first 15-minute break, there was a decrease in shoulder central fatigue and a decrease in thumb peripheral fatigue, but hand fatigue and thumb peripheral fatigue remained elevated. Prior to the 30-minute lunch break, hand fatigue, both central and peripheral, decreased. A test battery was collected immediately before resumption of activity in the afternoon. Thumb, hand, and shoulder peripheral and central fatigue were minimal after the 30-minute break. During early afternoon, thumb and shoulder peripheral fatigue, and hand peripheral and central fatigue increased. Immediately prior to the second 15-minute work break, peripheral fatigue of the hand, thumb, and shoulder remained elevated. Subsequent to the afternoon break there was a slight decrease in all fatigue measures in all body segments, with the exception of peripheral fatigue of the thumb, which remained elevated. Towards the end of the 8-hour pipetting task, indicators suggest that fatigue increased. More specifically, hand and thumb peripheral fatigue increased, shoulder peripheral and central fatigue increased, and cognitive fatigue increased.

The patterns exhibited by principal components demonstrate interplay between peripheral and central fatigue mechanisms, over the 8-hour period, in three body segments: thumb, hand, and shoulder. In chapter 7, both central and peripheral indices demonstrated interactions and different patterns over a fatiguing exercise in different task conditions. Therefore, the development of fatigue may be dependent on task parameters, including the task intensity, task duration, and type of contraction. Thumb and shoulder actions might be considered as concentric contractions, whereas hand force might be categorized as isometric. Thumb fatigue demonstrated changes at the periphery, prior to central responses, prior to the morning break. In the afternoon, a similar pattern emerged. Peripheral fatigue increased, was not alleviated by the afternoon break, and increased further towards the end of the day. During the morning, the shoulder demonstrated increases in fatigue that was central in nature. On the other hand, peripheral mechanisms were predominant in the early afternoon, with contributions from central mechanisms toward the end of the day. In study 5, shoulder intermittent isometric contractions at a duty cycle of 50% and cycle time of 6 seconds led to increases in central fatigue and subsequently peripheral fatigue. Although fatigue patterns, demonstrated by both studies, were not consistent with previous literature (i.e., expected intermittent isometric protocols), the shoulder responses were consistent with lower intensity activity. Hand fatigue responses, particularly in the morning, followed expected fatigue development during a sustained isometric contraction. With the hand, central fatigue progressed early morning followed by contributions mechanisms peripheral in origin. During the afternoon, both central and peripheral fatigue initially developed, but peripheral fatigue predominated towards the end of the day. Therefore, based on examples from study 5, the fatigue development of the three segments were consistent with expected patterns observed in activities at different intensities, segments, and contraction type.

5.3 Error Rates Over 8 Hour Light Precision Work: A Consequence of Fatigue?

During the first hour of pipetting, participants, on average, had an error rate of 3.83%. The error rate increased in the second hour (9:30 to 10:25 hrs), resulting in an error rate of 5.38%, and further increased in the third hour to 6.68%. Subsequently, towards the 30-minute lunch break, the error rate decreased to 5.38% at 11:45 to 12:40 hrs. After the lunch break, error rates were at a minimal, with an error rate of 3.78% for the 55-minute block of pipetting. Error rates increased thereafter, with an error rate of 6.60% at 14:15 to 15:10 hrs, 6.01% at 15:30 to 16:25 hrs after the afternoon break, finally 6.34% during the final hour of pipetting. The most common of the total errors were air bubbles in the micro-centrifuge sample, accounting for an average of 76% of errors in all time periods, followed by dispensing incorrect volume of solution (10%) and imprecision in aspiring and dispensing the desired solution (9.4%). Work efficiency and error rates have been shown to increase with time spent on mentally and physically demanding tasks. To support this, principal component analysis revealed error rates contributing to three components, accounting for 50.9% of the total variance. These principal components, in addition to error rate, reflect both physical and cognitive fatigue.

Mizuno and Watanabe (2008) measured the number of errors while participants performed visual search trials. These trials were part of the advanced trial-making test (ATMT), which evaluated the level of selective attention and spatial working memory. According to the authors, an increase in number of errors was more related to a decrease in selective attention rather than working memory. Selective attention is often referred to as cognitive tunneling, where mechanisms regulate the information that has most impact on behaviour by enhancing sensory processing while suppressing irrelevant information (Wickens & Hollands, 1999). It is this selectivity that enables for the flexibility of behaviour while preventing operators from reacting reflexively to stimuli. Although selective attention has been associated with features and characteristics of the stimuli or bottom-up attentional processing; more recently it has been linked to both top-down and bottom-up processes and is driven by goals, task demands, prior cognitive orientations, and top-down attentional processes (Ocasio, 2011). To further this, Boksem and colleagues (2005) have shown a relationship between mental fatigue and attentional processes. A decrement in performance was observed during a 3-hour visual attention task, including an increase in reaction time, missed targets, and number of false alarms. Since the number of missed targets increased, but not at the expense of a reduction in responses (i.e., the number of false alarms increased), the decrements in performance were a result of increasing difficulty to correctly identify targets rather than task disengagement. The 3-hour task resulted in an increased aversion to continue task performance (i.e., mental fatigue was elicited) and an increase in power in alpha, theta, and beta frequency bands of the EEG signal. Increases in alpha and theta band power were associated with decreases in arousal and increased effort to maintain an alert state (Boksem et al., 2005). To explain these findings, Boksem and colleagues (2005) proposed that mental fatigue might differentially affect top-down and bottom-up attentional processes, where with increased time on task, goal-directed selection of relevant stimuli is negatively affected. On the other hand, automatic or stimulus-driven processes were relatively unaffected by mental fatigue. Hence the efficiency to allocate attention is inhibited, which may account for observed increases in distractibility and decreased behavioural flexibility. Slips are related to states of attentional capture, either from internal preoccupation or external distraction (Styles, 2014). Therefore, it may not be surprising that the majority of errors in this study (air bubbles, volume, precision) were slips and may be related to deficits in attention.

When errors occur, it may lead to a cascade of error effects and might explain the increased number of errors during particular blocks of 55-minute pipetting. Post-error slowing is a phenomenon where the operator, after committing an error, slows down on the next decision. A number of competing proposals have served to explain post-error slowing, including perceptual distraction, time wasted on irrelevant processes, *a priori* bias against the response made in error, increased variability in *a priori* bias, or an increase in response caution (Dutilh et al., 2012). Preceding or following an error, the speed of response may change, implying that cognitive control levels can be dynamically regulated to optimize overall performance (Dudschig & Jentzsch, 2009). Typically, before an error, response speed is quick, allowing the individual to lower their response threshold and to achieve faster responses. Post-error, the response threshold is reset to a higher level to avoid future errors and to ensure more accurate future performance, and thus response speed is slower (Dudschig & Jentzsch, 2009). Recent reports have shown that post-error slowing may interfere with subsequent event processing (e.g., delay the start of evidence accumulation on the next event) particularly with trials in close succession. Interestingly, Boksem and colleagues (2006) observed that fatigued individuals did not demonstrate post-error slowing. Instead, the reduced ability to prepare for proceeding successive stimuli may lead to decreases in response speed and reduced accuracy.

In this study, oculomotor behaviour (i.e., eye blink frequency) and critical flicker frequency threshold may provide insight into the participants' cognitive state. As previously mentioned, eye blink frequency were associated with decrements in vigilance and increased fatigue, or reduced alertness due to sleepiness. Elevated blink frequency may also be indicative of increased level of arousal and self-perceived alertness (Stern et al., 1984). There is some prevailing evidence that suggests accident risk is a consequence of the level of arousal and alertness. In fact, Folkard and Åkerstedt (2004) proposed a non-linear U-shaped relationship between relative accident risk and alertness, indicating that high and low levels coincided with increased risk. The authors assert that being overly alert or aroused may lead to overconfidence and failure to sufficiently self-monitor. When alertness or arousal significantly decreased, fatigue may lead to increased accident risk. Accident risk may decrease at a level of arousal and alertness where operators are more cautious of their performance and engage in controlled processing of information (Folkard & Åkerstedt, 2004). In this study, increases in blink frequency occurred mid-morning at 10:30 hrs and towards the end of the 8-hour task (e.g., 16:30 and 17:30 hrs), which were found to be statistically significant from 8:30 hrs. Error rates coincided with changes in blink frequency, with increases between 10:45 and 11:40 hrs, and during late afternoon (14:15 to 17:25 hrs). Critical flicker fusion frequency threshold, on the other hand, remained relatively constant throughout the day.

There is a long-standing history linking physical fatigue with decrements in worker productivity and product quality. In the ergonomics literature, it has been speculated that poor ergonomics not only has an effect on the system, e.g., quality and production levels, but also on the operator, e.g., fatigue, pain, competency (Rose et al., 2013). A recent systematic review sought to empirically prove the relationship between ergonomics and production quality, and to also identify intermediary factors in this relationship (Kolus et al., 2014). The authors found twenty-six studies, related to manufacturing work environments, where fatigue, broadly defined, was an intermediary factor. Nine of these studies involved a measure of fatigue, and their results generally confirmed expectations, revealing an increase of fatigue with a concomitant increase in quality deficits. The authors found that fatigue, primarily physical in nature, was found to be most relevant in the ergonomics and work quality relationship in manufacturing assembly. However, in laboratory-controlled studies, there remains inconsistent evidence of the role of physical fatigue in product quality and productivity. For instance, minor changes in quality of work were observed before and after a laboratory-controlled fatiguing protocol during carpentry tasks (Hammarskjöld & Harms-Ringdahl, 1992). Although the quality of work was inferior during hammering (misses) and sawing (deviations from target), screwing performance (rate of turns) was preserved.

Additionally, the rate of hammering and sawing did not differ from pre-fatigue values. Quite possibly, task performance may be maintained due to compensatory mechanisms and changes in motor strategies (Côte et al., 2008).

In this study, we note that a number of measures reflecting change central or peripheral in origin, more specifically postural tremor of the finger, hand, and shoulder, increased early to mid-morning, decreased after lunch, and increased during the afternoon. Physiological tremor measurements, although not statistically significant at different time periods, also demonstrated increasing tremor amplitude in mid-morning. These trends in tremor, as described earlier, coincided with trends in error rate. In addition to neuromuscular fatigue, increased tremor amplitude may also be an indicator of elevated arousal (Hester & Fowler, 1980; Oxendine, 1970). With an increase in blink frequency, it is possible that increases in arousal or alertness, indeed, might have led to an increase in error rate in the morning. Increases in arousal might be driven by diurnal rhythms. Van Hilten and colleagues (1991) reported increases in tremor, both amplitude and duration, mid-morning at 10:00 hrs. Similarly, in study 4, we observed peak amplitude in the morning during hand steadiness tests, and a slight increase in physiological resting tremor at 10:00hrs. Van Hilten et al., (1991), however, asserted that sympathetic nervous system activity unlikely explained the circadian behaviour of tremor.

The available evidence suggests that increases in error rates may be a consequence of fatigue – both physical and cognitive, and/or changes in arousal levels. Since measures might reflect both phenomena, it is apparent that discerning the primary factor is challenging. With the exception of 13:15hrs, critical flicker fusion frequency remained relatively stable over the course of the day, at time periods coinciding with changes in tremor, blink frequency, and errors. This might indicate that arousal levels were constant. Ratings of perceived fatigue might also provide further insight. An increase in perceived fatigue was observed mid- to late- morning, decreased subsequent to the 30-minute lunch break, and increased significantly late afternoon. These increases in perceived fatigue, in a descriptive sense, followed changes in error rate. However, like most measures, perceived fatigue may be influenced by factors (e.g., motivation, specificity of body region, fatigue dimension of interest) that are not explicitly related to fatigue. These influences notwithstanding, at least indicate that fatigue, both physical and cognitive in nature, may play a central role in increased error rates over the course of the 8-hour simulated task. Patterns identified from principal component analysis revealed that errors contributed to the first three principal components, reflecting distal upper extremity central and peripheral fatigue, central and peripheral shoulder fatigue, postural sway, and cognitive fatigue. Therefore, patterns assessment supported the trends observed from physical and cognitive measures over the 8-hour period: errors were a consequence of both physical (central and peripheral) and cognitive fatigue and were not body segment-specific.

5.4 The Effects of Work Breaks

It is commonly understood that rest breaks provide amelioration of increased fatigue and deficits in work performance. Within-day breaks have been shown to not only alleviate musculoskeletal discomfort and strain associated with prolonged and repetitive tasks, but might also improve overall wellbeing (Trougakos & Hideg, 2009). Research in this area has mainly examined the frequency, timing, length, and content of work breaks. Generally, more frequent and/or longer breaks are associated with reduced strain, injury, and risk of accidents (Taylor, 2005). More recently, the content of work breaks have dominated interest in its design in the workplace. Strategies such as cognitive tasks between bouts of fatiguing work have been shown to accelerate physical recovery (Mathiassen et al., 2014), while active breaks (i.e., physical activity) may have substantial benefits (Taylor, 2005). In this study, we implemented two, 15-minute breaks in the morning and afternoon, and a 30-minute break at lunch hour. Although participants were given the opportunity to self-select activity during work breaks, all participants chose to sit comfortably and, at times, participants required restroom breaks.

There were observable decreases in arousal (i.e., CFF threshold) after a 30-minute lunch break. A decrease in critical flicker threshold frequency may be indicative of sleep deprivation or low arousal. Intuitively, the observed decrease contradicts the expected physiological response. What might explain this *decrease* in arousal after a 30-minute break? A “post-lunch dip”, a phenomenon where there is a reduction in cognitive function and performance after a mid-day meal (Gibson & Green, 2002), may serve as a possible explanation for the decrease in arousal after the 30-minute lunch break. Craig and Richardson (1989), in a multivariate approach, measured the effects of the size of a meal to participants’ performance and arousal. The authors found a significant drop in self-perceived alertness following a large meal (mean = 1380 Cal) but increased following a small meal (mean = 260 Cal). Surprisingly, 15-minute breaks in the morning and afternoon did not appear to effect cognitive indicators (i.e., blink frequency and CFF threshold). These results are in sharp contrast to earlier studies on perceptual-motor tasks in production work, which have shown detrimental effects on performance with the absence of short rest pauses or breaks. The lack of improved performance and cognitive state may instead be indicative of the intensity of the preceding workload rather than the effectiveness of the recovery break (Meijman, 1997).

Based on *physical* measures, tremor particularly postural hand and thumb, decreased significantly after the 30-minute lunch break. Trends generally revealed a decrease in amplitude following 15-minute breaks, but were not statistically significant. Based on trends, there is some evidence to suggest that breaks lead to reduced physical fatigue effects, which is consistent with previous observations in static work (Sundelin & Hagberg, 1989) and repetitive tasks (Fisher et al., 1993). Therefore it is tempting to suggest that 15-minute breaks during the morning and afternoon provided more benefit to reduce physical fatigue effects than cognitive fatigue effects.

The effects of rest breaks on error rates were found to be inconsistent throughout the 8-hour period. We found a decrease in error rate after the 15-minute afternoon break but an increase in the morning. An increase in error rate after the 15-minute break was inconsistent with Henning et al., (1997), who found a 5% increase in productivity with frequent, short breaks (e.g., 30 seconds, 3 minutes, 15-minutes). In this study, we observed a decrease in error rate following the lunch break, which conflicts with previous reports on the effect of the post-lunch dip on work performance. Craig and Richardson (1989) found that mid-day meals yielded changes in work performance: errors of omissions during a sustained attention task increased after a large meal. Possibly, a decrease in performance (i.e., increase in error rate) may be more pronounced for short, memory-loaded tasks rather than short perceptual tasks (Smith & Miles, 1987). Based on the types of errors that were typically committed, it appeared that the pipetting task was more susceptible to errors involving attention and perceptual failures. The size of the meal might have a differential effect on task performance, which might explain differences in error rates after breaks throughout the 8-hour task. In this study, lunch meals averaged 487 Cal, whereas breaks averaged 174 Cal in the morning and 106 Cal in the afternoon. However it remains uncertain whether a "post-lunch dip" is independent of time or is function of the time-of-day (Craig & Richardson, 1989).

The lack of significant cognitive and physical recovery effects after 15-minute breaks may be due to methodological limitations. Responses following 15-minute breaks were collected at the conclusion of 55-minutes of pipetting and indicative of the cognitive or physical state at that period. Therefore it is possible that significant effects, both physical and cognitive, would be clearly elucidated if measurements were immediately collected after breaks.

5.5 Study Limitations and Strengths

The lack of clear trends observed in measures that did not demonstrate significant time effects might be a consequence of the selected analytical technique and parameters. For instance, to evaluate postural sway, a number of analytical methods have been proposed, e.g., shifts, fidgets, drifts, etc., which have been shown to be sensitive measures of postural control. Traditional analytical methods of surface electromyography (e.g., amplitude and frequency) may be complemented with methods that consider the temporal pattern of muscle activity. For instance, EMG gaps analysis quantifies muscular rest and its time fraction and gap frequency has been linked to the risk of developing musculoskeletal disorders and muscle fatigue (Nordander et al., 2000). Although the objective of this study was to evaluate the temporal development of fatigue using a set of measures, reflecting different fatigue domains, and their traditional processing methods, future investigations should consider different analytical techniques in assessing measurement responsiveness in prolonged tasks. Additionally, this study focused on fatigue, primarily of the upper extremities and within the physical domain. Oculumotor behaviour and critical flicker frequency thresholds were collected to reflect changes in alertness, arousal, and vigilance. Complementing these selected measures with heart rate variability (i.e., to assess the state of the autonomic nervous system), electroencephalography (i.e., to assess the level of arousal and cognitive function), and other field-usable measures (e.g., psychomotor vigilance task) might provide further insight into cognitive fatigue development over the pipetting task. One methodological limitation is the duration of time from activity cessation to fatigue measure test. In study 3, measurement latencies were analyzed to help determine the length of time, after exposure, that a test battery can be collected while reasonably approximating cessation values. Measures of interest recovered from cessation within 1 to 4 minutes, and recovered to baseline values within 15 minutes post exercise. However, to the author's knowledge, there is no data on measurement latencies for other selected fatigue measures (e.g., postural sway, critical flicker fusion frequency, oculomotor behaviour). Measurement latencies might help inform decisions on test battery composition and arrangement.

This study contributes to a small body of literature that documented fatigue, reflecting multiple domains and both central and peripheral processes, over an 8-hour work task. Similar to study 2, the current study lends support to the need of a complementary set of fatigue measures to comprehensively detect fatigue from multiple processes. Relying on a single measure might lead to erroneous interpretations. Another strength is the investigation of cognitive fatigue from a prolonged monotonous task rather than application of a neuropsychological test (e.g., Stroop test).

This design may be more relevant to cognitive fatigue observed in realistic work. Interestingly, the Stroop test is a tool to understand various cognitive-perceptual processes, which has been utilized to challenge selective attention (Broadbent, 1979) and to act as a psychological or cognitive stressor (Renaud & Blondin, 1997). Although stress and cognitive (and physical) fatigue are intimately interrelated, arguably, they are interlinked but independent phenomena. Lastly, this study provides further insight into fatigue development in a light precision task, potential relationships between fatigue and work performance (i.e., errors), and the effect of work breaks (i.e., 15-minute morning and afternoon breaks, 30-minute mid-day break).

6. Conclusion

Fatigue was documented over an 8-hour pipetting task, employing a test battery of measures reflecting multiple domains and processes. Through this experimental design, we can gain further insight towards the responsiveness of a complementary set of fatigue measures in prolonged light precision work, the relationship between fatigue and work performance, and the effects of scheduled work breaks. Despite performing the pipetting task at a work pace determined from psychophysical frequency adjusted approach, 9 measurement parameters revealed significant increases in fatigue over the work period. Traditional field measures (i.e., MVC and EMG) did not lead to extraordinary time effects. Error rates followed similar trends to the 9 significant measurements: an increase from baseline towards mid-morning, a slight decrease prior to the lunch break, a nadir after lunch, and increasing fatigue effects over the course of the afternoon. Error rates, however, might not be sole consequence of fatigue – cognitive and physical; but might also reflect changes in arousal level (high and low). Scheduled work breaks had a significant effect in both cognitive indices and physical responses. Tremor decreased after a 30-minute lunch break, while 15-minute breaks shared similar but not significant trends. Arousal, on the other hand, decreased after the extended lunch break, which might be attributed to a post-lunch dip. Overall, the pipetting task involved a complex interplay between peripheral and central mechanisms in three body segments: thumb, hand, and shoulder of the pipetting limb. At a local level, the development of fatigue may be dependent on task parameters, including the intensity, duration, and type of contraction.

Chapter 9

Fatigue Measurement at the Workplace

1. Emerging Issues

The measurement and quantification of fatigue may play a significant role in reducing the extent of fatigue at the workplace. Due to a number of challenges with fatigue measurement, field-based fatigue studies have been far less extensive compared to laboratory settings. First, there is no single test to measure fatigue. Multiple mechanisms in central and peripheral domains may contribute to the manifestation of fatigue, and a single test to measure a single mechanism may lead to an erroneous interpretation (Saito, 1999). Second, not all measures of fatigue are field-usable. Some direct measures of fatigue (e.g., blood sampling, muscle biopsy) are invasive and multiple exposures to tissue trauma might not be feasible (Flodgren et al., 2009). Certain equipment may also be cumbersome to bring to a field setting and may encumber the worker as they perform their tasks. Additionally, field-settings may involve changing weather and environmental conditions; therefore robust and durable equipment are desired. Third, continuous measurement during work activity, which might be advantageous in providing information representative of work, may also be disruptive to the work process. Measures collected as part of a test battery can be administered during work breaks and control for factors that may affect interpretation (e.g., muscle length, movement velocity, magnitude of exerted force).

The objective of this thesis was to identify fatigue measures that might address fatigue-related outcomes and evaluate these detection methods for their responsiveness to different work exposures. To help accomplish this objective, a workshop was held to identify fatigue measures for field and laboratory settings, based on expert opinion; a set of fatigue measures were evaluated in an exploratory study in physically demanding work; a set of fatigue measures were evaluated for their reliability and sensitivity in a controlled experiment; the diurnal effects of a select number of fatigue measures were evaluated over a 12-hour period; a set of fatigue measures were evaluated in four exercise conditions representing differences in task intensity, type of contraction, and body segment/muscle group; and finally, an evaluation of a set of complementary fatigue measures in a light precision task, over an 8-hour work period. To meet these objectives, we compared measurement responsiveness (i.e., by comparing rate of response –

regression slopes), the temporal responsiveness for each measure in each condition (i.e., by comparing changes over time), and qualitatively described the pattern of fatigue development (i.e., by describing the projections after principal components analysis).

This chapter summarizes and synthesizes the results from preceding studies to help develop a battery of fatigue measures. Hypotheses stated in Chapter 1 will be revisited. There will be a discussion on the development of fatigue in realistic work, simulated work, and fundamental well-controlled exercise protocols. Based on the available evidence, there will also be a discussion on pertinent issues of collecting a test battery of measures, including but not limited to the influence of diurnal effects and the selection of measures based on task conditions.

2. Re-Visiting Hypotheses

A series of hypotheses were developed for studies that were the focus of this dissertation (study 3 to 6):

<u>Study 3 – Sensitivity and Reliability of Conventional and Novel Fatigue Measures</u>

Hypothesis 1: Novel fatigue measures and traditional measures will show strong (i.e., $0.61 \leq \alpha < 0.8$) to almost perfect reliability (i.e., $\alpha \geq 0.80$) over successive test batteries but novel measures will be more sensitive (i.e., quicker rate of response) to the fatiguing exercise than common methods.

Result: Eight measures exhibited almost perfect test-retest agreement (i.e., perceived fatigue measured by visual analog scale (VAS), action tremor, mechanomyography (MMG), and all handwriting metrics with the exception of pen pressure). Three measures demonstrated strong reliability (i.e., surface electromyography, maximum voluntary handgrip contraction, and pen pressure). The remaining 6 measures led to poor to moderate test-retest reliability, with tapping frequency exhibiting poor agreement (ICC = 0.184). Action tremor RMS amplitude, MMG RMS amplitude, postural tremor RMS amplitude, and VAS were highly responsive, and were statistically more responsive than the least responsive measures (i.e., handwriting and sensorimotor synchronization parameters). Of those that were highly responsive, three measures (i.e., action tremor, postural tremor, MMG) were considered novel and one was commonly used (i.e., VAS), based on citation count. Therefore, hypothesis 1 is rejected, as there was a considerable range of reliability of the selected fatigue measures and not all novel measures led to a quicker rate of response than commonly used methods.

Hypothesis 2: The responsiveness of the fatigue measure, as a test battery, will show no difference in response than when measured continuously.

Result: Four measures enabled for comparisons between test battery and continuous measurement (i.e., MMG, action tremor, EMG, and force variation). With the exception of surface EMG, there were no statistical differences between rate of responses collected as a test battery and as a continuous measurement. Surface EMG appeared to be variable and was muscle-specific, with a significantly higher response as a test battery than as a continuous measure for the flexor carpi radialis. Therefore, hypothesis 2 is rejected, as the response differed as a test battery than as a continuous measure for surface EMG amplitude.

Hypothesis 3: The novel fatigue measures will demonstrate prolonged latency effects (i.e., remain sensitive to fatigue for a longer duration of time after exercise) compared to commonly used measures. It is hypothesized that commonly used measures (e.g., EMG, MVC, rating of perceived fatigue) will recover immediately after activity (i.e., within 1 minute of recovery).

Result: All measures recovered from cessation within 4 minutes. Handwriting, tapping measures, and force variation did not demonstrate any statistical differences during recovery compared to cessation and compared to baseline values. In fact, these measures were not sensitive to differences between pre- and post- fatigue exercise. Commonly used measures, including perceived fatigue, maximum voluntary contraction, and surface EMG, were similar to cessation values 1 to 2 minutes after the end of exercise. Novel measures, such as physiological tremor and postural tremor, returned to baseline levels within 3 minutes and recovered from cessation within 1 minute. Action tremor and MMG amplitude required 2 to 4 minutes to recover from cessation and exhibited a quick recovery to baseline (1 – 2 minutes). To summarize, commonly used measures demonstrated prolonged duration to recover back to baseline values but returned from cessation within 1 minute. Novel measures, which exhibited pre- and post- increases in fatigue, recovered to baseline within 3 minutes and from cessation within 1 to 4 minutes. Therefore, hypothesis 3 is rejected, as novel measures did not demonstrate extraordinary prolonged latency effects compared to commonly used measures.

Study 4 – Does Diurnal Variation Affect Daylong Fatigue Measurement?

Hypothesis 1: Fatigue measures will demonstrate diurnal effects. More specifically, there will be fatigue effects during early morning due to sleep inertia, responses will maximize or minimize during mid-day, and tend towards non-optimal responses from late afternoon to early evening.

Result: Two measures, MMG amplitude and action tremor, exhibited rhythmicity based on cosinor analysis, with an observed nadir at 08:00 and acrophases at 18:28 and 18:56, respectively. Responses subsequently decreased towards 20:00. These measures also displayed a statistically significant time-of-day effect. Aggregate summary measures, based on muscle activity and all fatigue measures, exhibited rhythmicity with a fitted cosine model accounting for 97.4% and 89.9% of the overall variance, respectively. Therefore, hypothesis 1 is accepted on the basis of MMG, action tremor, summary muscle activity, and aggregate score of all measures.

Study 5 – Task Dependent Specificity of Fatigue Measures During Low-Load Exercise

Hypothesis 1: Based on concepts of task dependency, fatigue measures reflecting central components will be more responsive during a sustained isometric condition than an intermittent isometric condition.

Result: Both intermittent isometric and sustained isometric conditions led to increases in perceived fatigue and decreases in maximum voluntary force, over the exercise period. The intermittent isometric condition led to significant increases in EMG muscle activity, from baseline to cessation. The sustained isometric condition, on the other hand, did not lead to significant changes in EMG muscle activity. Based on continuous measurement rate of response and test battery measurement, hand tremor, however, was more responsive than muscle activity during the sustained isometric condition. These changes in tremor appeared to lead to global effects, with increases in amplitude not only at the body segment where force is exerted, but at distal segments as well. These observations appear to be consistent with the task dependent nature of fatigue, where central fatigue develops before peripheral fatigue during sustained isometric exercise, and the inverse pattern during a time varying exercise exercise. Therefore, hypothesis 1 is rejected, due to increases in selected central measures (e.g., rating of perceived fatigue) in both conditions. However, changes to peripheral measures (i.e., EMG – a central measure where increases in neural drive reflects changes at the peripheral level) during intermittent isometric activity, and a lack thereof during sustained isometric exercise, add support to the development of fatigue based on type of contraction.

Hypothesis 2: Peripheral measures will be more responsive during a condition without rest breaks (i.e., continuous intermittent at 15%MVC) than a condition with rest breaks (i.e., intermittent at 15%MVC with breaks at 10-minute intervals provided by a test battery).

Results: In both break and no break conditions, perceived fatigue and maximum voluntary force exhibited time effects. During the no break condition, tremor of the finger and hand, and MMG increased at cessation. Increases in MMG may be indicative of impairments in cross-bridge cycling and intrinsic mechanical properties of active muscle fibres. Therefore, hypothesis 2 is accepted, with increased work intensity (i.e., no rest break condition) leading to substantial increases in peripheral fatigue.

Hypothesis 3: Measures will be body-segment specific, at the shoulder and at the hand/forearm. This is due to differences in morphological and fibre composition between extrinsic muscles of the forearm and primary muscles involved in forward flexion of the shoulder.

Results: There were no differences, in either aggregate test battery or continuous measurement rate of responses, between shoulder and handgrip exercises. Based on test battery measurement, action tremor (with an accelerometer at the elbow) during shoulder exercise led to a quicker rate of response than other measures in hand and shoulder conditions. However, action tremor did not lead to significant changes over time periods. Based on continuous measurement, no fatigue measure was most responsive. Therefore hypothesis 3 is rejected. There were no differences observed between the two conditions but the lack of significant differences may be due to unintentional differences in the intensity of muscle activity.

Hypothesis 4: Based on task dependency, there will be no single measure that will be most responsive in all exercise conditions.

Results: There was no single measure that was common, in terms of responsiveness, in all exercise conditions. The comparability of measures, based on rate of response, might also differ if collected as a test battery or continuously with exercise. However, there were common measures that were responsive in most exercise conditions, as either a continuous or test battery measure. Action tremor, of the hand, shoulder, and elbow, was found to be the most responsive measure. Therefore, hypothesis 4 is accepted, and is consistent with the task-dependency nature of fatigue.

Hypothesis 5: Central measures will be more responsive at lower intermittent force conditions (i.e., intermittent at 15% MVC) than higher intermittent force condition collected in study 3 (i.e., intermittent at 30% MVC).

Results: In study 3, action tremor, MMG amplitude, postural tremor/steadiness, and rating of perceived fatigue were found to be highly responsive and significantly different from the least responsive measures. In this study, no measure appeared to significantly differentiate itself as a test battery during the reference hand intermittent exercise. Trends indicate a quick rate of response of action hand tremor (6.5%/Test Battery), postural tremor (1.6% - 12.0%/Test Battery), and rating of perceived fatigue (10.2%/Test Battery). MMG a peripheral fatigue measure, on the contrary, demonstrated a negative average rate of response but was close to zero. These comparisons, however, should be approached with caution as the test battery measures differed between studies, the measures were collected at different intervals of time, the mean force amplitude differed by 5% maximum voluntary force, and the possibility of inter-subject variation. Therefore hypothesis 5 is rejected, as central measures did not appear to be most responsive, based on rate of response, in this study. However, the significantly quicker rate of response in MMG amplitude and tremor may indicate that peripheral fatigue mechanisms dominate higher intensity activity (study 3), consistent with notions of fatigue task dependency.

<u>Study 6 – Responses During Simulated Light Precision Work: An 8-Hour Study</u>

Hypothesis 1: Peripheral and central measures will respond to physiological changes over the workday. Additionally, cognitive fatigue indices will increase over the course of the pipetting task. Test battery measures will demonstrate increasing fatigue response at hourly intervals and responses will be significantly different between pre- and post- simulated work sessions.

Results: Patterns exhibited by principal components demonstrate interactions between peripheral and central fatigue mechanisms in three body segments (i.e., thumb, hand, and shoulder). The development of fatigue was dependent on task parameters, including the task intensity, duration, and type of contraction. In fact, fatigue development of the three segments was consistent with expected patterns observed in study five. However, fatigue development was not simply a linear increase over the 8-hour task. Not all measures revealed a significant time effect, including before and after the pipetting task. For the 9 measures and measurement parameters that demonstrated a significant time effect, in general, physical and cognitive fatigue indices increased mid-morning (i.e., 9:30 or 10:30 hrs), decreased towards the 30-minute lunch break, demonstrated a nadir after the 30-minute break at 13:15 hrs, and increased thereafter towards the end of the day. Therefore the hypothesis is partially rejected, as we observed both changes in peripheral and central measures, and significant increases in fatigue response for a few, but not all, selected fatigue measures/measurement parameters.

Hypothesis 2: Although peripheral and central measures will respond over the course of the workday, central measures will be more responsive than measures reflecting peripheral responses due to the nature of the task.

Results: Nine fatigue measures/measurement parameters revealed a significant time effect: rating of perceived fatigue, postural finger, hand, arm, and shoulder tremor, blink frequency, and critical flicker fusion frequency. Of these measures, postural tremor and rating of perceived fatigue measured the physical dimension of fatigue. These measures also appeared to reflect changes in processes that are central in origin.

Hypothesis 3: Fatigue responses will recover towards baseline values after the 15-minute morning and afternoon break, and after the 30-minute lunch break. There will be a concomitant decrease in error rates subsequent to the scheduled breaks.

Results: There were observable decreases in arousal after the 30-minute lunch break. However, the morning and afternoon breaks did not affect blink frequency nor flicker fusion frequency threshold. Based on physical indices, postural tremor of the hand and thumb decreased significantly after the 30-minute break. Trends also indicated a decrease in amplitude after the 15-minute breaks but were not significant. The effects of rest breaks on error rates were found to be inconsistent throughout the 8-hour period. After the 30-minute lunch break and 15-minute afternoon break, there was an observable decrease in error rate. On the other hand, error rates increased after the morning break. The hypothesis is rejected for the following reasons: (1) Cognitive indices did not demonstrate recovery (i.e., higher arousal or alertness) and, in fact, led to a lower arousal state at the end of a 30-minute lunch break. (2) Physical indices recovered after the 30-minute break and trends indicated recovery after 15-minute breaks. (3) Errors did not decrease after all scheduled breaks.

Hypothesis 4: Fatigue and error rates will share similar trends. Error rates will concomitantly increase with increasing fatigue response. A decrease in error rate will follow a diminishing response in fatigue indices.

Results: Changes in error rates approximated changes in arousal and changes in fatigue – both physical and cognitive. Pattern of fatigue development also revealed that errors were associated with the first three principal components: distal and upper extremity central and peripheral fatigue, central and peripheral shoulder fatigue, postural sway, and cognitive fatigue. Together, trends indicate that error rates shared similar trends to fatigue, and thus the hypothesis was accepted.

3. Insights Towards Fatigue Development

With the goal of developing appropriate interventions, reducing the extent of the acute effects of fatigue at the workplace, and preventing possible long-term health outcomes (if fatigue is a precursor or biomarker), research should be devoted to understanding the temporal pattern of fatigue development (de Looze et al., 2009; Kajimoto, 2007). However, the development of fatigue is task dependent, and the contributions from processes central or peripheral in origin might differ based on task conditions. This dissertation examined fatigue development by manipulating task conditions in a well-controlled study (Study 5), in realistic physically demanding work, within- and across multiple workdays (Study 2), and in an 8-hour simulated light precision task (Study 6).

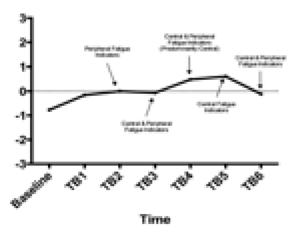
3.1. A Review of Study Findings

Previous studies have observed that fatigue development may be dependent on the task, more specifically the intensity, duration, muscle groups involved, and the type of contraction. Task conditions might dictate the predominant mechanisms and pattern of fatigue, and selection of fatigue measures in future workplace studies should account for these potential differences. Study 5 focused on the responsiveness of select fatigue measures by changing the type of contraction (intermittent isometric vs. sustained isometric), the intensity (rest breaks vs. no rest breaks), and body region (handgrip vs. shoulder flexion). A set of complementary fatigue measures, reflecting changes to central and peripheral processes, documented fatigue development in order to: (1) identify responsive measures over time (i.e., temporal responsiveness), and therefore predominant fatigue mechanisms, and (2) describe the pattern of fatigue development based on central and peripheral fatigue over the exercise or work period.

Study 5

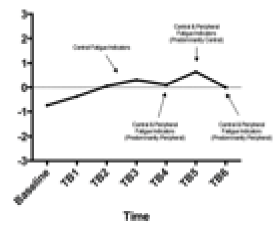
The intermittent isometric handgrip force (Table 9.1) demonstrated significant increases in EMG amplitude of a forearm extensor muscle, decreases in maximum voluntary handgrip contraction, and increases in rating of perceived fatigue over the 60-minute exercise period. Relative to baseline, EMG amplitude increased at cessation, whereas maximum contractions and perceived fatigue increased after 20 minutes into exercise and displayed elevated fatigue levels until recovery. Therefore, based on measurement responses over time, measures reflecting central and peripheral mechanisms (MVC) and predominantly central measures (perceived fatigue) were responsive earlier in the exercise period, followed by increases in peripheral fatigue (EMG amplitude). The pattern of fatigue development indicated increases in peripheral fatigue followed by increases in central fatigue. Increased peripheral contributions were observed towards the end of the 60-minute exercise protocol. This pattern of fatigue development was similar to previous investigations on concentric contractions (e.g., Babault et al., 2006). Together, these results might suggest that fatigue development followed expected patterns, but central mechanisms led to profound changes earlier than peripheral mechanisms.

Table 9.1 Intermittent Isometric Handgrip Contraction Summary

TB vs. TB	TB By Time	Continuous vs. Continuous	Fatigue Pattern Development
–	• EMG RMS – FCR • Maximum Voluntary Contraction • Rating of Perceived Fatigue	–	

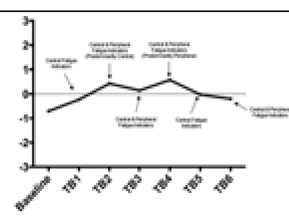
The sustained isometric handgrip contraction (Table 9.2) led to an inverted pattern of fatigue: central fatigue indicators increased prior to peripheral indices with contributions from central factors toward the end of the 60-minute protocol. This temporal pattern was consistent with previous studies. Six measures demonstrated an increase in fatigue response over time. Hand tremor amplitude during a test contraction (action tremor) increased after 30 minutes of exercise, and remained elevated until cessation. Proximal segments (e.g., wrist and shoulder during a handgrip test contraction) appeared to follow similar trends. MMG amplitude also increased after 30-minutes of exercise and did not recover to baseline values until after cessation. Maximum voluntary contraction and rating of perceived fatigue increased after 20-minutes of exercise. These results can be interpreted as a significant increase in central fatigue (i.e., MVC and perceived fatigue but predominantly central) soon followed by a significant increase in peripheral fatigue (i.e., MMG and action tremor but predominantly peripheral). As a result, unlike sustained isometric handgrip exercise, central fatigue developed prior to peripheral fatigue, with profound increases in central fatigue immediately followed by peripheral fatigue.

Table 9.2 Sustained Isometric Handgrip Contraction Summary

TB vs. TB	TB By Time	Continuous vs. Continuous	Fatigue Pattern Development
• Finger Tremor (Postural Arm)	• Hand Tremor (Action) • Wrist Tremor (Action) • Shoulder Tremor (Action) • MMG RMS – FDS • Maximum Voluntary Contraction • Rating of Perceived Fatigue	• Hand Tremor (Action)	

There were no statistical differences between test battery measures at 10-minute time periods during intermittent isometric shoulder exercise (Table 9.3). Patterns from principal component analysis revealed the development of central fatigue, followed by increases in peripheral fatigue, and contributions from central fatigue towards the end of the 60-minute protocol. This temporal pattern did not appear to be consistent with previous literature on time-varying protocols, but may be a better reflection of lower intensity exercise. The lack of significant increases in fatigue response over time might support this hypothesis. Therefore, although there was an observed temporal pattern of fatigue development, there were no predominant mechanisms that led to significant increases over the exercise period.

Table 9.3 Intermittent Isometric Shoulder Contraction Summary

TB vs. TB	TB By Time	Continuous vs. Continuous	Fatigue Pattern Development
• Finger Tremor (Postural)		–	

Finally, a no test battery condition (i.e., no 10-minute test batteries) represented a high intensity workload compared to the intermittent isometric condition (Table 9.4). Five test battery measures were responsive over successive 10-minute periods. At cessation, hand action tremor during a test contraction increased relative to baseline. This increase in action tremor amplitude remained elevated at recovery. Similarly, maximum voluntary handgrip contraction and rating of perceived fatigue demonstrated fatigue responses at cessation and recovery. Finger action tremor amplitude increased but after the cessation of exercise (i.e., at recovery). Patterns of fatigue development were not assessed due to the limited number of time series data points.

Table 9.4 Intermittent Isometric Handgrip Contraction (No Breaks) Summary

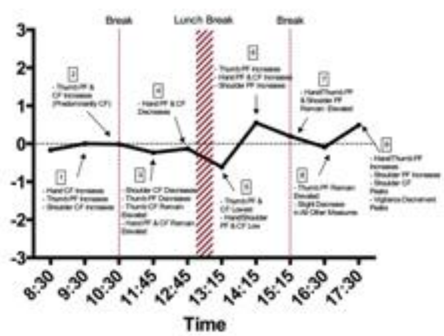
TB vs. TB	TB By Time	Continuous vs. Continuous	Fatigue Pattern Development
–	• Finger Tremor (Action) • Hand Tremor (Action) • MMG RMS – FDS • Maximum Voluntary Contraction • Rating of Perceived Fatigue	• Finger Tremor (Action)	–

Study 6

The patterns of fatigue development from study 5 helped inform the temporal dynamics in the 8-hour light precision task (Table 9.5). Over the pipetting task, there was interplay between peripheral and central fatigue mechanisms in three body segments: thumb, hand, and shoulder. Patterns indicate increasing hand and shoulder fatigue, primarily central in nature, during the first 2 hours. Thumb-related fatigue increased as well, first demonstrating increases in peripheral fatigue, and later predominantly central fatigue. After a 15-minute break, there was a decrease in shoulder central fatigue and a decrease in thumb peripheral fatigue, but hand fatigue and thumb peripheral fatigue remained elevated. Prior to the 30-minute lunch break, hand fatigue, both central and peripheral, decreased. After the 30-minute lunch break, thumb, hand, and shoulder peripheral and central fatigue were minimal, but thumb and shoulder peripheral fatigue, and hand peripheral and central fatigue increased during early afternoon. After a 15-minute afternoon break, there was a slight decrease in all fatigue measures in all body segments, with the exception of peripheral fatigue of the thumb, which remained elevated. Towards the end of the 8-hour pipetting task, indicators suggest that hand and thumb peripheral fatigue, shoulder peripheral and central fatigue, and cognitive fatigue all increased. Consequently, fatigue developed at a “local” level (i.e., at the three body segments) and was consistent with expected patterns observed in study 5, particularly if thumb and shoulder actions were considered concentric actions and the grip force was a sustained isometric contraction. Prevailing evidence suggest that local fatigue might eventually lead to global effects, including interjoint and intermuscular changes (e.g., Côté et al., 2008).

Nine test battery measures, representing physical and cognitive domains of fatigue, were found to be responsive over the pipetting task. Physical fatigue measures predominantly reflected changes that were central in origin. Trends of postural tremor measures generally demonstrated an increase in postural amplitude at the second test battery at 9:30 hrs, decreased before the morning break, and continued to decrease towards the lunch break. The lowest tremor amplitude occurred after the lunch break and tremor amplitude increased towards the end of the workday. Blink frequency and critical flicker fusion frequency threshold were indicative of cognitive fatigue. Eyeblink frequency increased mid-morning, slightly decreased prior to the lunch break, slightly decreased after lunch, and increased significantly towards the end of the pipetting task. Critical flicker frequency threshold generally remained constant throughout the 8-hour pipetting task but significantly decreased after the lunch break. These results indicate that central mechanisms of neuromuscular fatigue and cognitive fatigue indices were predominant over the course of the work period and patterns of fatigue were localized to body segments.

Table 9.5. Eight-Hour Light Precision Task: Micro-Pipetting Summary

TB By Time	Fatigue Pattern Development
• Rating of Perceived Fatigue • Finger Tremor (Postural Finger) • Finger Tremor (Postural Finger) • Hand Tremor (Postural Hand) • Finger Tremor (Postural Arm) • Wrist Tremor (Postural Arm) • Hand Tremor (Postural Shoulder) • Oculomotor Behaviour (Blink Frequency) • Critical Flicker Fusion Frequency Threshold	

Study 2

Lastly, fatigue was documented over a workday and between multiple workdays in physically demanding work, i.e., residential plumbing (Table 9.6). In this study, measures were recorded at three time periods: beginning of the work shift, mid-shift before lunch, and at the end of the workday. Two measures, rating of perceived discomfort and grip strength, indicated significant differences within a work day, notably an increase at the beginning and end of the shift (perceived discomfort) and a decrease between mid-shift and end of shift (grip strength). It was speculated that within-day trends were consistent with central fatigue mechanisms. Over multiple workdays, both central and peripheral components displayed a significant day effect. Fatigue accumulation over the workweek was observed with grip strength, physiological resting tremor, and postural tremor measures, particularly between day 1 (Tuesday) and day 4 (Friday).

Table 9.6 Fatigue Development Related to Work Performance

Within-Day Measures	Between-Day Measures
• Rating of Perceived Discomfort	• Maximum Voluntary Contraction
• Maximum Voluntary Contraction	• Physiological Resting Tremor
	• Postural Tremor

3.2 Synthesizing the Information

To summarize, a collection of studies investigated the effects of task parameters on the development of fatigue (neuromuscular – central and peripheral and cognitive). These findings support earlier investigations on the pattern of fatigue development in isometric and time-varying contractions. In both isometric and intermittent isometric contractions, both central and peripheral fatigue measures were responsive over the exercise period. Generally, relative to baseline, a significant increase in central fatigue preceded those detected by peripheral measures. In this study, sustained isometric exercise, measuring predominantly reflecting central mechanisms increased after 20 minutes, peripheral measures were responsive after 30 minutes. During an intermittent isometric condition, central measures were responsive after 20 minutes but a peripheral measure did not show increased fatigue until cessation (60 minutes). The temporal responsiveness of central and peripheral measures may be a better reflection of the intensity of the task, where low intensity activity is dominated by central mechanisms (Gandevia, 1998) and high intensity activity is dominated by peripheral mechanisms (Westerblad et al., 2010).

A condition with increased task intensity (i.e., no periodic breaks at 10-minute intervals) was performed to help clarify observations in sustained and intermittent isometric temporal responsiveness. Both central and peripheral measures were responsive, but with only baseline and cessation values, the temporal responsiveness could not be discerned. However, it appeared that, similar to sustained isometric, tremor during the exercise condition (i.e., a form of action tremor) led to the quickest rate of response. If action tremor predominantly reflects peripheral factors, there is some evidence to suggest that peripheral fatigue played a central role in overall fatigue development in both higher intensity and sustained isometric conditions. The shoulder intermittent condition was not consistent with the expected pattern for an intermittent isometric contraction. Fatigue development was predominantly central in origin, with contributions from peripheral mechanisms mid-way through the exercise period. Additionally, there were no significant changes in either central or peripheral measures over the exercise period. One hypothesis, as previously mentioned, is that the study protocol may have inadvertently generated lower muscle activity, and therefore the extent of fatigue may have been minimal. Consequently, although it might be convenient to suggest that the type of contraction might determine the pattern of fatigue development, and the task intensity might govern the temporal responsiveness of the type of fatigue, results from the shoulder intermittent isometric condition demonstrate the need to understand complex combinations of task-dependent factors in both fatigue development and temporal responsiveness.

This dissertation also observed fatigue development over time. In an 8-hour light precision task, the predominant mechanisms were central in origin, with concurrent changes in cognitive indices. Fatigue development was localized to body segments, and its pattern was dependent on the type of contraction, which support earlier findings. In realistic physically demanding work, similar to the controlled light precision task study, central fatigue measures were responsive over the day. Between multiple consecutive workdays, both central and peripheral fatigue measures were responsive, and were able to discriminate accumulated fatigue over a workweek.

The effects of work breaks, within- and between- a workday, could be observed by investigating fatigue responses prior, and subsequent, to breaks. In study 6, three work breaks were scheduled during the 8-hour pipetting task: two, 15-minute breaks in the morning and afternoon, and a 30-minute lunch break. The mid-day break led to observable decreases in arousal, which may be consequence of the “post-lunch dip” phenomenon, but surprisingly, both 15-minute breaks did not affect cognitive indicators. Based on physical indices, fatigue decreased after the 30-minute lunch break and, although not statistically significant, trends indicated decreasing fatigue after 15-minute breaks. The effects of work breaks on error rates, on the contrary, appeared to be inconsistent over the day. Therefore, it appeared that work breaks provide amelioration of increased fatigue over the day but its effect on error rates were unpredictable. Between-day fatigue responses may be indicative of recovery from the burdens associated with work, however little research has been devoted to the role of weekends in recovery (Trougakos & Hideg, 2009).

In study 2, fatigue responses indicated incomplete recovery after a weekend break. However, such response might be a consequence of, among many factors, the "unique Monday" effect, which is linked to higher rates of injury and reduced arousal and alertness, possibly due to a re-adjustment from weekend sleep-wake schedules. Research on end-of-day breaks have shown that engaging in work-related activities resulted in reports of a higher need of recovery and greater fatigue (Sonnentag & Zijlstra, 2006). In the exploratory, realistic work study, activities during leisure time were not controlled and could have factored into between-day differences. But perhaps, not surprisingly, fatigue did not recover over consecutive workdays.

4. Fatigue Measurement

An important and recurring theme is that fatigue may be task dependent. Consequently, measures that reflect unique processes might be responsive to different task conditions. In this dissertation, fatigue measures were identified, the responsiveness of select measures was evaluated in different task conditions, and pertinent issues in test battery collections were addressed. The results from these studies might provide a preliminary guide to the selection of fatigue measures for work exposure assessment. Study 1 reported the results from a workshop of expert fatigue researchers, identifying practical, reliable, sensitive, and valid measures of fatigue. A selection of fatigue measures was then evaluated during realistic physically demanding work (i.e., residential plumbing) to preliminary assess their responsiveness over a workday and workweek (Study 2). Select measures were then evaluated for their test-retest reliability and responsiveness during an intermittent isometric handgrip contraction at mean force amplitude of 30%MVC (Study 3). The same measures underwent daylong reliability assessment to identify possible effects of diurnal changes in study 4. Measures were taken at 2-hour intervals, from 08:00hrs to 20:00hrs, over two consecutive days in a traditional time-of-day protocol. A select number of fatigue measures were also evaluated after manipulating task conditions and compared to an intermittent isometric handgrip contraction at force levels relevant to work and the development of work-related musculoskeletal disorders. In study 5, the responsiveness of these measures were assessed in exercise conditions representing changes to contraction type (intermittent vs. sustained isometric), changes to work intensity based on rest allowances (break vs. no break), and changes to muscle group (hand vs. shoulder). Finally, a select number of complementary measures, representing physical (neuromuscular) and cognitive fatigue, were evaluated in a light precision task over an 8-hour work period.

4.1 A Review of Study Findings

The objectives of the aforementioned studies were to: (1) identify measures responsive at different task conditions, (2) investigate the influence of circadian effects on daylong fatigue measurement, (3) assess the test-retest reliability of select fatigue measures, and (4) provide evidence to help clarify ambiguous origins or mechanisms of select fatigue measures.

<u>Study 1</u>

Fifty-seven measures were identified based on outcomes and/or effects of fatigue in the workplace. Expert researchers who participated in the workshop were subsequently asked to rate these measures, based on their previous experience and knowledge, on the perceived validity, reliability, and practicality in laboratory and field investigations. The researchers arrived to four measures that were recommended for both settings: maximum voluntary contractions, questionnaires and fatigue scales, Borg's rating of perceived exercise or discomfort, and visual analog scales. On the other hand, twenty-five measures were not recommended for field studies, including methods traditionally recognized as "gold standard" in measuring cellular and metabolic changes. For the purpose of this dissertation, maximum voluntary contractions, Borg's rating of perceived discomfort, and visual analog scales were included as part of a test battery in all studies. Additional fatigue measures were selected on the basis of the following criteria: (1) relationship to tangible fatigue outcomes (i.e., work performance), (2) complement other selected fatigue measures to reflect multiple domains and processes central or peripheral in origin, (3) the novelty of measure in documenting fatigue responses.

<u>Study 2</u>

Fatigue was documented in realistic physically demanding work while employing a set of measures to provide a comprehensive picture of fatigue development. Not all measures revealed increasing fatigue over the workday or over the workweek, which may be a result of fatigue measures reflecting different processes of fatigue. Thus, the study reinforced the need of a complementary set of measures, reflecting multiple domains, to measure and interpret the temporal development of fatigue. It appeared that measures reflecting central mechanisms were responsive within a workday, while measures reflecting both central and peripheral mechanisms were responsive over the workweek.

Study 3

A select number of fatigue measures were compared to evaluate their reliability and sensitivity, the degree in which a test battery can approximate continuous measures, and examine measurement responsiveness after cessation activity to ascertain the length of time in which measures may be sensitive to fatigue effects. Test-retest reliability ranged between "poor agreement" and "almost perfect agreement". In terms of sensitivity, action tremor, MMG RMS amplitude, postural tremor, and rating of perceived fatigue were highly responsive. Perceived fatigue remained elevated, relative to baseline, until 11 minutes post-exercise. Postural and physiological tremor persisted from baseline until the third minute of recovery. Action tremor, however, quickly recovered within the first minute of recovery. This current study found that for most of the measures, there were no statistical differences between test battery and continuous measurement, but a few measures were approaching statistical significance. Action tremor and mechanomyography collected during a test contraction, and perceived fatigue assessed by a visual analog scale, were found to be most reliable, most responsive, comparable to continuous measures, and sensitive after the fatiguing activity. This preliminary evidence suggests that action tremor, MMG, and perceived fatigue should be considered with other measures of interest, as part of a test battery when measuring fatigue.

Study 4

The aim of this study was to better understand the effects of diurnal changes on recorded signals for a range of fatigue measures. Only two measures revealed a statistically significant time-of-day effect: mechanomyography of a flexor forearm muscle and action tremor at 30% MVC. These two measures exhibited rhythmicity based on cosinor analysis. In both MMG and action tremor responses, the observed nadir of the oscillatory function occurred at 08:00 hrs and acrophases at 18:28 and 18:56 hrs, respectively. MMG and action tremor measurement values were below the daily average during the morning (08:00 – 10:00 hrs), were above average during the afternoon (12:00 – 18:00 hrs), and decreased to the daily average, or below average, in mid-evening (20:00 hrs). Therefore there is evidence that a degree of caution might be required when interpreting daylong fatigue with these two measures, whereas the other measures may not be susceptible to significant diurnal effects. Although the remaining measures did not reveal statistically significant time effects, most measures were characterized with similar patterns to those found in previous literature.

Study 5

This study evaluated selected fatigue measures during time varying intermittent isometric and sustained isometric exercises, with breaks and no breaks, and at both hand and shoulder at force ranges relevant to the development of work-related musculoskeletal disorders. There was no one universal measure that was common, in terms of responsiveness, in all exercise conditions. Additionally, we also found that the comparability of measures, based on rate of response, might differ when collected as a test battery or continuously with exercise. Therefore based on this study, it may be reasonable to suggest that test batteries might provide alternative information relative to measures collected continuously and simultaneous to exercise, even when comparing similar measurements, and the comparability between test battery and continuous measurement might be task dependent. Although no single measure was found to be most responsive in *all* conditions, there were measures responsive in *most* exercise conditions as either a continuous or test battery measure. This was the case with action tremor. A maximum voluntary contraction, which is dependent on processes in both central and peripheral domains, was similarly responsive. Rating of perceived fatigue, which has been cited as a centrally mediated indicator, was also found to increase with exercise progression in hand conditions. Therefore fatigue measures, reflecting changes to both central and peripheral processes, may be useful in measuring tasks and exercises of varying parameters.

Study 6

Both cognitive and physical fatigue, including central and peripheral neuromuscular fatigue indices, was documented over an 8-hour light precision task. The overall aim was to investigate the responsiveness of this set of fatigue measures, and to determine which measures revealed underlying physiological changes in a psychophysically determined frequency-adjusted micropipetting task. A secondary objective was to track work performance and relate these changes to fatigue responses. Nine measurement parameters revealed significant increases in fatigue over the work period. Traditional field measures (i.e., MVC and EMG) did not lead to extraordinary time effects. Error rates followed similar trends to the 9 significant measurements: an increase from baseline towards mid-morning, a slight decrease prior to the lunch break, a nadir after lunch, and increasing fatigue effects over the course of the afternoon. Error rates, however, might not be a sole consequence of fatigue – cognitive and physical; but might also reflect changes in arousal level.

4.2. Synthesizing the Information

Collectively, the studies support the need of a test battery of complementary fatigue measures to provide a comprehensive picture of fatigue development in work. As was demonstrated in study 5, fatigue development is task dependent, and the selection of measures should reflect multiple fatigue processes involved with a particular task. However, if selection of fatigue was limited to a single measure, the data might be susceptible to erroneous interpretations. Consequently, the studies argue for both neuromuscular and cognitive indices, and in the case of neuromuscular (physical) fatigue, both central and peripheral measurements.

The selection of measures, however, is not trivial. Fifty-seven unique measures were identified by a group of experts in fatigue research, each reflecting a physiological mechanism, an effect, and an outcome. Yet not all measures are suited for field use, and these measures differ in their practicality, reliability, and sensitivity. The selection of measures in this dissertation was informed by workshop results, but was also selected based on their relationships to workplace performance, their capability to reflect different processes in the causal chain of fatigue, and their utility as a test battery measure.

There are distinct advantages in documenting fatigue with a test battery. First, in realistic work, it may be infeasible to obtain continuous measurement without encumbering workers. Second, test batteries can be administered during work breaks to avoid disruptions to work activity, Third, test batteries provide a standardized measure to allow for comparisons between time periods and possibly tasks. However, there remains uncertainty whether test batteries can approximate continuous responses. In study 3, with the exception of EMG, most of the selected measures did not exhibit statistical differences between test battery and continuous measurement. EMG continuous responses led to a quicker rate of response than test battery measurements. Similarly, MMG responses, although not statistically different, approached statistical significance. In study 5, it appeared however that the rate of response as a test battery provided alternative information compared to the rate of response collected continuously with exercise. This comparison was made between measures to characterize conditions rather than a direct comparison between rate of response as a test battery or continuous measurement. Although study 5 might appear to contradict study 3, in fact, this might not be the case. Rate of responses between test battery and continuous measurement may not have been statistically different, but their magnitudes were also not identical. Therefore comparing different measures under the same collection strategy (i.e., test battery or continuous methods) might then lead to extraordinary differences. Furthermore, in study 3, test batteries were collected at shorter intervals (i.e., 1-minute), which might better approximate the continuous rate of response. Lastly, it was observed, in study 5, that the comparability between test battery and continuous measurement might itself be task dependent. Therefore, although collecting test batteries may be advantageous when quantifying cumulative fatigue, continuous measurement might provide complementary information and might be directly representative of the workload. However, if test batteries were collected at shorter time intervals, they may reasonably approximate measurement responses collected as a continuous measure. As a test battery measure, the time interval between cessation of activity and test battery collection may have implications on the representativeness of the cumulative fatigue effect. In study 3, perceived fatigue, physiological resting and postural tremor, and surface EMG amplitude measures did not approximate cessation values, 1 minute after activity. Both maximum voluntary contractions and action tremor recovered from cessation values 2 minutes after activity, whereas MMG recovered from cessation within 4 minutes. Accordingly, test batteries measurements obtained within a minute should reasonably approximate levels of fatigue observed at cessation. However, the observed latencies may not be generalizable if fatigue response and recovery is task dependent. In study 3, longer latency times were observed for measures that predominantly reflected peripheral fatigue after an intermittent isometric contraction at mean force amplitude of 30%MVC until volitional fatigue.

The reliability and responsiveness of measures should be considered when selecting fatigue measures. Reliability may be in the form of a test-retest repeatability analysis over a short period of time or an assessment at defined periods of the day over an extended period of time. In study 3, a test-retest analysis revealed fair to moderate repeatability for most test battery measures. Tapping frequency, as means to measure sensorimotor synchronization, resulted in poor reliability. The most repeatable measures (i.e., almost perfect reliability) were perceived fatigue, handwriting tests, action tremor, and MMG. In study 4, daylong reliability was evaluated to determine whether measures were susceptible to diurnal effects. Diurnal fluctuations of physiological functions might challenge the interpretation of fatigue measures and their responses over the course of a workday. In that study, action tremor and MMG, in a traditional time-of-day protocol, exhibited rhythmicity and a significant time-of-day effect. Intuitively, these results are conflicting: a highly repeatable short-term response demonstrated a significant change and diurnal effect over an extended period. In fact, a highly repeatable and sensitive (discussion forthcoming) measure might be better suited to reveal underlying circadian effects, whereas a less repeatable measure might have high within-subject variance. Thus, it is possible that circadian effects exist in general circumstances, but can only be measured by indices that are highly repeatable and sensitive. And consequently, a certain degree of caution should be in place when interpreting MMG and action tremor responses, whereas the remaining measures were not significantly affected by intrinsic diurnal variability.

As mentioned, sensitivity of measures (i.e., responsiveness) may be largely dependent on task parameters, including intensity, duration, cycle time/duty cycle, and type of contraction. This dissertation investigated measurement responsiveness in realistic physically demanding work (study 2), in light precision work (study 6), by manipulating task parameters in a well-controlled laboratory study (study 5), and during a time-varying exercise, at a mean amplitude typically carried out in laboratory fatigue studies, until volitional fatigue (study 3). An exploratory study in realistic physically demanding work (i.e., residential plumbing) provided insight towards measures that have potential to document fatigue as a test battery measure. From that study, perceived discomfort and maximum voluntary contractions were responsive indices of within-day fatigue. Over the workweek, grip strength, physiological resting tremor, and postural tremor were responsive indices of cumulative fatigue. Due to the apparent responsiveness and utility of these measures for field use, these measures were selected for inclusion in a test battery in subsequent studies. We observed that MMG, action tremor, postural tremor, and rating of perceived fatigue were highly responsive during an intermittent isometric handgrip exercise at mean force of 30%MVC. These measures were also significantly different between baseline and cessation when comparing test battery responses between the two time periods. Although maximum voluntary contraction did not lead to an exceptionally high rate of response, there was a statistical difference between pre- and post- exercise values. Action tremor of the segment proximal to the exerting force was found to be particularly most responsive during a sustained isometric and no break (high intensity) intermittent handgrip exercise. Action tremor was also found to be responsive during the shoulder intermittent exercise. A maximum voluntary contraction was responsive, with changes over time in intermittent isometric handgrip, intermittent isometric handgrip with no breaks, and sustained isometric handgrip conditions. Ratings of perceived fatigue, measured from a visual analog scale, similarly displayed significant differences over successive test batteries, in the same three conditions. Therefore, overall, there was no single measure that was found to be most responsive in *all* conditions but the aforementioned measures were responsive in *most* conditions as either a test battery or continuous measure. To summarize, based on the laboratory studies, it appeared that action tremor, rating of perceived fatigue, and maximum voluntary contractions were most responsive in many of the task conditions. MMG was responsive, but observed only in the intermittent handgrip condition at higher mean force amplitude.

Finally, fatigue measures were evaluated over an 8-hour period in light precision work (i.e., micro-pipetting). Although the rate of response between test battery measures was not compared, the responsiveness over time was assessed for each measure. Measures that appeared to be responsive, even in a psychophysically frequency-adjusted 8-hour task, were predominantly central fatigue indices and cognitive measurements. These nine measures include: perceived fatigue, finger amplitude during a postural finger test, finger and hand amplitude during a postural hand test, finger and wrist amplitude during a postural shoulder test, oculomotor behaviour, and critical flicker fusion frequency threshold. Consequently, daylong collections (studies 2 and 6) were consistent: central (physical) indices were responsive at multiple time periods over the workday. However, this might be surprising as the realistic work task involved physically demanding work but the simulated laboratory study comprised of a light precision task. Possibly, while residential plumbing involves many physically demanding tasks characterized by a number of manual material handling exposures, construction workers, in real-life work, have both scheduled and discretionary breaks, and opportunities to vary muscle forces, postures, and work pace. Moreover, real-life work is also performed not until exhaustion. Therefore, although residential plumber consists of non-routinized tasks that are physically demanding, the observed cumulative fatigue response of the dominant upper extremity may have been more similar to a lower intensity level.

From principal components analysis, measures were grouped based on their representation of the processes along the causal fatigue chain. For instance, a measure reflecting peripheral processes distal to the neuromuscular junction were categorized as “peripheral measures”, and conversely, central processes proximal to the neuromuscular junction were “central measures”. There were measures that reflect both central and peripheral components, such as maximal voluntary contractions and based on the available evidence, possibly tremor. Tremor was a recurring measure, responsive in most of the studied task conditions. However, tremor can be categorized according to its appearance and the method to obtain tremor response. Three types of tremor were obtained: physiological tremor (i.e., resting), postural tremor (i.e., limb held against gravity), and action tremor (i.e., tremor during an exerted force). According to PCA, action tremor was predominantly grouped with peripheral measures, including increases in EMG and MMG amplitudes. Postural and physiological resting tremors were often grouped together with perceived fatigue. Based on these groupings, the predominant fatigue mechanism(s) and fatigue development patterns can be ascertained for each task condition. As previously described, the temporal responsiveness and pattern of fatigue development were consistent with previous literature.

If these findings hold true, then action tremor may be indicative of motor unit firing and recruitment, or changes in interstitial K^+, or stretch-reflex responses. Postural and physiological resting tremor might then describe changes associated with oscillations originating from the CNS. Although Renshaw cell inhibition is a central mechanism, it might actually reflect compensations to peripheral fatigue. Renshaw cell inhibition offers an intriguing explanation for the increased amplitude of action tremor during a fatiguing task. As a variable gain control, during low contraction levels, recurrent inhibition allows supraspinal centers to operate over a large working range to cause small changes in muscle force, thereby improving resolution and control of motor output. Over higher level of forces, a decrease in Renshaw cell inhibition will allow central command to generate larger force output for a given drive (Pierrot-Deseilligny & Burke, 2005). However, during fatigue, to produce the same force output, recurrent inhibition is decreased, allowing for the recruitment of motoneurones to compensate for cellular impairments of fatigue (Pierrot-Deseilligny & Burke, 2005). Consequently, action tremor amplitude increases as the motorneuron pool is synchronized at a recruitment frequency of 8 to 12 Hz, which matches the resonant frequency of the upper limbs.

Measures were assessed by the described criteria (Table 9.10). Selection of measures for inclusion to the test battery might have varied, study-by-study, mainly due to the need to control the number of measures, while enabling the collection of measures of interest. Four measures, which were found to be responsive in the exploratory plumbing study, were common in all studies: physiological tremor, postural tremor or steadiness, MVC, and rating of perceived fatigue. Three measures (i.e., action tremor, EMG, MMG) were collected in all laboratory studies. Based on the available evidence, rating of perceived fatigue and action tremor scored highly on all criteria tests. Postural tremor or steadiness and MVC appeared to be moderately responsive and reliable. Handwriting kinematics, oculomotor behaviour, and critical flicker fusion frequency threshold displayed a change over time but were only assessed under a single condition. Physiological tremor, force variation, EMG, MMG, sensorimotor tapping tests, postural sway, and Semmes-Weinstein monofilament tests led to lower test-retest reliability ratings or responsiveness over time.

Table 9.10 Notes:

1. *Responsive*: Based on calculated rate of response of test battery data (High/Moderate/Low/Very Low)
2. *Change*: Based on statistical differences over exercise period. Temporal Responsiveness. (Yes/No)
3. Measures reflect changes at body segments exerting force
4. Normalized (z-scores) for each condition to allow equitable ratings between conditions.
    - High: >1.00
    - Moderate: 0 – 1.00
    - Low: -1.00 – -0.01
    - Very Low: <-1.00
5. Abbreviations: PDW = Physically Demanding Work, Mod = Moderate

Table 9.10 Summary Table of Fatigue Measures

	Criterion									
Fatigue Measure	Test-Retest	Responsive Handgrip Intermittent at 30% MVC	Responsive/ Change Handgrip Intermittent at 15% MVC	Responsive/ Change Handgrip Sustained at 10% MVC	Responsive/ Change Handgrip Intermittent No Breaks at 15% MVC	Responsive/ Change Shoulder Intermittent at 15% MVC	Circadian Effect	Change Over 8 Hours in Light Precision Work	Change Over 8 Hours in PDW	Change Over Multiple Days in PDW
Physiological Tremor	Fair	Mod	Mod to High/No	Low to Mod/No	High/No	Low/No	No	No	No	Yes
Postural Tremor or Steadiness	Mod	High	Low to High/No	V. Low to High/No	Low to Mod/No	Low to High/No	No	Yes	No	Yes
MVC	Strong	Low	Low/Yes	Low/Yes	Low/Yes	Low/No	No	No	Yes	Yes
Rating of Perceived Fatigue	Almost Perfect	High	High/Yes	Mod/Yes	Mod/Yes	Mod/No	No	Yes	Yes	No
Action Tremor	Almost Perfect	High	Low to Mod/No	Mod to High/Yes	Low to Mod/Yes	Low to High/No	Yes	No		
Force Variation	Mod	Mod	Low/No	Low/No	Low/No	Low/No	No		No	Yes
EMG	Strong	Low	V. Low to Mod/Yes	Mod/No	Low/No	Low/No	No	No		
MMG	Almost Perfect	High	V. Low/No	Low/Yes	Low/Yes	Low/No	Yes	No		
Sensorimotor Tapping Test	Poor to Fair	Low					No			
Handwriting Kinematics	Almost Perfect	Low					No			
Oculomotor Behaviour								Yes		
Postural Sway								No		
CFF								Yes		
Semmes-Weinstein			No	No	No	No				

4. Summary of Key Findings

<u>Major Findings:</u>

- Fifty-seven unique fatigue measures were identified by a group of expert fatigue researchers, but not all measures are suited for field use, and these measures differ in their practicality, reliability, validity, and sensitivity.
- Perceived fatigue, action tremor, mechanomyography, and handwriting tests were highly repeatable in a test-retest reliability test over a 60-minute period at 5-minute intervals. In a daylong reliability study, to determine the diurnal effects on selected fatigue measures, action tremor and MMG exhibited rhythmicity and a significant time-of-day effect.
- The responsiveness of fatigue measures appears to be dependent on task parameters (i.e., intensity, duration, body segment, type of contraction, etc.). There was no single measure that was found to be most responsive in *all* conditions (i.e., handgrip or shoulder flexion exercise) but there were measures responsive in *most* conditions as either a test battery or continuous measure. Action tremor, rating of perceived fatigue, and maximum voluntary contractions were responsive in most conditions.
- Measures that were responsive over the course of a workday were cognitive indicators and reflect, predominantly, central neuromuscular fatigue. In physically demanding work, perceived discomfort and maximum voluntary contractions were responsive over three periods: beginning of shift, mid-shift, and end of shift. In a light precision task, perceived fatigue, postural tremor, oculomotor behaviour, and critical flicker fusion frequency threshold were all responsive measures. Measures responsive over multiple workdays were both peripheral and central fatigue indices, including grip strength, physiological resting tremor, and postural tremor.
- By utilizing a complementary set of fatigue measures, central and peripheral processes can be documented to describe the temporal development of fatigue. A sustained isometric handgrip condition led to an increase in central fatigue indicators prior to peripheral indices, with contributions from central factors toward the end of the 60-minute protocol. An intermittent isomeric handgrip led to an inverted pattern: increases in peripheral fatigue followed by central fatigue. However, in terms of temporal responsiveness (i.e., significant change over time), which may be an indicator of predominant fatigue mechanisms, both protocols led to significant increases in central fatigue followed by increases in peripheral fatigue. For the sustained condition, central mechanisms significantly increased after 20 minutes, and

peripheral measures were responsive shortly afterwards at 30 minutes. Intermittent conditions led to an increase in central fatigue after 20 minutes and peripheral fatigue increased after 60 minutes. Therefore, a hypothesis is that the pattern of fatigue development might be contingent on the type of contraction while the task intensity might determine temporal responsiveness.

- Fatigue development might be localized to body segments during a prolonged, 8-hour, light precision task. At each body segment, fatigue development was dependent on the type of contraction, supporting earlier findings.
- In general, increases in tremor amplitude might reflect processes central and/or peripheral in origin. The predominant mechanism to explain an increase in amplitude, however, may be dependent on the type of tremor. It appeared that physiological resting and postural tremor might be associated with central fatigue. Action tremor might better reflect changes to the peripheral system.

Supplementary Findings

- The shoulder intermittent condition was not consistent with the expected fatigue pattern for an intermittent contraction. Fatigue development was predominantly central in origin, with contributions from peripheral mechanisms mid-way through the exercise period. Additionally, there were no significant changes over 60-minutes in either central or peripheral measures. Possibly the extent of fatigue was minimal. Consequently these results underscore the need to understand complex combinations of task-dependent task factors in both fatigue development and temporal responsiveness.
- Work breaks provided amelioration of increased fatigue over the day but its effects on error rates were inconsistent. Based on physical indices, fatigue decreased after the 30-minute lunch break and, although not statistically significant, trends indicated decreasing fatigue after 15-minute breaks. The mid-day break led to observable decreases in arousal, which may be consequence of the “post-lunch dip” phenomenon, but surprisingly, both 15-minute breaks did not affect cognitive indicators.
- Fatigue responses between consecutive days can provide insight towards the effects of between-day breaks. A “unique Monday” phenomenon was observed after a weekend break. This may be due to re-adjustments from weekend sleep-wake schedules.

5. Tentative Recommendations for the Field Study of Fatigue

- Collecting measures as part of a test battery is advantageous when documenting fatigue in realistic work. Test batteries can be collected during breaks to avoid work disruptions and provide a degree of standardization to compare between time periods. Collecting a test battery within 1 minute from cessation of activity should reasonably approximate levels of fatigue observed at cessation.
- Test batteries provide complementary information to continuous measurement. Test batteries quantify cumulative fatigue whereas continuous measurement might provide information directly representative of workload. Test batteries recorded at shorter intervals reasonably approximate continuous measurement.
- To gain a comprehensive picture of fatigue development, a complementary set of physical (i.e., central and peripheral) and cognitive measures are recommended.
- Based on the available evidence and under the studied exercise conditions, rating of perceived fatigue and action tremor rated highly on all criteria tests. Postural tremor or steadiness and MVC also achieved higher than moderate ratings when considering the collective assessments.
- A degree of caution is required when interpreting MMG and action tremor when measured over the course of a day. Both measures exhibited diurnal rhythm during a traditional time-of-day protocol.

6. Conclusion

For the ergonomist or health and safety practitioner, this dissertation provides insight towards the utility of a test battery of fatigue measures to complement current task analysis techniques. For workplace researchers, this dissertation provides insight towards the temporal development of fatigue in various task conditions and the reliability and responsiveness of select measures in both short and longer-term work-studies. This research might elicit future investigations in the relationship between work exposure, fatigue development, and outcomes (i.e., acute – risk of accidents, work performance, and longer-term – work-related musculoskeletal disorders, chronic fatigue syndrome, burnout, etc.). After elucidating these relationships, fatigue may then be a relevant biomarker for cumulative exposure to repetitive and/or sustained work, a useful risk indicator, and a design and evaluation tool.

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Appendices

Appendix A: Study 1 Graphical Representation of Links

Appendix B: Study 5 Matrices of All Statistical Data & Alternative Graphical Representation of Pre/Post Difference of Measures

Appendix C: Study 6 Psychophysical Instructions and Test Battery Responsiveness Over 8-Hour Pipetting Task

Appendix A

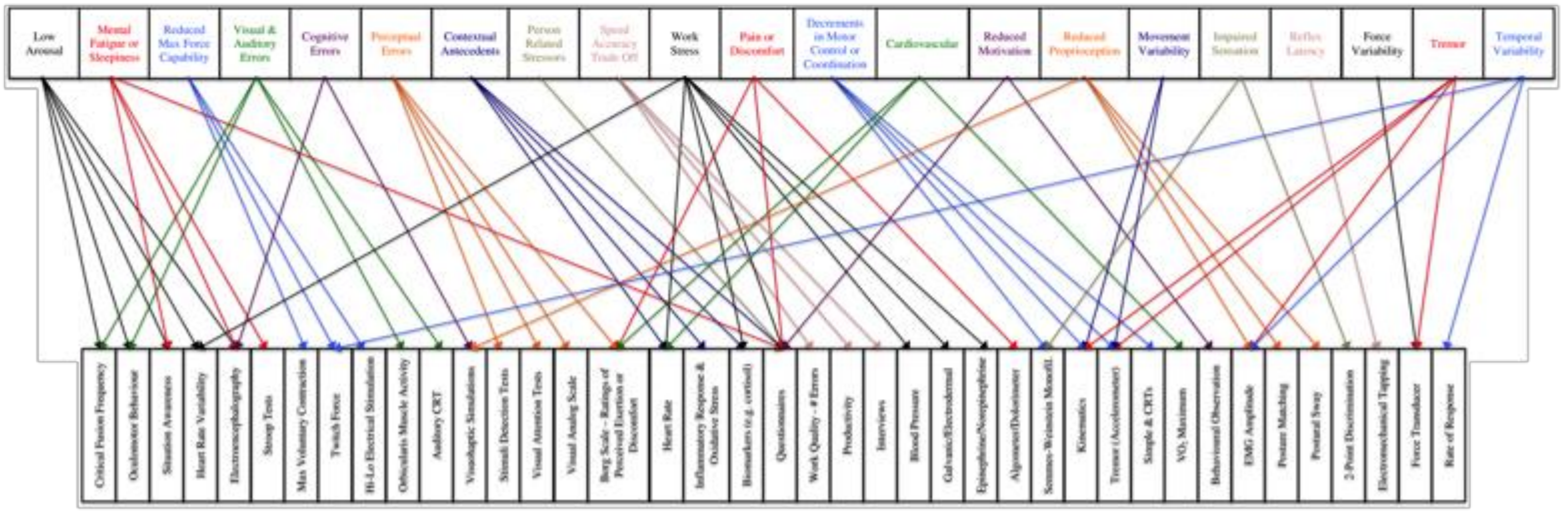


Figure 1. Fatigue measures and detection methods linked to causes or mechanisms of fatigue-related performance and quality outcomes.

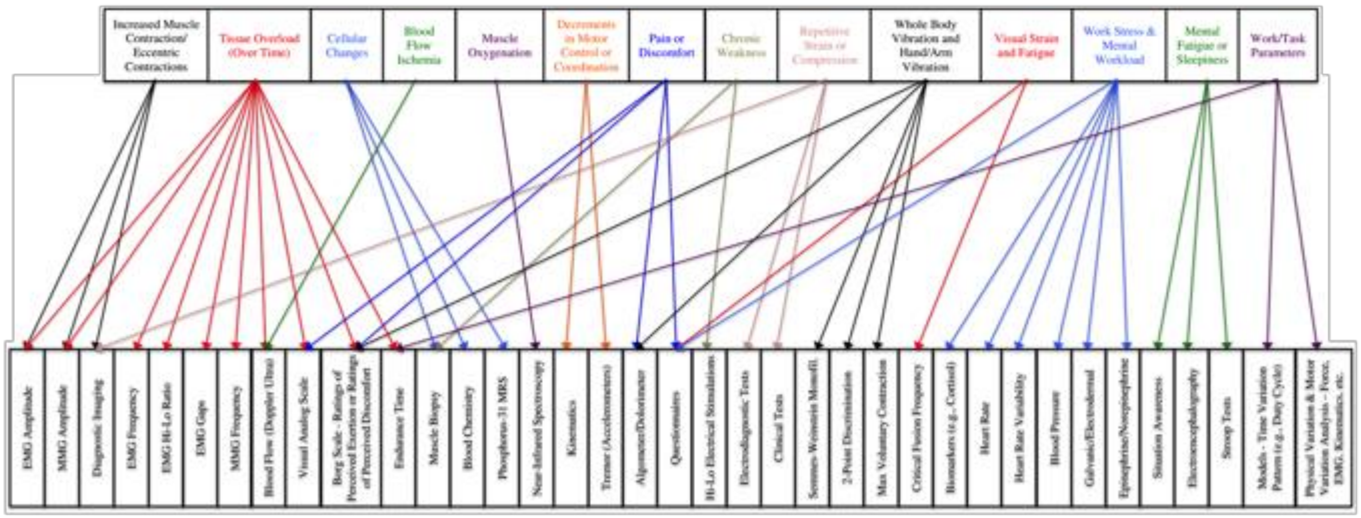


Figure 2. Linking fatigue measures and detection methods with causes or mechanisms for fatigue-related injury disorder outcomes.

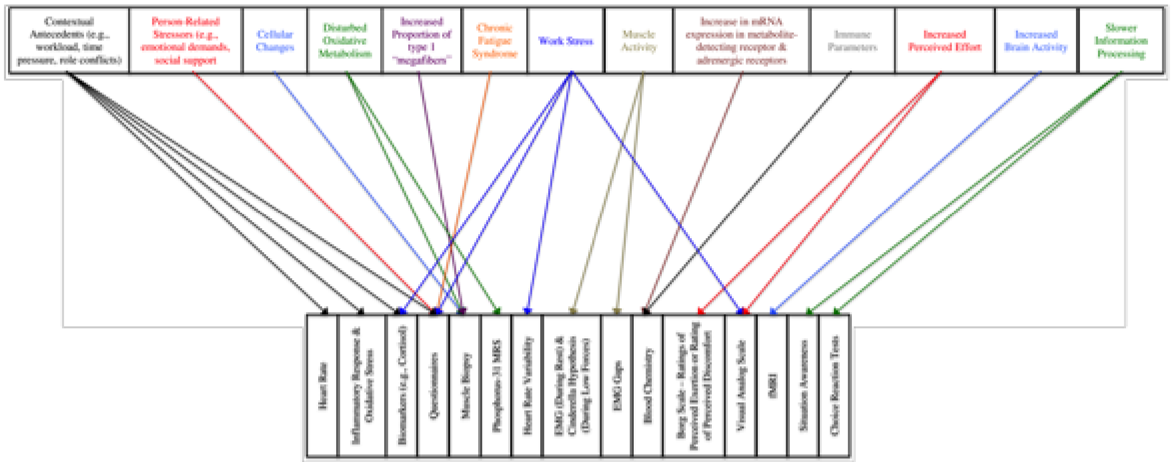


Figure 3. Fatigue measures and detection methods linked to causes or outcomes of fatigue-related illness and wellness outcomes.

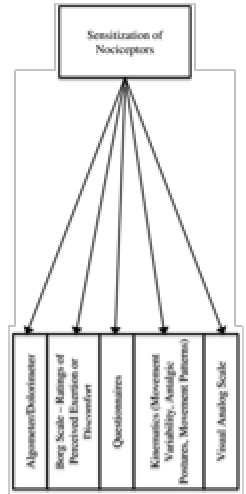


Figure 4. Linking fatigue measures and detection methods with causes or mechanisms of fatigue-related discomfort outcomes.

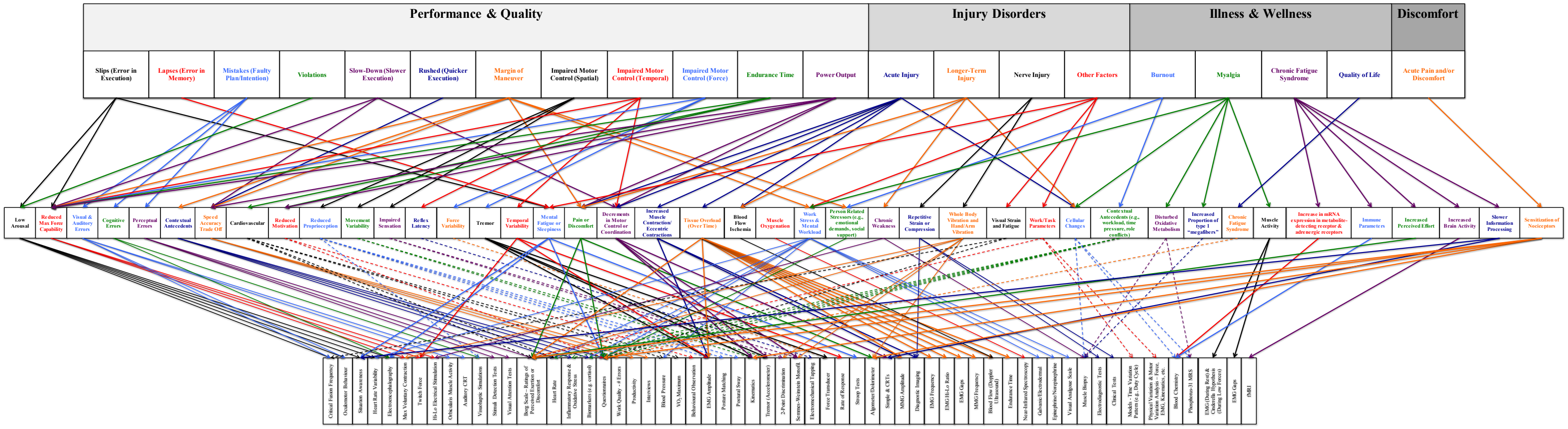
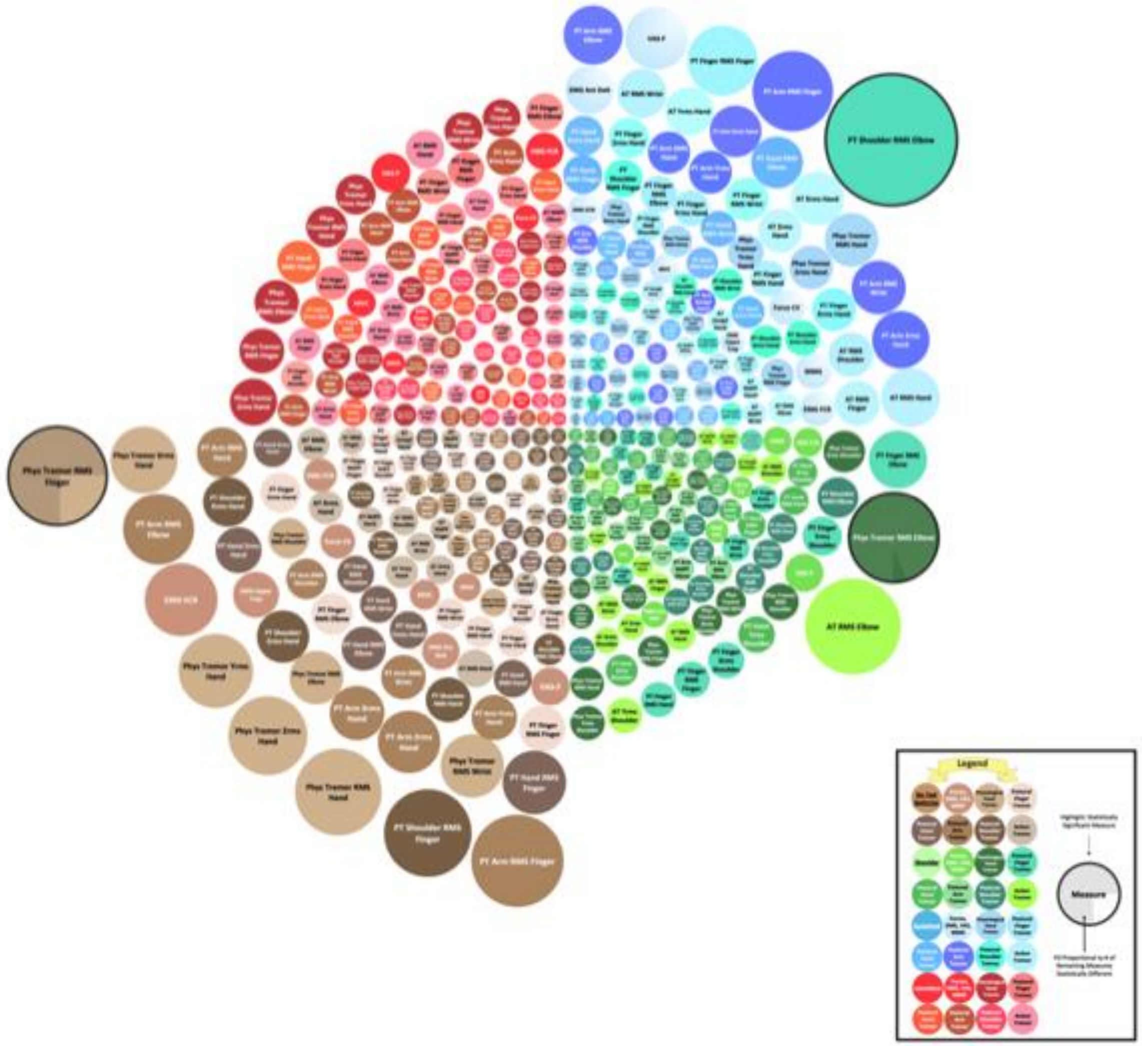


Figure 5. Summary of links between fatigue outcomes, effects, mechanisms, and measures.

Appendix B

Description: The accompanying Excel spreadsheet contains 14 worksheets of data (see "Content" worksheet). For each worksheet, the coloured cells are the mean values of a slope or test battery. Cells highlighted in yellow are statistically significant values at alpha = 0.05.

Filename: Supplementary File – Statistics Matrices.xlsx (Available Upon Request)



This is a visual representation of fatigue test battery measures recorded before and after four different exercise conditions. Each circle represents a test battery measure, the pre- and post- exercise difference as a percentage normalized to baseline. The relative magnitude of the difference is proportional to the size of the circle, which was logarithmically transformed. The four conditions (sustained handgrip at 10%MVC, intermittent handgrip at mean 15%MVC, intermittent handgrip at mean 15%MVC without test batteries, and intermittent shoulder flexion at mean 15%MVC) are coloured blue, red, brown, and green tones, respectively. Statistical analysis indicates that conditions were statistically different (sustained vs. intermittent, sustained vs. shoulder, intermittent vs. no test battery, and no test battery vs. shoulder) based on all measures. When all conditions are collapsed, RMS tremor amplitude of the elbow during postural shoulder tremor, exhibited statistically significant differences compared to 97 other measures/measurement parameters. After stratifying based on condition, RMS amplitude of the accelerometer mounted on the elbow measured during the postural shoulder tremor test was statistically different from all other measures/measurement parameters in the sustained condition ($p < 0.0007$). In the no test battery condition ($p < 0.0001$), RMS tremor amplitude of the finger during physiological tremor test was statistically different from 75 of the 104 measures/measurement parameters. RMS amplitude of the elbow demonstrated statistical differences compared to 96 other measures/measurement parameters, in the shoulder condition ($p = 0.0008$), when recorded during the physiological shoulder tremor test.

Appendix C

Psychophysical Frequency-Adjusted Instructions:

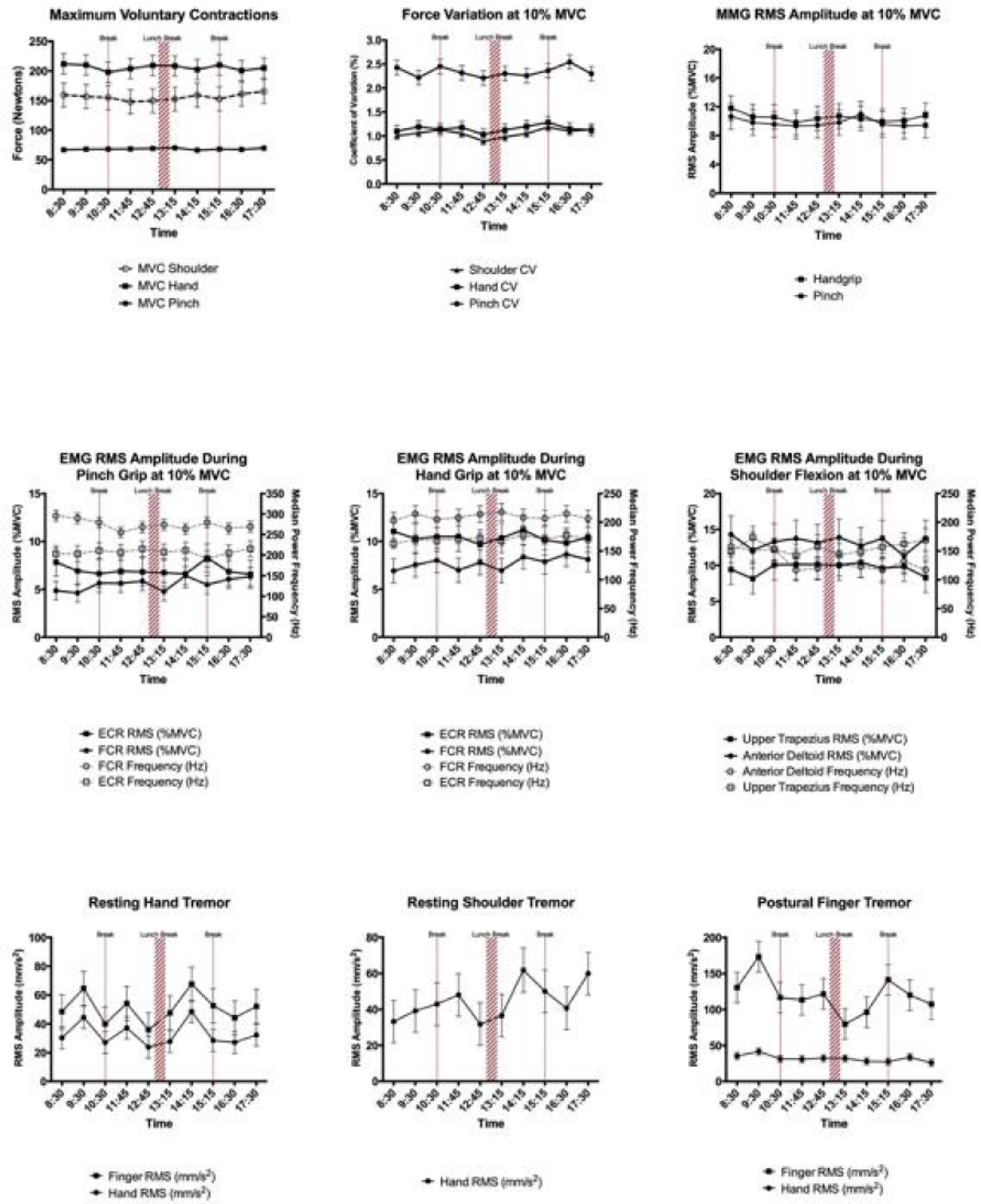
Your job is to transfer liquid from the test tube to the microcentrifuge tube. Every time you hear a beep, you will attach a disposable tip to the pipette, aspire the liquid, dispense, and eject the tip. You will adjust the workload according to the guidelines below:

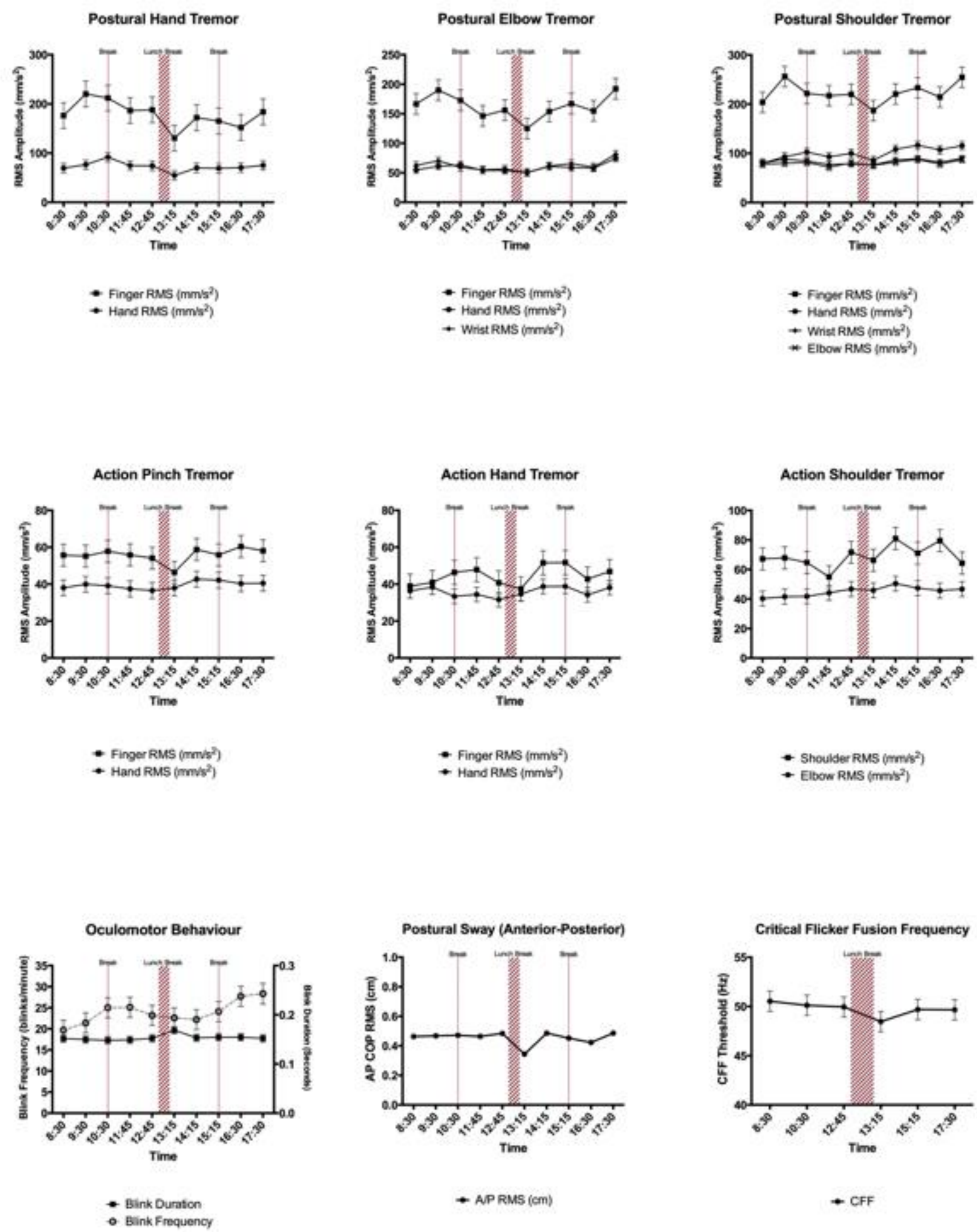
- Perform the pipetting cycle smoothly and at a moderate speed – not too fast and not too slow.
- Ensure you produce quality transfers; avoid aspiring and dispensing dish liquid into the microcentrifuge.
- We depend upon you for successful results, and greatly appreciate your participation!

Instructions for Adjusting Workload:

- We want you to imagine that you are getting paid for the amount of work that you do (i.e., piece work). However, you will work for an 8-hour shift that allows you to go home without unusual discomfort in the hands, wrists, forearms, and shoulders.
- In other words, you will work as hard as you can without straining your hand, wrist, forearm, and shoulder.
- **You will adjust your own workload.** You will work at the sound of the beep. You will adjust the frequency by telling the research facilitator to adjust the speed at which you complete a cycle.
- Adjusting your workload is not an easy task. Only you know how you feel.
- If you feel you are working too hard, reduce the frequency by telling the research facilitator to decrease the speed.
- However, we don't want you working too lightly either. If you feel you can work harder, as you might on piecework, adjust your speed to increase your work pace.
- Make as many adjustments as you can.

Remember…this is not a contest.
Everyone is not expected to do the same amount of work.


Maximum Voluntary Contractions
Force (Newtons)
Time
MVC Shoulder
MVC Hand
MVC Pinch
Force Variation at 10% MVC
Time
Shoulder CV
Hand CV
Pinch CV
MMG RMS Amplitude at 10% MVC
RMS Amplitude (%MVC)
Time
Handgrip
Pinch
EMG RMS Amplitude During Pinch Grip at 10% MVC
RMS Amplitude (%MVC)
Median Power Frequency (Hz)
Time
ECR RMS (%MVC)
FCR RMS (%MVC)
FCR Frequency (Hz)
ECR Frequency (Hz)
EMG RMS Amplitude During Hand Grip at 10% MVC
RMS Amplitude (%MVC)
Median Power Frequency (Hz)
Time
ECR RMS (%MVC)
FCR RMS (%MVC)
FCR Frequency (Hz)
ECR Frequency (Hz)
EMG RMS Amplitude During Shoulder Flexion at 10% MVC
RMS Amplitude (%MVC)
Median Power Frequency (Hz)
Time
Upper Trapezius RMS (%MVC)
Anterior Deltoid RMS (%MVC)
Anterior Deltoid Frequency (Hz)
Upper Trapezius Frequency (Hz)
Resting Hand Tremor
RMS Amplitude (mm/s²)
Time
Finger RMS (mm/s²)
Hand RMS (mm/s²)
Resting Shoulder Tremor
RMS Amplitude (mm/s²)
Time
Hand RMS (mm/s²)
Postural Finger Tremor
RMS Amplitude (mm/s²)
Time
Finger RMS (mm/s²)
Hand RMS (mm/s²)


Postural Hand Tremor
Postural Elbow Tremor
Postural Shoulder Tremor
Action Pinch Tremor
Action Hand Tremor
Action Shoulder Tremor
Oculomotor Behaviour
Postural Sway (Anterior-Posterior)
Critical Flicker Fusion Frequency
RMS Amplitude (mm/s²)
Blink Frequency (blinks/minute)
Blink Duration (Seconds)
AP COP RMS (cm)
CFF Threshold (Hz)
Time
Break
Lunch Break
Finger RMS (mm/s²)
Hand RMS (mm/s²)
Wrist RMS (mm/s²)
Elbow RMS (mm/s²)
Shoulder RMS (mm/s²)
Blink Duration
Blink Frequency
A/P RMS (cm)
CFF