Eccentrically Induced Skeletal Muscle Damage in Patients With Chronic Fatigue Syndrome (CFS), With Reference to Overtrained Athletes

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ECCENTRICALLY INDUCED SKELETAL MUSCLE DAMAGE IN PATIENTS WITH CHRONIC FATIGUE SYNDROME (CFS), WITH REFERENCE TO OVERTRAINED ATHLETES

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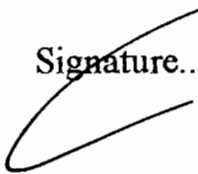The Use of Thesis statement is not included in this version of the thesis.

Abstract

Chronic fatigue syndrome (CFS) and Overtraining syndrome (OTS) are separate, complex conditions which have so many similar debilitating effects that it has led some researchers to conclude that OTS is a sub-condition of CFS. The purpose of this research was to compare the force and damage-recovery characteristics of skeletal muscle in CFS patients and control normals, after a single damaging bout of eccentric contractions in the non-dominant forearm flexors. The subjects (n = 25), a convenience sample were assigned to three groups; [1] CFS + eccentric damage (n = 8), [2] Control Damage (CD) + eccentric damage (n = 10), and [3] Control (ND) + no damage (n = 7). The research was carried out over a four week period using the following format. CFS & CD groups received eccentrically induced muscle damage of the forearm flexors by 35 isokinetic eccentric (7 x 5, 2 minutes recovery between sets) contractions at $90°$ sec^{-1} with the forearm returning passively at $15°$sec^{-1}. Testing was undertaken pre-damage and 1, 2, 4, 6, 8, 12, 16, 20, 24, & 28 days post-damage, by measurements of voluntary maximal concentric isokinetic force at $150°$sec^{-1}, isometric maximal voluntary contraction at approximately $90°$ elbow flexion, electrically stimulated 20 : 50Hz isometric force ratio at approximately $90°$ elbow flexion, muscle pain, and blood CK. Groups were compared on these variables using Students independent t-test and repeated measures two way ANOVA with simple contrasts. Alpha was set at 0.05 level. The results of this study were significant for the eccentric force produced in the

damage bout with the CFS group producing less force after the 4th set ($p < 0.05$). Serum CK concentration, which following eccentric damage was significantly higher in the CFS group than the CD group ($p < 0.01$), and the ND group ($p < 0.001$). The low frequency fatigue (LFF) ratio was significantly lower in the CFS group 2, 4, 6 & 8 days post-damage when compared to the CD group. Maximal isometric voluntary force and isokinetic concentric peak torque (PT) & average peak torque (AT) loss was significantly greater in the CFS group compared to the CD group (isometric $p < 0.01$, PT $p < 0.01$; & AT $p < 0.001$) and ND group (isometric $p < 0.01$; PT $p < 0.001$; & AT $p < 0.001$). The intensity of delayed onset muscle soreness (DOMS) was significantly less 6 days post-damage in the CFS group, when compared to the CD group ($p < 0.05$). The combination of an increased CK efflux and low frequency fatigue, that is of both greater depth and longer lasting, together with greater isometric and concentric force losses, indicates that the subjects with CFS have a lower threshold for muscular damage, that is more profound and slower to recover than in healthy individuals.

Declaration

"I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any institution of higher education; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except were due reference is made in the text."

Signature..

Date........ 9/2/ 1995

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CHAPTER 1

INTRODUCTION

1.1 The Background & Significance of the Study

Chronic fatigue syndrome (CFS) is a very complex and debilitating condition that has been described as having various possible aetiologies including psychological (Krupp, Mendelson, & Friedman, 1991), viral (Behan & Behan, 1993), combined viral and psychological (Byrne, 1991), immunological, neuro-physiological (Parker & Brukner, 1994) and a hypothalamic disorder (Lee, 1994). Due to its complexity, CFS is generally diagnosed by exclusion of psychiatric or possible other pathogenesis (Behan & Behan, 1993), though recent research (McGregor, Butt, Zerbes, Dunstan, Roberts, & Klineberg, 1994) claims to have isolated a urinary biomarker which the researchers have titled CFSUM1.

Overtraining syndrome (OTS), like CFS, is also a clinical condition of uncertain aetiology and apparent complexity which can result in many symptoms including depression, central fatigue, and immunosuppression (Parry-Billings, Matthews, Newsholme, Budgett, & Koutedakis, 1993). Diagnosis is generally made by "monitoring physiological markers such as aerobic capacity, changes in muscle force [in prolonged contractions], and by comparing [performance] times" (Sharp & Parry-Billings, 1992, p. 34), as well as by reduction of the performance attainable at the 4 mmol blood lactate concentration

(Lehmann, Foster, & Keul, 1993), which indicates a reduced anaerobic threshold in the athlete.

Whilst being acknowledged as separate syndromes both CFS and OTS share common symptoms, in particular profound fatigue, and myalgia. In fact, so similar are the two diseases that many researchers (Eichner, 1991; Fitzgerald, 1991; Fry, Morton, & Keast, 1991a, Fry, Morton, & Keast, 1991b; Gross, 1992; Keast & Morton, 1992; Lehmann, et al., 1993; Parker, 1990; Parker & Brukner, 1994) feel that overtraining syndrome can be classified as a sub-condition of CFS.

Myalgia is often, but not always, associated with muscle damage (Byrnes & Clarkson, 1986). Edwards, Newham, & Peters, (1991) indicate that the serum biochemistry of the intramuscular enzymes creatine kinase (CK), lactate dehydrogenase (LDH), and aspartate transaminase (AST), are consistently found to be within the normal range (CK: 60-200, AST: 11-35, LDH: 80-190 UI/L, Nosaka, Clarkson, & Apple, 1992) in persons diagnosed with post viral fatigue syndrome (PVFS) a condition which has been reclassified as CFS. On the other hand in OTS it is sometimes reported that there is elevated CK serum concentration (300 UI/L) when compared to the normal concentration for a trained athlete (200 UI/L), which may be due more to the effects of acute training overload, than as a symptom of OTS (Fry, et al., 1991a). Therefore, it seems that although there may be myalgia present in CFS and OTS, generally there is no syndrome related muscle damage in either CFS or OTS as in many of these cases the plasma CK, AST and LDH

concentrations are within the normal range (Edwards, et al., 1991), (refer to Table 2.3 for normal ranges).

From a patho-physiological view-point the similarities between CFS and OTS pose the questions; To what extent can the symptom of myalgia, be reflected in the degree of damage? Does CFS (including OTS) affect the normal recovery processes occurring during muscle regeneration?

1.2 Purpose of the Study

The overall objectives of this research are twofold 1) attempt to establish a physiological diagnostic protocol and 2) indicate the pathology for CFS (including OTS), based on the damage-recovery characteristics of skeletal muscle.

1.3 Hypotheses

1. After damage, muscle force characteristics of subjects with CFS will be different from the Control Damage (CD) group.

2. After damage, the contractile properties of skeletal muscle as determined by the level of low frequency fatigue (LFF), will differ in subjects with CFS when compared to the CD group

3. The time course of serum CK efflux, and the serum CK concentration in subjects with CFS will be different from the CD group.

4. The time course of delayed onset muscle soreness (DOMS) during recovery in subjects with CFS will be different from the CD group.

5. The degree of DOMS in subjects with CFS will be different from the CD group.

1.4 Organisation of the Thesis

An overview and the purpose of the study, outlining the hypotheses to be tested is covered in Chapter 1. This is followed by the review of the literature with reference to the methodological rationale and theoretical framework in Chapter 2. Methodology of the thesis is covered in Chapter 3. Results and findings of significance of the research are provided in Chapter 4 with the discussion of these results in Chapter 5. A summary of the study including recommendations for future research are included in Chapter 6.

CHAPTER 2

REVIEW OF THE LITERATURE

2.1 Introduction

The task of providing relevant information on CFS, and the relationship of OTS to CFS, as well as the physiology of muscle damage is a complex one. Therefore, each of these topics will be dealt with separately.

2.2 Chronic Fatigue Syndrome (CFS)

2.2.1 Overview.

CFS, which can have a myriad of debilitating conditions (Manu, Lane, & Matthews, 1992) has a long recorded history. The main features of the illness were first described by Manningham in the 18th century, and later discussed as a persistent illness following infections, by George Beard in 1869 (cited in Behan & Behan, 1993). Since then it has been known under a number of different names such as Post-Viral Fatigue Syndrome, Chronic Epstein-Barr Virus, Royal Free Disease, and Myalgic Encephalomyelitis, (Parker & Brukner, 1994), with a more complete list of names used for CFS shown in Table 2.1. More recently in Australia the syndrome has been generally referred to as CFS, though it is still commonly referred to as Post Viral Fatigue Syndrome (PVFS) in Europe. The Prince Henry's Hospital (Sydney, NSW) criteria for the diagnosis of CFS are shown in Table 2.2.

Table 2.1

Conditions which have been described as chronic fatigue syndrome

Addington disease	Neurasthenia
Akureyi disease	Neuromyasthenia
Allergic fatigue syndrome	Neurocirculatory asthenia
Allergic tension fatigue syndrome	Post viral fatigue syndrome
Anxiety neurosis	Postinfection fatigue synd.
Anxiety reaction	Post viral exhaustion synd.
Autonomic imbalance	Post viral syndrome
Benign myalgic encephalomyelitis	Psychoneurosis
Cardiac neurosis	Royal Free disease
Chronic Epstein-Barr virus infect.	Shell shock
Chronic hyperfatiguability synd.	Soldier's heart
Chronic mononucleosis	Somatization reaction gen.
Chronic mononucleosis-like synd.	Somatization psychogenic
Combat fatigue	asthenic reaction
Da Costa syndrome	Somatization psychogenic
Disordered action of the heart	cardiovascular reaction
Effort syndrome	Somatization reaction
Epidemic myalgic encephalomyelitis	psychogenic cardiovascular
Epidemic vegetative neuritis	reaction
Epidemic neuromyasthenia	Syndrome X
Icelandic disease	Tapanui flu
Irritable heart	Vaso regulatory asthenia
Lake Tahoe mystery disease	Vasomotor instability
Myalgic encephalomyelitis	Vasomotor neurosis
Nervous exhaustion	Yuppie flu
Nervous tachycardia	20th century disease
Neuritis vegetiva	

(Fry, Morton, & Keast, 1991c, p. 77)

Table 2.2

Criteria for diagnosis of CFS

---

1.   Chronic persisting or relapsing fatigue exacerbated by minor exercise, causing significant disruption of usual daily activities, present for greater than 6 months

2.   Neuropsychiatric dysfunction, including, impairment of concentration and short-term memory and depressed mood.

3.   Exclusion of common medical and psychiatric disorders (Prince Henry's Hospital, 1988/93)

(Parker & Brukner, 1994, p. 15)

The relationship between CFS and OTS are increasing and OTS is viewed as a sub-condition of CFS by some researchers (Fry et al, 1991b). There are two basic types of OTS. Firstly, there is Classic, sympathetic or Basedowoid OTS, which is relatively rare and tends to occur more often in anaerobic type sports. And secondly, Modern, parasympathetic or Addisonoid OTS, which is the most common form of OTS and occurs mainly in the aerobic type sports (Lehmann, et al., 1993). The general symptoms for OTS, like CFS are varied with elevated pulse rate, painful and heavy muscles, gastrointestinal disorders, upper respiratory tract (URT) infections, delayed healing from cuts and bruises, as well as central fatigue, irritability, depression and sleep disturbances being common (Parry-Billings, Budgett, Koutedakis, Blomstrand, Brooks, Williams, Calder, Pilling, Baigrie, & Newsholme, 1992). More specifically the main symptoms of the sympathetic form of OTS including restlessness and excitation in conjunction with performance decrements, whereas inhibition and depression in

conjunction with performance decrements are indicative of the parasympathetic form of OTS (see Table 2.3).

Table 2.3

Findings in the "classical" and "modern" forms of overtraining syndrome for which conformation is still lacking in part.

Overtraining Syndrome	
Classic, Sympathetic or Basedowoid Form	Modern, Parasympathetic, or Addisonoid Form
Performance reduction	Performance reduction
Easily fatigued	Easily fatigued
Restlessness excitability	Depression, inhibition
Disturbed sleep	Sleep not disturbed
Loss of weight	Constant weight
Accelerated resting HR	Bradicardic HR
Delayed recovery	Good recovery capacity

(Lehmann, et al., (1993, p. 856)

Fry, et al., (1991b, p.48) stated: "Athletes who are exposed to excessive training, psychological, environmental, nutritional or lifestyle stressors may suffer performance decrements and other stress related symptoms reflective of a state described in the literature as overtraining". If recognised in the early stages (up to 2 weeks) a full recovery from overtraining may be attained after only a few days to two weeks rest. On the other hand, if the overtraining

persists for longer it may take weeks or even months for recovery, and it is this condition that is known as OTS (Lehmann, et al. 1993), which can be considered as a sub-condition of CFS.

2.2.2 Serum Biochemistry of CFS.

From a biochemical viewpoint, Edwards, et al., (1991) indicate that cytoplasmic enzymes of skeletal muscle, notably CK, LDH, and AST are consistently found to be within the normal range in persons diagnosed with PVFS (Table 2.4), so although there may be myalgia present in CFS there is no indication of muscle damage. On the other hand there is sometimes a reported elevation in LDH or CK serum levels (Table 2.4) in persons with OTS (Fry, et al., 1991b), though this may well be more due to acute overload of training than to the effects of OTS (Fry, et al., 1991a).

Table 2.4

Biochemical markers for muscle damage, adults normal range. *

CK	60 - 200	U/L
LDH	80 - 190	U/L
AST	13 - 35	U/L
Myoglobin	6 - 85	ng/ml

* method of assay and test principles are shown in Appendix A.
(Modified from Nosaka, et al., 1992, p. 184)

2.2.3 Physiological Parameters.

Research by Stokes Cooper & Edwards, (1988) found that muscles of patients with effort syndromes were no weaker or more fatigable than that of healthy controls. Similarly, Lloyd, Hales, & Gandevia, (1988) found normal isometric strength and dynamic force capabilities in patients with CFS when compared to healthy controls, though with an impaired recovery. Kent-Braun, Sharma, Weiner, Massie & Miller (1993) whilst generally supporting Lloyd et al. (1988), also found that CFS patients showed an inability to fully activate muscle during intense sustained exercise, which they concluded was due to central fatigue. Later research by Lloyd, Gandevia & Hales (1991), concluded that failure of the contractile properties of skeletal muscle in patients with CFS was not important in the pathogenesis of fatigue in CFS. Patients with CFS in the form of PVFS have been found to have a reduced aerobic capacity, which in turn pre-disposes these patients toward a reduced work capacity (Behan & Behan, 1993; McCluskey, 1993) and as such CFS patients have been shown to have a limited exercise capacity in graded exercise tests (Buchwald & Komaroff, 1991). Further, research by Arnold and co-workers, (1984) cited by Behan & Behan (1993) suggests an increased level of glycolytic metabolism due to an excessive level of acidosis during exercise. And finally, whilst other metabolic studies (Byrne & Trounce, 1987 cited by Buchwald & Komaroff, 1991; Kent-Braun, et al., 1993) have concluded that adenosine tri-phosphate (ATP) levels are not effected in patients with CFS, Wong, Lopaschuk, Zhu, Walker, Catellier, Burton, Teo, Collins-Nakai, & Montague, (1992) suggest that from their research using 31P nuclear magnetic resonance spectroscopy, there is a oxidative metabolism defect

within skeletal muscle in patients with CFS determined by a significantly lower ATP level in skeletal muscle of patients with CFS at the point of exhaustion when compared to healthy subjects during exercise testing. Though they conclude that the aetiology of profound fatigue in CFS is unclear and could be as a result of deconditioning, post-viral effect, or due to some other cause.

There are numerous physiological symptoms of OTS (for a full review refer to Fry, et al., 1991a, 1991b), some of which include: a) A reduced 4 mmol blood lactate threshold whereby the lactate curve shifts to the left and becomes more vertical (Fry, et al., 1991a; Lehmann, et al., 1993; O'Brien, 1993) which results in a reduced anaerobic threshold of the athlete. b) An increased heart rate for the same workload (McKinnon & Hooper, 1992; O'Brien, 1993). c) A reduced VO_{2max} by as much as 5-10% (McKinnon & Hooper, 1992), with a concurrent increase in ventilation (Fry, et al., 1991a). And d) a reduction in the amount of muscular force that can be applied in prolonged contractions (Sharp & Parry-Billings, 1992).

2.2.4 Electrophysiological Effects.

Kent-Braun, et al., (1993) indicate that electromyograph (EMG) activity is generally normal in patients with CFS, though research cited by Behan & Behan, (1993), found a reduction in the recruitment patterns of voluntary motor units as well as abnormal single fibre electromyograph (EMG) in patients with PVFS with the peripheral component of the motor unit (muscle fibre) as the most likely site. This indicates a likely myopathic disease involvement affecting contractile tissue in PVFS rather than

neurogenic disease affecting the motoneurone (Rothwell, 1994). Similarly, Newsholme (1990) cited by Fry et al. (1991a) proposes that due to reduced glutamine release from skeletal muscle in OTS there is a resultant decrease in motor unit recruitment with an increased level of fatigued myofibres during rest. Other nervous system abnormalities in OTS include: a) an increased difficulty in temperature control (Parker, 1990) which may be related to 5-HT (serotonin) levels (Behan & Behan, 1993); b) sensory nerve disturbances including hypaesthesia (numbness) and paraesthesia (pins & needles); c) vertigo; and d) palpitations and tachycardia (Parker, 1990).

2.2.5 Pathology of CFS.

A significant proportion of patients with PVFS, following muscle biopsy, show mild to severe atrophy of Type 2 muscle fibres and mitochondrial degeneration in oxidative muscle fibres (Behan & Behan, 1993). Conversely Edwards, et al., (1991, p. 826) state: "Clinical examination of muscle bulk reveals normal findings in PVFS patients, particularly in early stages of the disorder." Therefore, whether the cause of these aforementioned myopathies is due to CFS or due to immobilisation as a result of de-conditioning is not clear. In OTS, Fry, et al., (1991a, p. 52) concludes that. "Most muscle damage [in OTS] reflects acute overload and is therefore more likely to be associated with overreaching than with advanced overtraining".

2.2.6 Immunology of CFS.

The immunology of CFS is varied (Table 2.5) and often shows many abnormalities such as increased auto-antibodies, abnormal

complement metabolism, and abnormal concentrations in various immunoglobulins (Behan & Behan, 1993; Wessely & Thomas, 1991). Other responses include an abnormality in the cell-mediated response with either an increase or decrease in absolute numbers of T-helper (CD4) or T-suppressor (CD8) cells, an imbalance in CD4 : CD8 ratio, and a reduced hypersensitivity skin response (Lloyd, et al., 1991). These immunological findings suggest that the immune system of patients with PVFS is compromised by a persistent viral infection (Behan & Behan, 1993). Horrobin (1990) hypothesises that levels of Ω-3 and Ω-6 essential fatty acids (EFA's) found in patients with PVFS may be inadequate due to the inability of an individual with PVFS to correctly metabolise the Ω-3 linoleic acid (Figure 2.1)

Linoleic
↤ Viral infections block this step
↤ This step defective in atopic eczema
Gamma-Linolenic

Dihomogammalinolenic ⟶ Prostaglandins
Interferon activates this step
Arachidonic ⟶ Prostaglandins

Figure 2.1. The interactions between essential fatty acid (EFA) metabolism, viral infections, atopic eczema and interferon. (Horrobin, 1990, p.214).
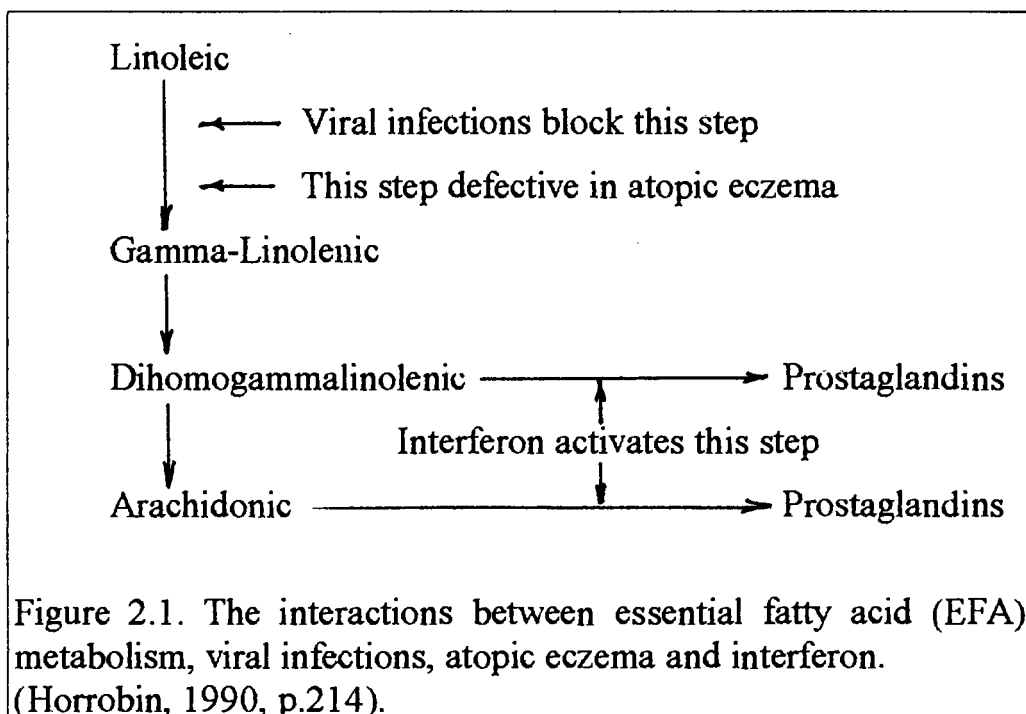
It is generally accepted that moderate exercise can enhance the immune system, whereas excessive exercise levels as undertaken

by many elite athletes can damage the immune system (Fitzgerald, 1991). The immunological effects in OTS are markedly similar to that of CFS shown in Table 2.5, with significant variations in CD4 to CD8 ratio common (Fry, et al., 1991a). Any reduction in CD4 or CD8 numbers may be linked to a possible decrease in nocturnal catecholamine secretion, particularly epinephrine (Lehmann, Schnee, Scheu, Stockhausen, & Bachl, 1992) as CD4 and CD8 lymphocyte proliferation is enhanced by catecholamines (Weicker & Werle, 1991).

Table 2.5

Immune dysfunction in CFS

Humoral immune responses;
    1) elevated antibodies to viral proteins,
    2) low antibodies to EBNA or EBMA-1,
    3) partial hypogammaglobulinaemia,
    4) normal immunoglobulin,
    5) elevated circulating immune complexes, and
    6) decreased immunoglobulin release in vitro from mitogen
       stimulated lymphocytes.
Lymphokine and interleukin responses;
    1) increased leucocyte 2-5-oligoadenylate synthase,
    2) decreased interleukin-2 synthesis in vitro,
    3) decreased immune (gamma) interferon synthesis
       in vitro by mitogen-stimulated lymphocytes, and
    4) normal gamma interferon production.
Lymphocyte number and function;
    1) increased helper (CD4) to suppressor (CD8) ratio from
       decrease CD8 count,
    2) increased CD8 and decreased CD4, and
    3) normal CD4 to CD8 ratio.

(Modified from Wessely & Thomas, 1990, p. 109).

Research (Parry-Billings, et al., 1993) found significantly lower levels of plasma glutamine in conjunction with significantly higher levels of glutamate in overtrained athletes when compared to healthy controls and they propose that the level of glutamine, which is the primary metabolite of the immune system, is reduced due to being metabolised as a substrate within the skeletal muscle rather than being released from skeletal muscle so as to become available for the immune system.

As a result of the imbalances that occur in the immune system overtrained athletes become more susceptible to upper respiratory tract infections (URTI), (MacKinnon, 1994) which can be illustrated by Figure 2.2, with the cause of the immunological imbalance may well be as a result of reduced glutamine levels.

Figure 2.2. Modified "J-shaped" model of the relationship between the amount of exercise and the risk of upper respiratory tract infection (MacKinnon, 1994, p. 192)
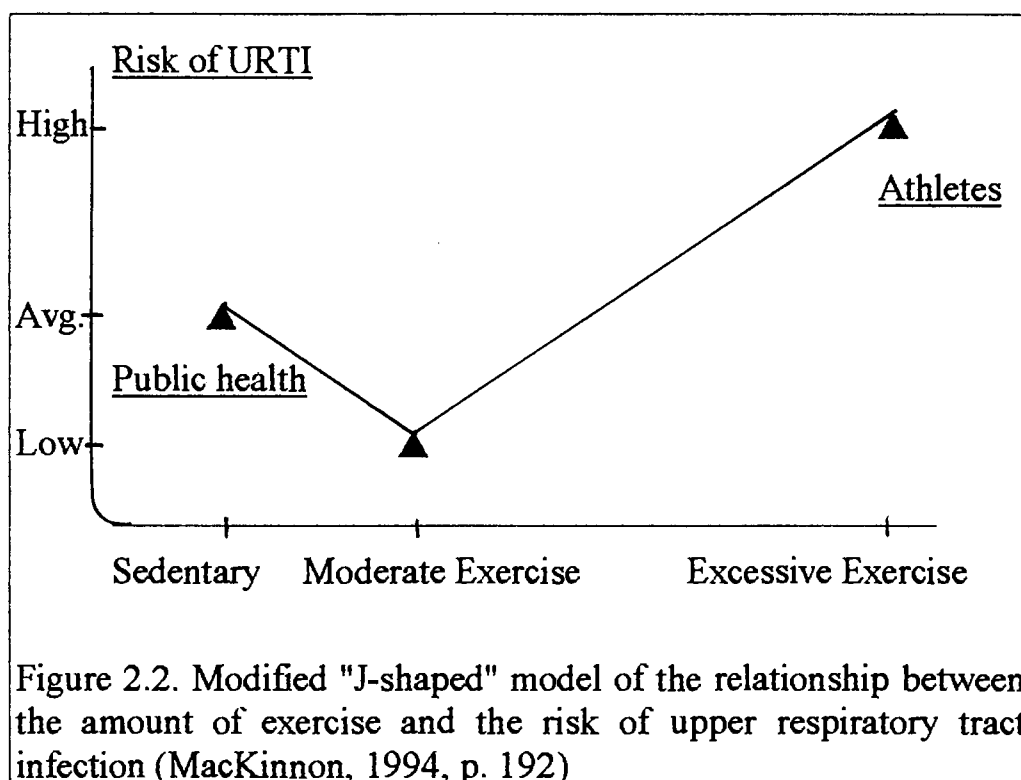
2.2.7 Neuroendocrine Effects.

Hans Selye's General Adaptation Syndrome (GAS) whereby the neuroendocrine system responds to increased stress levels by release of hormones that enable physiological repairs to be carried out (Powers & Howley, 1994), is of importance to CFS and OTS. In that, these hormones, catecholamines, and glucocorticosteroids all have a significant role in immunoregulation (Keast & Morton, 1992), and in a healthy individual react positively.

However, in CFS or OTS the hormonal balance may be lost. Fry, et al., (1991a) indicate that hormonal imbalances in OTS sufferers may result in various responses including: a) an increase in resting levels of catecholamines (epinephrine and norepinephrine); b) higher concentrations of the neuropeptides (including endorphins and encephalins); c) increased resting levels of cortisol (Fitzgerald, 1991); d) increased resting levels of thyroid hormones (Keast & Morton, 1992); e) decreased resting testosterone level; f) increased insulin resistance, and; f) a decreased glucose tolerance that may be related to growth hormone release. (O'Brien, 1993).

Some interesting research into the role of the neurotransmitter 5-hydroxytryptamine (5-HT or serotonin) which is a derivative of the amino acid tryptophan, and its involvement in CFS and OTS has been recently carried out (Newsholme, Blomstrand, McAndrew, & Parry-Billings, 1992; Parry-Billings, et al., 1992; & Parry-Billings, et al., 1993). Brain levels of 5-HT are thought to influence sleep and tiredness and has been implicated in central fatigue (Newsholme, et al., 1992), other functions that may involve 5-HT

include memory, appetite, mood, and temperature regulation (Behan & Behan, 1993).

The 5-HT receptors in patients with PVFS have been shown to be more active when compared to a healthy control group and a control group with primary depression, and as such depression in PVFS is likely to be different from primary depression (Behan & Behan, 1993). Whereas in OTS researchers (Newsholme, et al., 1992) propose that 5-HT, which is widely spread in the brain is involved in three main physiological functions of; a) wakefulness and mood, where it is thought to have a role in disturbing sleep and in central fatigue; b) motor neurone excitability where 5-HT has a role in increasing monosynaptic reflexes and decreasing polysynaptic reflexes which could be involved in a reduction of work capacity; and c) autonomic and endocrine function where it has been implicated in the reduction in the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) which are used to regulate the levels of testosterone.

2.2.8 Psychological Aspects of CFS.

In a review of the pathophysiology of CFS conducted on 32 research publications, Manu et al., (1992) confirmed the following trends found, though the cause-effect relationship is not evident. These trends included findings that CFS patients are more likely to be: a) middle aged Caucasian females, b) have a major depression and lifetime somatization disorder, c) may have a abnormal personality trait such as histrionic, schizoid or avoidance personalities, and (d) have the general belief in physical causation of chronic fatigue. Parker (1990, p. 580) states. "Like all chronic

illnesses, mental ramifications of the illness [CFS] naturally occur and add to the debility of the disease. Extreme mood swings, depression, anxiety, anger, frustration and consequently low self-esteem are common secondary aspects faced by CFS sufferers." She goes on to conclude that the psychological depression associated with CFS is reactive and as such is a symptom and not synonymous with CFS (see also Sect. 2.2.7).

The psychological aspects of OTS are very similar to those of CFS or primary depression (Fry, et al., 1991a), with mood swings, depression and irritability common (Lehmann, et al., 1993; MacKinnon & Hooper, 1992). Moreover, the link between psychological stress and the immune system has been well documented (Fitzgerald, 1991). As with CFS, the cause-effect relationship between psychological stress and the symptoms of OTS is not clear. However, it is reasonable to assume that elite level athletes may feel extreme pressures to perform during particular meets.

2.2.9 Conclusion.

It is evident from the literature, that the aetiology of CFS (including OTS) is probably multi-factorial. Consequently, the psychoneuro-immunologic (PNI) model (La Perriere, Antoni, Schneiderman & Fletcher, 1992) which deals with the interaction between psychological factors and the nervous and the immune systems (Figure 2.3) is an attractive model to use in the pursuit of understanding the dynamics of CFS. The PNI model was suggested by La Perriere et al., (1992) for the progression of HIV-1 and later

refined to include other chronic diseases (La Perriere, Ironson, Antoni, Schneiderman, Klimas, & Fletcher, 1994),

Figure 2.3: A suggested psychoneuroimmunologic model for stress-related immuno-modulator effects (La Perriere, et al., 1994, p. 183.
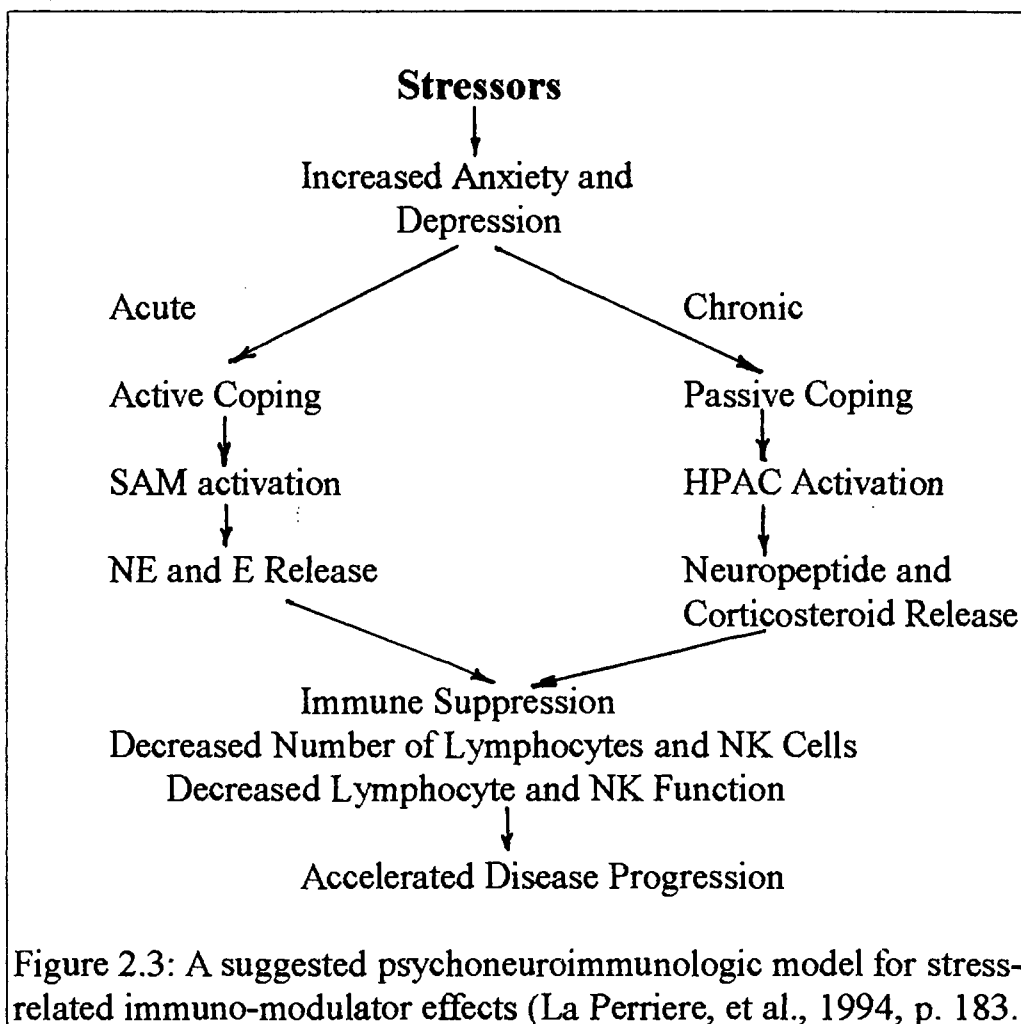
La Perriere, et al., (1992, 1994) explain Figure 2.3 as follows; a) Stressors of a physical and/or mental nature can increase anxiety and/or depression, and how these stressors are perceived is dependent on the psychological coping mechanism (active or passive) of the individual. b) An active coping mechanism is generally considered adequate and in this instance the sympathoadrenomedullary (SAM) system is activated to release the catecholamines epinephrine and norepinephrine to meet the demands of the stress. c) Should the stressors become too much for

the individual by becoming uncontrollable, unrelenting or unpredictable, then the individual tends to withdraw and adopt a passive coping mechanism. d) This results in activation of the hypothalamic-pituitary adreno-cortical system which results in increased secretion of corticotropin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) which in turn result in increased cortisol levels, which along with catecholamines is a known immunosuppressant.

2.3 Physiology of Muscle Damage
2.3.1 Overview.

It has been suggested that muscle damage and the associated pain, occurs as a result of exercise involving high force contractions (Friden, Sjostrom, and Ekblom, 1983; Newham, Jones, Tolfree & Edwards, 1986; Newham, Mills, Quigley, & Edwards, 1983). This is particularly so when the exercise is of a novel nature or it has been some time since this particular type of exercise has been undertaken by the individual (Newham, et al., 1986). Recent research (Lieber & Friden, 1993) has failed to support the high force-damage notion, instead they propose that the damage is caused by active muscle strain. That is, the magnitude of the strain on the muscle during the lengthening process is the determinant of damage, not the force. Either way, damage still occurs and is evidenced by; a) reduced force production (Ebbling & Clarkson, 1989; Jones & Round, 1993); b) increased serum levels of muscle proteins, (Newham, Jones, & Clarkson, 1987); and c) increased tenderness of the muscle and possibly central fatigue (Ebbling & Clarkson, 1989; Jones & Round, 1993).

2.3.2 Force Characteristics.

Immediately following an eccentrically-induced damage bout there is a loss of force (isometric and concentric) in the muscle, which can return to pre-damage levels from 24 hours to some weeks depending on the level of damage (Clarkson, Nosaka, & Braun, 1992; Ebbling & Clarkson, 1989; Ebbling & Clarkson, 1990; Newham, Mills, et al., 1983). This loss of force may be bought about due to one or a combination of the following: a) low-frequency fatigue (LFF); b) possible fatigue, both central & peripheral; c) perceived pain; and d) damage within the muscle, which may be due to sarcomere "creep" whereby sarcomeres of shorter length situated at the end of myofibres, which have greater innate strength than longer sarcomeres situated in the middle of the myofibre, cause damage to these longer fibres during eccentric stretch (Jones & Round, 1993), therefore effectively reducing the cross sectional area of muscle and thus the force that can be applied. The first two points will be discussed in the next two sections dealing with fatigue and contractile properties of the muscle.

2.3.3 Fatigue.

Both central and peripheral fatigue that arises as a result of exercise, reduces the force that can be applied in isometric and concentric contractions. Conversely, with peripheral fatigue the level of force that can be produced in eccentric contractions may increase with fatigue, due to the action of metabolites at the crossbridge (Jones & Round, 1993). In the fatigued state peak power from concentric contractions decreases and moves to the left of the power curve which means the individual can no longer

maintain a similar performance level, which is of course the rationale behind training. Appell, Soares, & Duarte (1992, p. 108) state: "A good training status may attenuate the clinical signs of fatigue and muscle damage".

Jones & Round, (1993) separate central fatigue into two main areas; a) the sense of effort, and b) Central nervous system (CNS) factors. Sense of effort (Figure 4) is an area that is poorly understood though there are two main trains of thought. Firstly it is thought that a signal that originates in the motor centre, radiates to the area responsible for the perception of effort. The other view held deals with the notion that sensory receptor afferents in muscle provide feedback information in much the same way as proprioceptors do (Jones & Round, 1993), which may explain the increased electro myograph (EMG) activity following eccentric exercise bouts (Ebbling & Clarkson, 1989). Moreover, things such as motivation and attitude certainly effect the individual and may well have an effect on the individual's sense of effort.
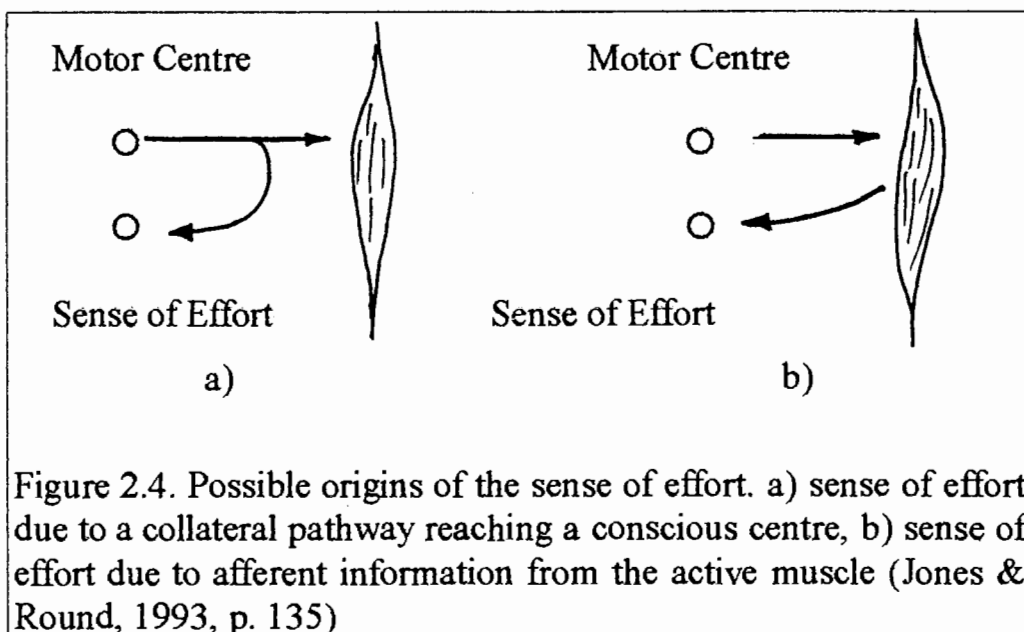
Figure 2.4. Possible origins of the sense of effort. a) sense of effort due to a collateral pathway reaching a conscious centre, b) sense of effort due to afferent information from the active muscle (Jones & Round, 1993, p. 135)

CNS involvement in fatigue can be determined by the use of electrical or magnetic stimulation of the cerebral cortex, direct electrical stimulation of a peripheral nerve, or stimulation of a muscle by percutaneous means. All of these methods provide information as to the integrity of the CNS distal from the point of stimulation, with the use of superimposed stimulation providing data as to the level of central fatigue (Jones & Round, 1993).

In exercise there is an generally only overall small reduction in the level of ATP, therefore it is unlikely that ATP levels have much impact on fatigue (Jones & Round, 1993), though this may not be the case in CFS whereby recent research (Wong, et al., 1992) using 31P NMR revealed significantly lower muscle ATP levels in CFS subjects at peak exercise levels when compared to healthy controls. On the other hand changes in the pH levels in muscle which can reduce from a pH of 7.4 to 6.5 in exhaustive exercise which place significant stress on the buffering system, inhibits glycolysis; and in combination with increased phosphate (Pi) levels, particularly in the monobasic form, results in fatigue (Cady, Jones, Lynn & Newham, 1989). Moreover, at lower pH levels (pH 6.5) the sensitivity to calcium of troponin reduces. All of these factors are in turn associated with a reduction of 10 - 30% in maximal muscular force, particularly in type 2 fibres which in turn results in a reduction in performance.

2.3.4 Contractile Properties.

In a healthy individual, prolonged repetitive activity such as extensive sub-maximal exercise, can result in low-frequency fatigue

(LFF or 20 Hz fatigue). LFF is force loss in electrically stimulated muscular contractions, which is greater at lower frequencies than higher frequencies indicating a reduced force output per action potential (Jones & Round, 1993). LFF most probably results from damage occurring at the excitation-contraction coupling (Jones, Newham & Torgan, 1989), specifically at the electron dense feet (EDF) (Figure 2.5). These are receptors sensitive to T-tubule depolarisation which transduces the electrical action potential into a release of Ca^{2+} from the intracellular sarcoplasmic reticulum (SR). Damage to the EDF could result in a reduction of Ca^{2+} release for each action potential (Ebbling & Clarkson, 1989; Lee, 1994). Because of this damage, a higher stimulation frequency is required to elicit the same intracellular Ca^{2+} induced force response. Thus by comparing the electrically stimulated responses at 20 & 50Hz, damage at the EDF can be deduced. LFF is more pronounced following eccentric exercise and may take up to 3-4 days for an individual to fully recover (Jones, et al., 1989).

Figure 2.5: Site of damage in LFF (Adapted from Lee, 1994, p.2)
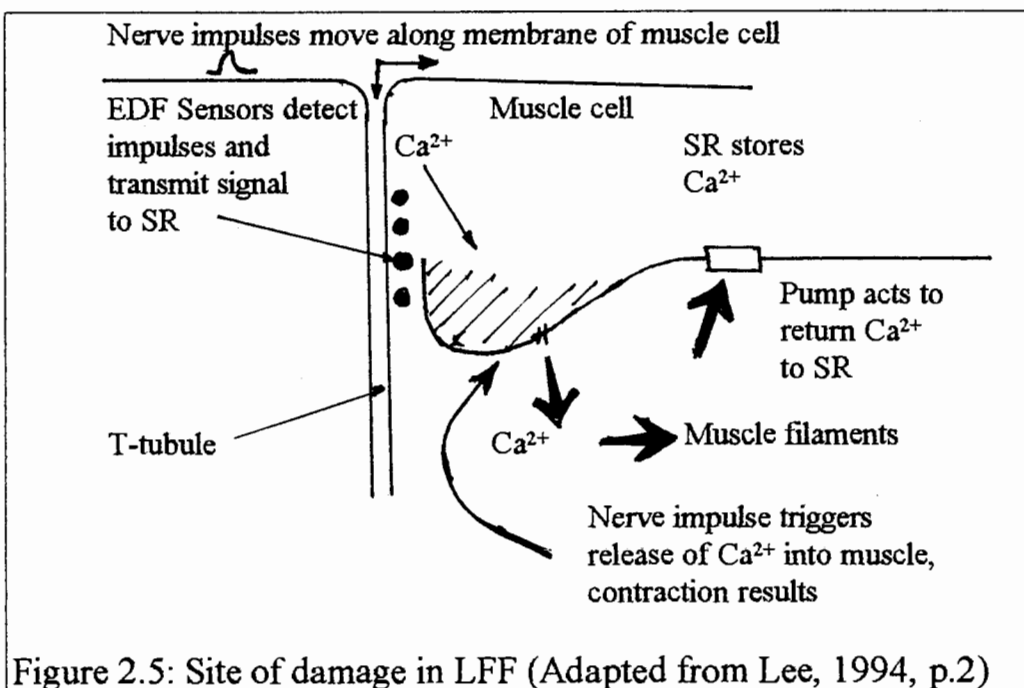
2.3.5 Creatine Kinase Release.

Creatine Kinase (CK) is an intracellular enzyme that as the name suggests is involved in the phosphorylation of adenosine diphosphate (ADP) to ATP (Jones & Round, 1993). Edwards, et al., (1991) indicate CK is consistently found to be within the normal range in persons diagnosed with PVFS (Table 2.4). On the other hand in OTS it is sometimes reported that there is elevated CK serum concentration (300 UI/L) when compared to the normal concentration for a trained athlete (200 UI/L), though it is possible that this may be due more to the effects of training, than as a symptom of OTS (Fry, et al., 1991a).

Following muscle damage the muscle cell membrane becomes more permeable and it results in CK being released into the interstitium and then into the blood via the lymph system. As a further result of cell membrane permeability sodium ions accumulate in the cytoplasm followed by an increase in cytosolic and mitochondrial Ca^{2+}, beginning the process of muscle cell breakdown (Byrd,. 1992; Knochel, 1993; Soares, Duarte, Carvalho, & Appell, 1993).). In severe cases this condition involving increased membrane permeability and resultant muscle fibre breakdown is known as rhabdomyolysis (Knochel, 1993; Poels & Gabreels, 1993).

Muscle cell lysis takes place immediately following high force eccentric exercise, myofibrillar disruption occurs, histologically demonstrated by Z-line disruption which is often termed Z-line streaming (Armstrong, 1990). Three to six hours post exercise there is in increased efflux of intracellular proteins (CK, LDH, AST

and myoglobin) into the blood. This efflux generally peaks between 2 - 5 days but in some instances may not occur until 7 days post exercise (Ebbling & Clarkson, 1989).

Whilst all serum levels of these aforementioned proteins rise, CK has the most dramatic increase and can increase x 100 from resting (Jones, & Round, 1993), and is thus the most common intracellular marker used to confirm that muscle damage has taken place. However, care needs to be taken when assessing the amount of muscle damage based upon CK results for the following reasons: a) Standard spectrophotometry does not differentiate between the CK isoenzymes and this can result in significant under or over estimation of the serum concentration of CK from skeletal muscle (Galasso, Litin, & O'Brien, 1993). b) Research (Manfredi, Fielding, O'Reilly, Meredith, Lee, & Evans, 1991; Nosaka & Clarkson, 1992) has shown that the level of serum CK does not correspond wholly to the level of skeletal muscle damage. Manfredi, et al., (1991) showed that whilst there was no significant difference between the levels of CK attained in two separate groups, based upon age (20-30, 59-63 yrs), undergoing exercise-induced damage, there was a significant difference in damage based on electron (EM) and light microscopy (LM) examination, with the older subjects showing damage in > 90% of examined fibres compared with 5-50% of fibres in the younger group showing damage. In similar research, Nosaka & Clarkson, (1992) failed to show any significant difference in serum CK levels of subjects who underwent eccentrically-induced muscle damage in both upper limbs when compared to subjects who underwent damage in only one upper limb.

Figure 2.6. Summary of some mechanisms involved in the response of an exercise-induced injury (Almekinders & Almekinders, 1992, p154).
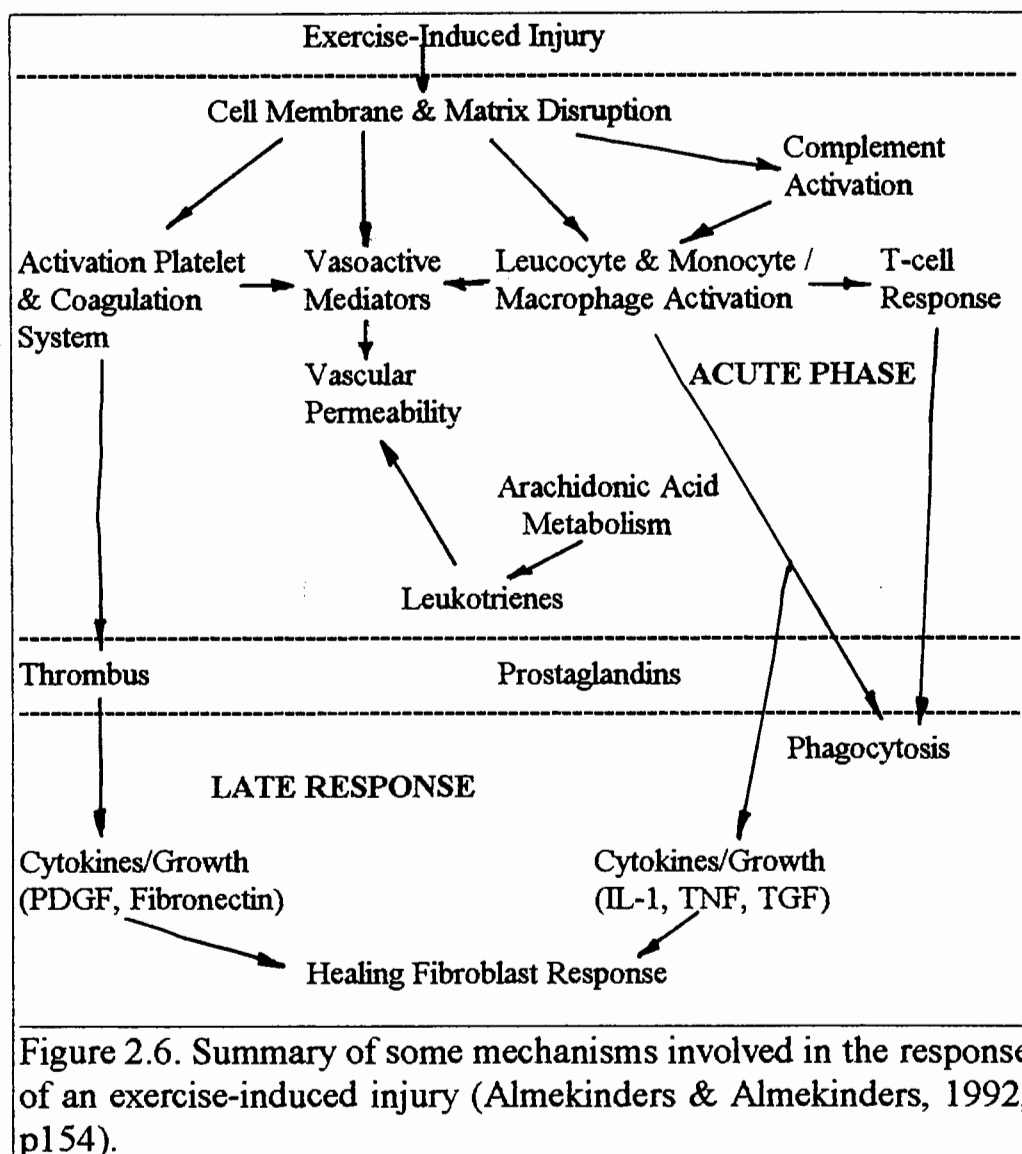
During the post-damage period, a series of immunological and biochemical processes take place (Figure 2.6) in which muscle fibres that have reached a "threshold" value of damage are lysed via a raised intracellular Ca^{2+} signal that activates intracellular phospholipase A_2 which in turn activates prostaglandins and leukotrienes (Almekinders & Almekinders, 1992; Armstrong, 1990). Damaged muscle fibres are then either repaired or replaced

by the activation of satellite cells to provide new myofibres (White and Esser, 1989).

2.3.6 Delayed Onset Muscle Soreness (DOMS).

Pain is a sensation, which occurs as a result of activation of nociceptors by chemical (refer to Table 2.6), mechanical or thermal stimuli (Jessell & Kelly, 1991). Following activation the threshold for a painful response may be lowered and the magnitude of pain response to a supra-threshold stimuli may increase. Thus, the sensation of pain following damage may be increased by these two avenues and this phenomenon is called hyperalgesia. Equally the sensation of pain may be modulated through methods such as Wall & Melzack's "Gate Control Hypothesis" (cited by Jessell & Kelly, 1991) and due to neurotransmitter involvement through supraspinal modulation of nociceptive transmission.

In the "Gate Control Hypothesis" the sensation of pain is modulated as follows. Activation of Type C un-myelinated afferents results in activity of the projection neurons, which are responsible for the sensation of pain. However, simultaneous activation of Aα/Aβ myelinated non-nociceptive afferents also occurs, which results in suppression of the activity of these projection neurons by activation of inhibitory neurons.

Regarding supraspinal modulation of nociceptive action, Jessell & Kelly, (1991) indicate a number of points. Firstly, direct administration of 5-HT or norepinephrine to the spinal cord produces analgesia. Secondly, serotonin [5-HT] is a very common neurotransmitter, with norepinephrine being the neurotransmitter

used in a descending pathway from the pons. These points are of particular interest when one considers that both 5-HT and norepinephrine can be elevated in individuals with CFS or OTS.

The phenomenon of DOMS, which is experienced by most people at some time, was first studied by Theodore Hough in the early part of the 20th century. Hough, (1902, p. 76) states: "When an untrained muscle makes a series of contractions against a strong spring, a soreness frequently results which cannot be regarded as a phenomenon of pure fatigue". In his study Hough outlined how pain came on eight to ten hours after extensive exercise and did not abate for some four to seven days. Hough was describing what we now know as DOMS.

DOMS can be described as a "sensation of discomfort or pain in the skeletal muscles following unaccustomed muscular exertion" (Armstrong, 1984, p., 529), that only occurs after the first or second bout of novel exercise (Byrnes & Clarkson, 1986). The time course of DOMS is from 1 to 7 days with the first phase being the development of a sensation of stiffness and painful skeletal muscles in 24 to 72 hours following novel exercise, that can result in a reduction in both voluntary effort and the contractile capacity of the muscle, which usually subsides within 5 to 7 days post-exercise (Armstrong, 1984). The aetiology of DOMS is unclear though it is related to over-use of the muscle concerned and is thought to occur as a result of high-tension structural damage, though as Byrnes & Clarkson, (1986, p. 605) state: "Damage in itself, however, will not always result in pain. There are numerous myopathies such as muscular dystrophies, myotonic disorders and most congenital

myopathies in which muscle damage is evident but no pain is found". Lastly, whilst DOMS follows a similar time course as CK release in novel exercise there is no significant relationship between DOMS and CK release (Byrnes, Clarkson & Katch, 1985), rather the mechanism behind DOMS is thought to involve the accumulation of the histamine, kinins and potassium in the interstitium in the area of group IV un-myelinated afferent fibres (Armstrong, 1984).

Table 2.6

Some of the naturally occurring agents that activate or sensitise nociceptors.

Substance	Source	Enzyme involvement
1. Potassium	Damaged cells	
2. 5-HT	Platelets	Tryptophan hydroxylase
3. Bradykin	Plasma kininogen	Kallikrien
4. Histamine	Mast cells	
5. Prostaglandins	Arachidonic acid-damaged cells	Cyclo-oxygenase
6. Leukotrienes	Arachidonic acid-damaged cells	5-Lipoxygenase
7. Substance P	Primary afferent	

Substances 1 - 4 activates primary, and 5 - 7 sensitise primary afferent fibres

(Modified from Jessell & Kelly, 1991, p. 387).

2.3.7 <u>Morphological Changes & Time Course of Recovery.</u>
Morphology, a term which is sometime used synonymously with anatomy, is the study of the structure of living organisms (Martin, 1992). Whereas sub-cellular Z-band disruption is the major morphological change that occurs in skeletal muscle following eccentric exercise, no changes are evident after concentric exercise when the muscle is actively shortened (Newham, McPhail, Mills & Edwards, 1983).

A brief review of some research undertaken into human muscle damage follows. Friden, Sjostrom, Ekblom, (1981) conducted research into delayed onset muscle damage (DOMD) via electron microscopy and histology on muscle biopsies taken from human soleus 2 weeks prior to, and 2 & 7 days post an eccentrically-induced damage bout. They found no cellular level changes, determined by the absence of ischaemic fibre necrosis or fibre rupture. However, sub-cellular morphological changes were evidenced by frequent focal disturbances originating from Z-line disruption, being most evident 2 days post-exercise by a factor of 3 : 1 when compared to pre-damage and 7 day post-damage muscle biopsies. Later research (Newham, et al., 1983) showed that the Z-line disruption that occurs following eccentric exercise does not occur following concentric exercise, and unlike Friden et al., (1981), they concluded that sub-cellular damage continues to develop after 2 days post-damage and not during the exercise period as previously thought. Jones, Newham, Round, & Tolfree, (1986) conducted a morphological study into eccentrically-induced muscle damage with muscle biopsies being taken at a time when CK response was expected to peak (4 to 8 days post-damage), 14

days post-damage, and 20 days post-damage. The biopsies taken when CK was expected to be at its peak generally show little morphological changes, however the biopsies taken 14 days post-damage generally show small degenerating fibres, increased acid phosphatase activity, increased cellular infiltration, and regenerating fibres, with the Type 2 fibres being more severely affected than Type 1 fibres. The biopsy taken on day 20 showed muscle that was predominantly recovered or recovering. This led Jones et al., (1986) to conclude several things. Firstly, whilst CK is a marker for muscle damage it cannot be used to judge severity of damage as CK had returned to normal by approximately day 8 post-damage however the peak of myofibre damage had not been reached and would not occur until about day 14 post-damage. Secondly, cellular infiltration was seen as a response to damage and not the cause, with the increase in acid phosphatase activity indicating that macrophages make up the majority of infiltrators.

2.3.8 Conclusion.

High force exercise results in a degree of skeletal muscle damage. This damage is more evident from exercise involving eccentric contractions, and can be determined by various factors including: a) force characteristics; b) cellular enzyme efflux, c) DOMS, and d) morphology. Whilst damage is involved in altering each of these parameters, they do not follow the same time course of change, consequently causal relationships between any two parameters, such as CK release and DOMS cannot necessarily be drawn.

2.4 Methodological Rationale

Eccentric contractions result in the most noticeable damage to muscle (Ebbling & Clarkson, 1989) and thus are commonly used in studies of muscle damage and regeneration. The histological and immunocytological evidence suggests that eccentric damage is a useful research parallel to the immunological actions that occur in inflammatory myopathies (Jones, et al., 1986; Jones & Round, 1993) and which may occur with CFS. The use of 20 : 50 Hz tetanic stimulation will indicate the presence of damage at the EDF of the subjects, and thus provide evidence as to the state of the contractile properties of the muscle. Further, in conjunction with muscular force characteristics, biochemical indicators of gross damage, such as CK, LDH, AST and myoglobin, are used to determine that skeletal muscle damage has actually taken place (Atwell, McNaughton, Gorringe, and Kaufman, 1991). In this research serum CK alone was used as the biochemical determinant for the following reasons: a) The muscle specific isoenzyme CKMM represents 98% of all CKMM found in the body (Painter, Cope, & Smith, 1994); b) it is only this isoenzyme that will change as a result of skeletal muscle damage; c) it is the most common method used by other researchers, and; d) the other enzymes offer no other advantages. In conclusion, serum CK is consistently found to be within the normal range (Table 3) in persons diagnosed with PVFS (Edwards, et al., 1991), and is thought to be elevated in persons with OTS only as a result of acute training overload (Fry, et al., 1991b). It then follows that it is reasonable to utilise these factors, as any elevation of serum CK in the subjects will be as a result of eccentrically induced muscle damage, and the time taken

for CK to return to normal ranges will indicate the time course of the degenerative stage during the recovery from this damage.

2.5 Summary & Conclusion

CFS and OTS are complex and debilitating conditions that have many similar symptoms, in particular profound fatigue and myalgia. The similarities in symptoms has led many researchers (Eichner, 1990; Fitzgerald, 1991; Fry et al., 1991a, 1991b; Gross, 1992; Keast & Morton, 1992; Lehmann, et al., 1993; Parker, 1990; Parker & Brukner, 1994) to feel that OTS may be a sub-condition of CFS. The presence of myalgia in CFS that is unrelated to ongoing damage, unlike myalgia that occurs with inflammatory myopathies (Jones & Round, 1993), it is possible that damage and recovery characteristics of skeletal muscle in patients with CFS (including OTS) are affected by having a lower "threshold" to damage and thus may be damaged easier, and if the immune system is depressed may be slower to repair. Early diagnosis and knowledge of a muscular site of action in CFS and thus OTS increases the possibility of prevention in CFS/OTS and a further step in the elucidation of this disease, making a diagnosis more positive and enabling overtraining to be objectively discovered prior to its catastrophic phase.

2.6 Theoretical Framework

Through the use of eccentric muscle damage and by monitoring markers of the damage, such as intracellular proteins, force characteristics, and the time course of recovery, it is proposed that any differences in muscle regeneration dynamics between subjects with CFS/OTS and subjects without symptoms of CFS or OTS will

be defined. A diagrammatical representation of the theoretical framework of this thesis is shown in Figure 2.7.
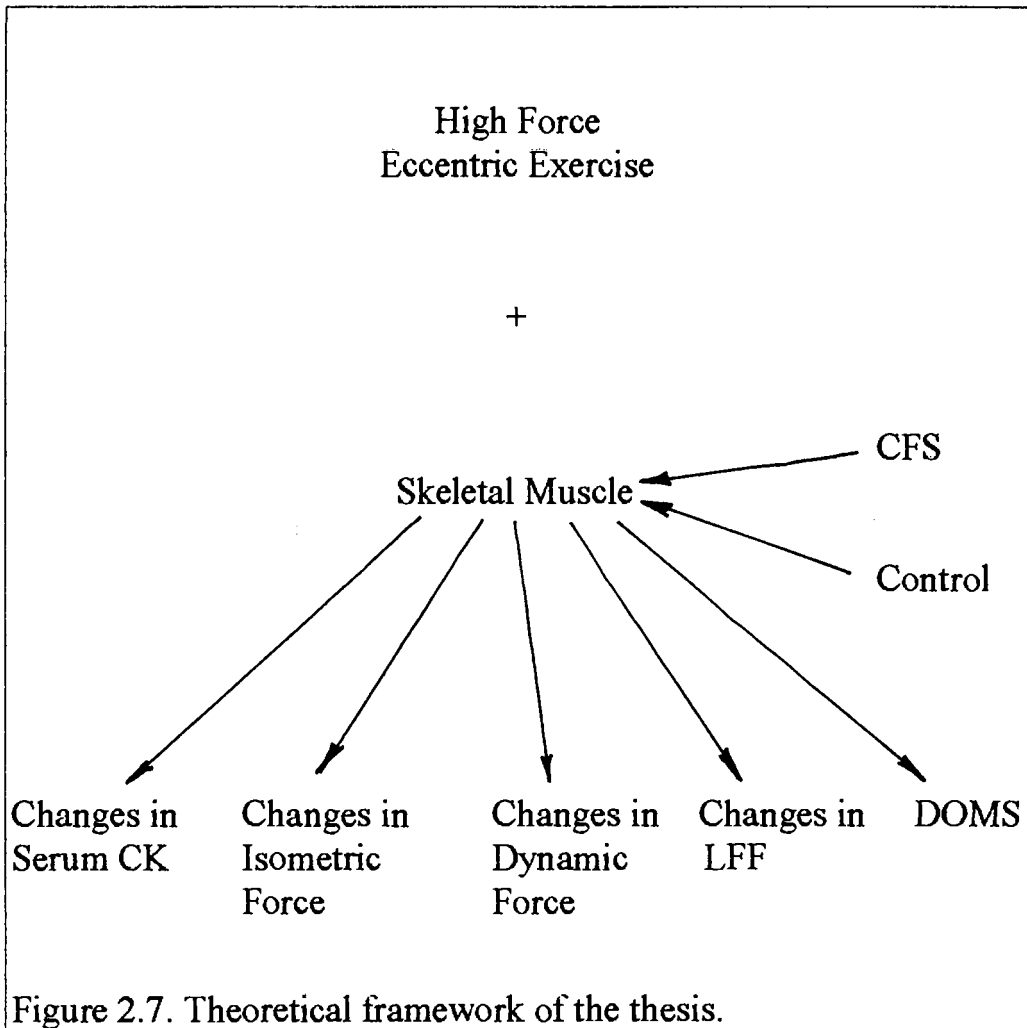
Figure 2.7. Theoretical framework of the thesis.

CHAPTER 3

METHODOLOGY

3.1 Design of the Study

The research utilises quasi-experimental design of an untreated control group with pre-test and post test (Burns and Grove, 1993). A diagrammatical representation of the design is shown in Table 3.1.

Table 3.1

Untreated control group with pre-test and post-test

Subjects	Pre-test	Intervention	Post-test	Number
1 - CFS patients	yes	damage	yes	n = 8
2 - Healthy Controls	yes	damage	yes	n = 10
3 - Healthy Controls	yes	control	yes	n = 7

3.2 Subject Sample

Recruitment of 25 subjects was undertaken. From these 25 subjects three experimental groups were formed of; Chronic Fatigue Syndrome (CFS) + eccentric damage n = 8, Control Damage (CD) + eccentric damage n = 10, and Control (ND) + no-damage n = 7, as shown in Table 3.1.

The subjects of the study were a convenience sample selected via responses from an advertisement (Appendix B) placed in the local press for volunteer subjects who had been diagnosed as suffering from CFS or PVFS, and from Edith Cowan University student and staff response to a flyer distribution (Appendix C). Though the subjects are a convenience sample, the subjects who volunteered for the control groups were randomly assigned to CD and ND groups.

Subjects that presented with CFS confirmed that they had been diagnosed with CFS, or as with CFS3 Fibromyalgia, by a General Practitioner (GP) or Specialist. In addition CFS subjects were requested to voluntarily complete an additional questionnaire (Appendix D) regarding their illness that provided information on: a) the longevity of their CFS; b) whether heavy bouts of exercise were implicated in their CFS; c) the presence or not of myalgia, and; d) what, if any medications were being taken by the subject, so that known effects of medications being taken could be accounted for.

3.3 Time Course of Data Collection

The commencement of data collection was staggered over a 7 week period. This was in line with subject response, and to allow sufficient time for each subject to attend on 11 occasions over the 4 week time course of the study . Consequently the time course of the data collection was a 11 week period with key dates shown below;

1.   4.10.94   commencement of pilot study

2.   11.10.94   commencement of actual study

3.   7.11.94   completion of pilot study

4.   12.12.94   completion of actual study

3.3.1 Pilot Study.

Due to the possibility of a hyper-immunological response following the eccentric damage bout in the patients with CFS, a pilot study was undertaken with a subject diagnosed with PVFS so as to establish what minimum, exercised caused, damage bout protocol was required. The damage bout of the pilot study consisted of 2 x 10, & 1 x 5 sets of maximal isokinetic eccentric contractions of the non-dominant forearm flexors at $90°\text{sec}^{-1}$, with the limb passively returning at a velocity of $15°\text{sec}^{-1}$, and a 1 minute rest break between each set giving a work-rest ratio of 1 : 4. The damage bout protocol for the main study was subsequently amended to 7 x 5 sets of maximal isokinetic eccentric contractions at $90°\text{sec}^{-1}$, with the limb passively returning at a velocity of $15°\text{sec}^{-1}$, and a 2 minute rest break between each set. The 1 : 4 work-rest ratio, with 2 minute rest breaks between sets, was adopted in order to minimise fatigue and enable the subjects to perform the isokinetic eccentric and concentric tests in a fatigue free state.

3.4 Instruments

The instruments used in data collection were as follows:

Cybex 6000 Isokinetic dynamometer (Cybex INC, N.Y.);

Force Chair and restraining straps;

   Tensiometer-strain gauge (fixed length);

   Goniometer;

Preacher bench (45°);

IBM Microprocessor;

Digitimer Stimulator DS7;

    Thandor 170C pulse generator;

    Tubigrip bandage;

    Carbon compound electrode pads (3 x 6 cm);

    Electrode gel;

Spectrophotometer (Reflotron);

    Isotonic saline;

    Eppendorf 5 ml tubes;

    Micro pipette;

    Medi swabs;

    Cotton wool balls;

    CK reagent carrier strips;

Data test sheet;

Pain proforma; and

CFS information questionnaire.

3.4.1 Instrument Reliability.

Prior and post all of the testing sessions conducted over the 4 week period of the research, all instruments in use, where necessary (ie Cybex, tensiometer, spectrophotometer), were calibrated for measurement. The calibration for the Cybex and spectrophotometer involved internal systems, whereas the tensiometer required manual calibration. Procedures and results of the tensiometer calibration are shown in Appendix E.

The Cybex 6000 (Cybex, INC, N.Y.) is software driven and has a published system error of < 1% for force, angle and angular velocity. Research on previous models (Sapega, Nicholas, Sokolow, & Saraniti, 1982) has shown Cybex error to be ± 1% at full scale

(488Nm). Measurement of each muscular contraction on the Cybex should be fatigue free and exhibit a coefficient of variance of < 5% between repeated measurements. The subjects were seated on the preachers bench and located adjacent to the Cybex in the same position for every testing session by recording, and emulating subject position at pre-test, positioning being the major cause of error in isokinetic dynamometry.

The force chair and tensiometer (strain gauge) were used to obtain maximal isometric forces and percutaneous isometric tetanic stimulation ratios. The subject was secured in the force chair in the same position for each test, this was achieved by recording the subject position at pre-test and ensuring that same positioning for all subsequent tests. The strain gauge was calibrated on a weekly basis, with an error of < 1% (Appendix E).

Dual plasma CK levels were measured on a Reflotron spectrophotometer (Boehringer & Mannheim) calibrated by reagent strip and with a published accuracy of ± 5% within a range of ; 9.8 - ca. 600 International Units/Litre (U/l) (25°C), 15.1 - ca. 900 U/l (30°C), 24 - ca. 1400 U/l (37°C). For [CK] >1400 U/l serial dilution with isotonic saline are required, where $A = XA_M$ [A_M = measured activity; A = plasma activity; and X = dilution factor].

3.4.2 Instrument Validity.

The validity of isokinetic dynamometry conducted in vivo is reduced due to activation of stabilising muscles, the use of a preachers bench will help to isolate the forearm flexors (see Figure

3.3) to some extent and the results will be as valid as possible with peak torque, total and peak work being least affected (Kannus, 1994).

The subject was restrained in the force chair (Figure 3.1) with sideways movement reduced as much as possible, though as with Cybex some stabilising musculature would be activated. The strain gauge which is of full bridge manufacture with dual 4 x 120 ohm resistance, was calibrated on a weekly basis with known weights and returned a error of < 1%.

CK activity falls in serum stored at; + 4°C : 2% after 7 days, +25° C : 2% after 24 hours. Chemical reagents on the carrier strip used to quantify CK levels are specific to all CK's (Braun, H., P., Deneke, U., & Rittersdorf, W. 1987).

3.5 Testing Protocols
3.5.1 Training.
To avoid any anomalies due to an unawareness of expectations, prior to testing all the subjects (control & experimental) were familiarised with the equipment and procedures used in the research.

3.5.2 Serum Creatine Kinase.
Plasma CK concentration was established as follows: a) 30 µL mixed venous blood samples were taken following lancet finger prick from the index finger of the non-dominant hand, in accordance with the protocols for taking blood samples outlined by Minikin, (1991). b) The blood was then placed on to the red zone

of the reagent strip, ensuring that the pipette did not touch the reagent strip. c) The reagent strip was then placed into the spectrophotometer for analysis (Appendix A for assay protocol). d) As the need arose (CK > 1500 UI/L) the spectrophotometer would return a Dilute message, in this case a fresh sample of blood was then taken and serial diluted with a set quantity of isotonic saline with a zero concentration of CK, 30 μL samples of the diluted mixture was then placed on to the red zone of the reagent strip, again ensuring that the pipette did not touch the reagent strip. This whole process, including serial dilution as required was completed in less than 3 minutes per test.

3.5.3 Isometric Strength.

Isometric strength of the non-dominant forearm flexors, as measured by peak force was determined by 1 isometric MVC of 5 seconds duration (Sale, 1991) as follows: a) The non-dominant arm was held in the sagittal plane, with approximately 90° of flexion at the elbow with the humerus held horizontally. The angle of flexion of the elbow was then measured by goniometer and recorded onto a test-sheet (Appendix F) so as to enable subsequent isometric MVC's testing to be undertaken at the same degree of flexion as at pre-test. b) A fixed length tensiometer was attached to the wrist (distal styloids), and a pre-set weight was placed at the same site so as to remove any slack from the tensiometer (see Figure 3.1). c) The subjects completed isometric MVC's and peak forces were measured from a strain gauge force transducer utilising an analog to digital converter in an IBM PC and using a Status-30 (Version 2.07) computer software package, results were then

recorded and transposed onto test sheet as well as Excel 5 spreadsheet for later analysis.
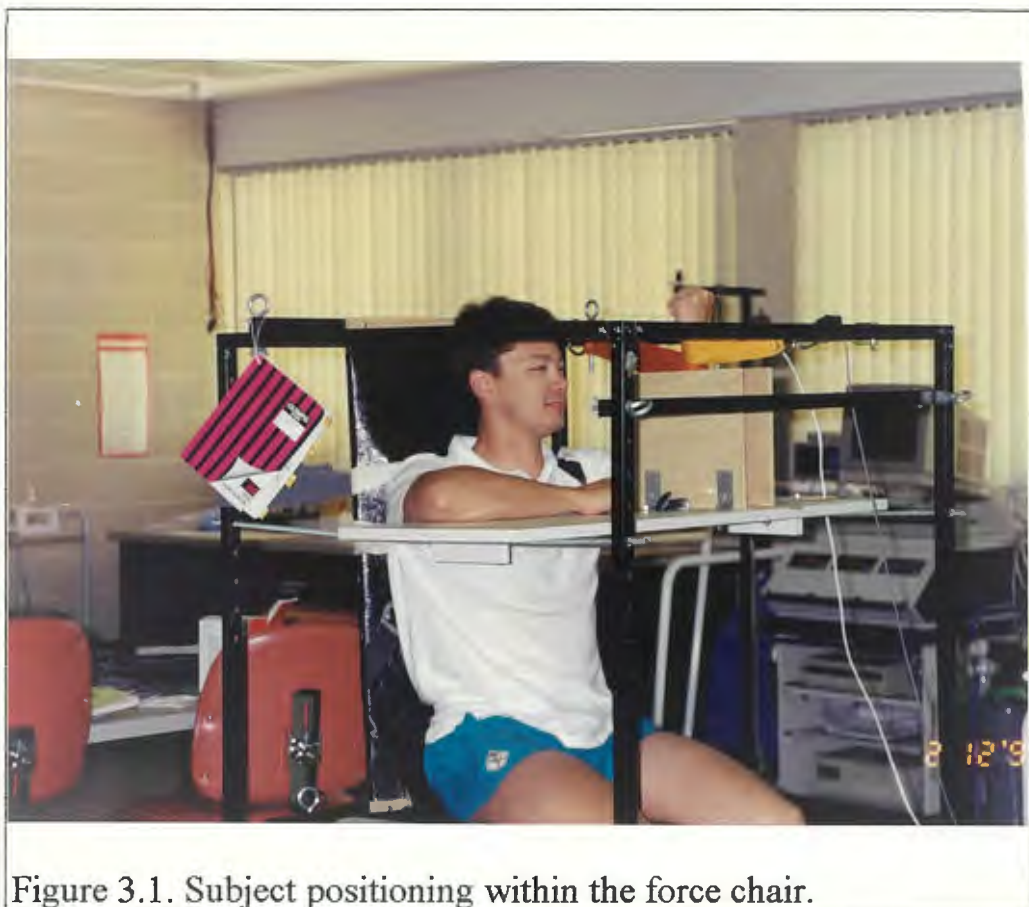
Figure 3.1. Subject positioning within the force chair.

3.5.4 Low Frequency Fatigue.

Low frequency fatigue (20 : 50Hz ratio) of the biceps brachii was measured with the subject sitting in the force chair (see section 3.5.3). This was carried out at the same general time that the isometric forces were tested and was determined by carrying out 4 tetanic stimulated isometric contractions at each frequency (4 x 20Hz, 4 x 50Hz). The frequency of stimulation was controlled by a Thandor 170C pulse generator. The stimulating pulses were produced by a Digitimer Stimulator (DS7), with a pulse width set at 50 microseconds. The intramuscular nerves were percutaneously

stimulated by 2 carbon compound electrodes (3 x 6 cm), smeared with electrode gel and then placed across the muscle belly, and held in place by a length of tubigrip (Figure 3.2).

Figure 3.2. Positioning of electrodes for 20:50 Hz stimulation

Prior to the 20 : 50 Hz stimulation, amperage threshold that the subject could endure was established as follows: a) 1 Hz twitches were given, every 5 seconds with the amperage being increased by 25/1000 of an amp each twitch. b) The current was increased until the subject indicated that the discomfort was barely tolerable. c) At this time the amperage was reduced by 50% and 20 : 50 Hz percutaneous stimulations were given and the subject questioned as to the comfort level of the stimulation. d) Trial 20 : 50 Hz stimulations were then given to the subject with the level of

amperage being increased by 25/1000th of an amp per test until the subject indicated the level of maximal tolerance. e) For percutaneous stimulation to be effective at least 10% and preferably 30% of the isometric MVC was required. f) The pre-test amperage level was used during subsequent testing, though it was found with a majority of CFS subjects that additional amperage was required to elicit sufficient muscle contraction (see Chapter 4 on results).

3.5.5 Isokinetic Concentric Force.

Dynamic forces measured were; isokinetic concentric peak torque (PT) in Newton metres (Nm) that was reached in any of the 3 MVC's, and average peak torque (AT) in Nm, of the 3 x 1 sets of MVC's (Sale, 1991). Measurements were taken from the 3 isokinetic concentric MVC's of the forearm flexors at an angular velocity of $150°sec^{-1}$ using Cybex 6000 as follows:

a) With the shoulder fixed at 45° flexion by utilisation of the preacher bench, the dynamometer axle was positioned at the centre of rotation of the elbow, and the lever arm attached to the wrist (distal styloids).

b) Three (3) concentric MVC's were made through a range of motion (ROM) of 130° at an angular velocity of $150°sec^{-1}$ (Figure 3.3) c) All force signals were raw signals, digitised and recorded in "real time" onto an IBM PC.
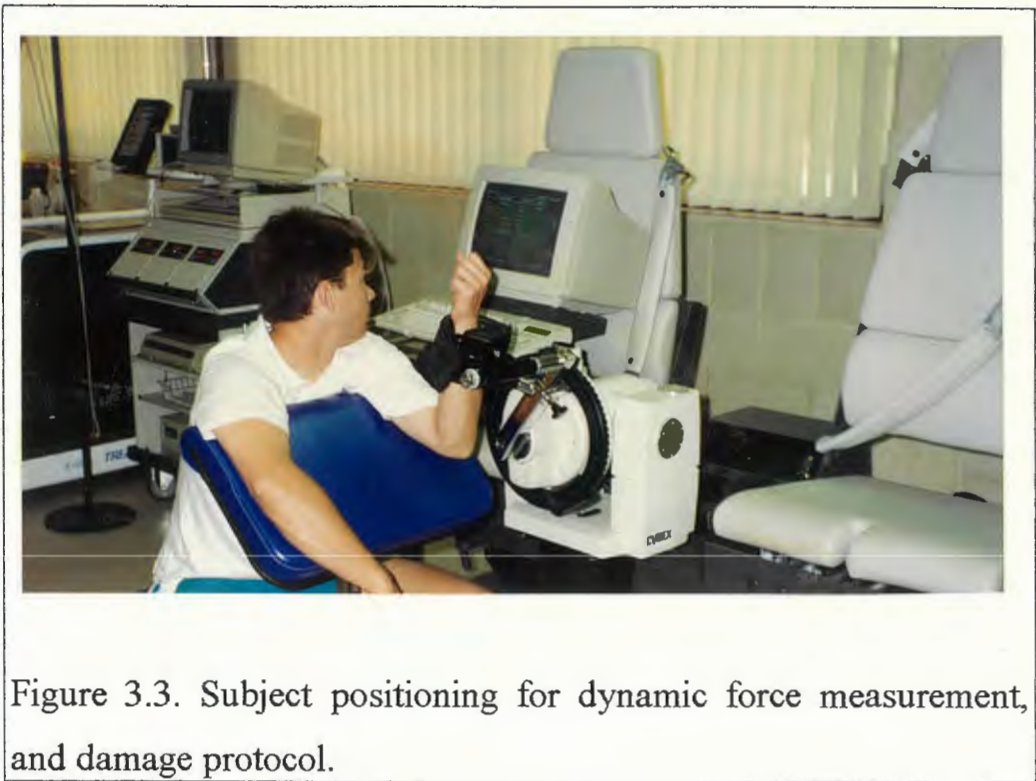
Figure 3.3. Subject positioning for dynamic force measurement, and damage protocol.

3.5.6 Delayed Onset Muscle Soreness (DOMS).

Pain was determined by palpation of the damaged biceps brachii with a 0 - 10 response as to the subjective level of pain being given by the subject, with 0 = no pain, and 10 = very, very painful. The location of the pain was recorded onto a grid proforma (Appendix G) and the response recorded onto Excel 5 spreadsheet.

3.5.7 Damage Protocol.

After 5 minutes to allow for recovery from any fatigue that may have occurred as a result on isometric and concentric tests, subjects from the CFS and CD groups underwent muscle damage by completing 35 maximal voluntary isokinetic eccentric contractions, at $90°sec^{-1}$. To minimise fatigue and enable subjects to consistently produce high forces the limb was passively returned at a velocity of $15°sec^{-1}$, giving a work-rest ratio of 1 : 4, and the contractions were

divided into 7 sets of 5 with a 2 minute recovery between sets (Figure 3.3).

3.5.8 Testing Schedule.

Measurements of force were conducted pre-damage and on day + 1, + 2, + 4, + 6, + 8, + 12 and then every four days for 4 weeks. LFF and Pain were measured at every testing session until they had returned to base line (approximated in Figure 3.4), and again at post-test 28 days post-damage. Serum CK was measured at every testing session. The majority of subjects had not fully recovered isometric or dynamic forces by the scheduled end of data collection, and some isometric and dynamic force data was collected after this point. This is discussed at length in Chapters 4 & 5.

	Pre-Test	+1	+2	+4	+6	+8	+12	+16	+20	+24	+28
CK	*	*	*	*	*	*	*	*	*	*	*
Pain	*	*	*	*	*	*					
LFF	*	*	*	*	*	*	*	*	*		*
Isometric Forces	*			*		*	*	*	*	*	*
Dynamic Forces	*			*		*	*	*	*	*	*
Eccentric Forces	*										

Figure 3.4: Testing schedule matrix

3.6 Data Analysis

For convenience the hypotheses being tested are reproduced below.

1. After damage, the muscle force characteristics of subjects with CFS will be different from the CD group.

2. After damage, the contractile properties of skeletal muscle as determined by the level of low frequency fatigue, will differ in subjects with CFS when compared to the CD group

3. The time course of serum CK efflux, and the serum CK concentration in subjects with CFS will be different from the CD group.

4. The time course of delayed onset muscle soreness (DOMS) during recovery in subjects with CFS will be different from the CD group.

5. The degree of DOMS in subjects with CFS will be different from the CD group.

Data analysis was conducted using Statistical Package for Social Sciences (SPSS) for Windows Version 6.0. Hypothesis 1, 2 & part of 3 were analysed by repeated measures two way analysis of variance (ANOVA) with group x time interactions used to detect any significant difference between the groups and their response over time. Simple contrasts were used if results were significant. Part of hypothesis 3 and hypothesis 4 & 5 were analysed by Students independent t-test. In all cases the probability level at which significance difference was accepted was set to < 0.05. Throughout the time course of the data collection, either due to illness of subjects or instrument malfunction, some data points were missed. Subsequent procedures of using prior knowledge or

mean values for the treatment of missing data points were adopted (Tabachnick & Fidell, 1989). All raw data is shown in Appendix H. Results are described in text quoting p values only, F values and full statistical findings are shown in Appendix K.

3.7 Limitations

1. The level of muscle pain is subjective.
2. Due to repeated testing it is possible that some training effect may occur.
3. The presence of neuropsychiatric dysfunction, and prescribed drugs in CFS subjects may result in less than maximal efforts in the testing and damage sessions.
4. Total CK is measured, not CKMM specifically.

3.8 Assumptions

1. The subjects diagnosed as suffering from CFS, actually have CFS.
2. The subjects will perform the eccentric, isometric and concentric tests to the best of their ability.
3. That the subjects will not alter their levels of activity throughout the period of data collection.
4. That changes in total CK will predominantly come from skeletal muscle.

3.9 Ethical Considerations

In healthy people the damage that occurs to muscle as a result of exercise is a fact of life. On every occasion a muscle is contracted it is likely that some micro-damage occurs. In this study the subjects

perceived damage as delayed onset muscle soreness (DOMS), the details of which is covered in Chapter 4 & 5.

This study attempts to ascertain the time course of recovery from experimentally induced muscle damage in people diagnosed with CFS by measuring force and pain. The subjects were able to withdraw from the study at any time without prejudice. All of the CFS subjects completed an additional questionnaire regarding their illness (Appendix D). The University policy for the conduct of ethical research involving humans (Committee for the Conduct of Ethical Research, 1994) was strictly adhered to and all of the subjects were made fully aware of any potential risks involved in the study, and informed consent (Appendix I) was obtained. The names and addresses of the subjects were kept confidential, with subjects only being identified by subject number, with master list and control sheets kept under lock and key by the principal investigators.

CHAPTER 4

RESULTS

4.1 Physiological Data

The physiological aspects of subjects from the three groups are as follows, Chronic Fatigue Syndrome (CFS) + eccentric damage (Table 4.1), Control Damage (CD) + eccentric damage (Table 4.2) and Control (ND) + no-damage) (Table 4.3).

Table 4.1

Physiological parameters of subjects diagnosed with CFS (n = 8).

Subject	Age	Gender	Mass (Kg)	Height (cm)	Race	Diagnosed	Iso. MVC (N)
CFS1	29.5	Male	63.9	169	Cauc.	1993	165
CFS2	48.6	Male	65.6	168	Cauc.	1992	214
*CFS3	48.2	Female	130.0	155	Cauc.	1987	222
CFS4	41.8	Male	89.0	179	Cauc.	1993	329
CFS5	36.8	Female	48.7	157	Cauc.	1994	174
CFS6	16.4	Female	62.0	166	Cauc.	1991	175
CFS7	45.1	Female	59.6	161	Cauc.	1986	189
CFS8	24.0	Male	79.0	193	Cauc.	1993	237
Mean	36.3		74.7	168.4			213
± SD	11.9		25.5	12.3			53

* Subject diagnosed with fibromyalgia

4.1.1 Additional Data CFS Subjects.

Of the 8 CFS subjects, 2 (CFS2 & CFS5) indicated that they regularly underwent heavy training bouts, with CFS2 training and participating in marathons, and CFS3 training for triathalons. Due to the high volumes of training known to occur in these sports, overtraining cannot be discarded from an involvement in the pathogenesis of CFS in these two subjects. CFS3 also indicated a overtraining diagnosis in the additional questionnaire completed, however due to the physiological make up of the individual, the presence of the "Modern" or parasympathetic form of OTS is questionable.

Six of the subjects were taking some form of supplement with multivitamin, iron, calcium, vitamin C and glutamine supplements being taken. Three subjects were under current prescription medications: a) CFS2 Keflex, antibiotic for a urinary tract infection (UTI); b) CFS4 Anatranil, anti-depressant, and; c) CFS7 Aropax 20, microgynon 50.

Five of the subjects (CFS1, CFS2, CFS3, CFS4, & CFS7) indicated that they do suffer from CFS induced myalgia in the limbs from time to time but all indicated that at the time of undergoing the eccentrically-induced damage bout none of these subjects was suffering from the effects of myalgia in the upper limbs.

Table 4.2

Physiological parameters of CD subjects (n = 10).

Subject	Age	Gender	Mass (Kg)	Height (cm)	Race	Iso. MVC (N)
CD1	21.3	Female	58.7	162	Cauc.	220
CD2	26.3	Male	82.2	188	Cauc.	282
CD3	29.8	Male	81.6	184	Cauc.	368
CD4	27.3	Female	60.7	163	Cauc.	229
CD5	24.8	Female	56.2	159	Cauc.	210
CD6	19.4	Female	61.3	170	Cauc.	146
CD7	31.8	Male	71.6	176	Cauc.	243
CD8	19.0	Male	95.0	185	Cauc.	305
CD9	37.3	Female	57.8	166	Cauc.	236
CD10	35.3	Male	83.3	171	Cauc.	302
Mean	27.2		70.8	172.4		254
± SD	6.4		13.8	10.4		62

Table 4.3

Physiological parameters of ND subjects (n = 7).

Subject	Age	Gender	Mass (Kg)	Height (cm)	Race	Iso MVC (N)
ND1	35.4	Female	52.8	163	Cauc.	187
ND2	26.0	Female	65.4	178	Cauc.	207
ND3	30.6	Male	66.5	170	Cauc.	312
ND4	22.3	Male	67.3	177	Cauc.	367
ND5	22.2	Female	53.7	162	Asian	207
ND6	23.5	Male	81.6	185	Cauc.	329
ND7	25.5	Male	73.3	176	Asian	287
Mean	26.5		65.8	173.0		271
± SD	4.9		10.2	8.4		70

4.2 Data Exclusion

Of the 25 subjects, all data was excluded from analysis for 3 subjects (CFS1, CFS3, & ND2) and partial data from 2 subjects (CFS5 & CD9) for the following reasons.

Subject CFS1 took part in the pilot study and as such received a different damage protocol. Consequently analysis of any data obtained from this subjects would be inappropriate. Subject CFS3 presented with fibromyalgia, and though individuals with fibromyalgia are considered to be no more susceptible to eccentrically induced muscle damage than are healthy people

(Jubrias, Bennett, & Klug, 1994), this disease has many shared symptoms with CFS including myalgia and fatigue, and is so similar that is considered to overlap with CFS (Goldenberg, 1994). As a consequence of the similarities of CFS to fibromyalgia this subject was subsequently accepted for the study, however, CFS3 failed to damage following eccentric bout, as illustrated by CK and force analysis. Serum CK did not exceed 86.1 (UI/L) throughout the time course of the study, and isometric force which although reduced to 93.5% of pre-test values 4 days post damage, reached 113.5% of pre-test values by 8 days post damage. ND2 failed to attend for any sessions after pre-test.

CFS5 & CD9 both withdrew from the study due to illness 16 days post damage, far enough advanced to have returned to base line in LFF, DOMS and CK, though dynamic and isometric forces had not. Consequently, CK, DOMS and LFF were used in data analysis and force data excluded.

4.3 Isokinetic Eccentric Torque

Though not strictly a post damage test, it became evident during data collection that the level of eccentric torque produced by the CFS group reduced at a faster rate, and reduced further, than the control-damage group. This was evidenced by the CFS group torque output declining to 59.1% ($\pm$ 1.8% SEM) in the 7th set of the mean fresh value (1st set), compared to a mean 84.8% ($\pm$ 3.5% SEM) in the 7th set in the CD group (Figure 4.1). Data was normalised to minimise individual variance and analysed by Students independent t-test. The results revealed a significant difference between the CFS and CD groups during the 3rd through

to the 7th set of eccentric contractions, with p < 0.05 in the 3rd set and p < 0.001 in the 4th to the 7th sets.

a)
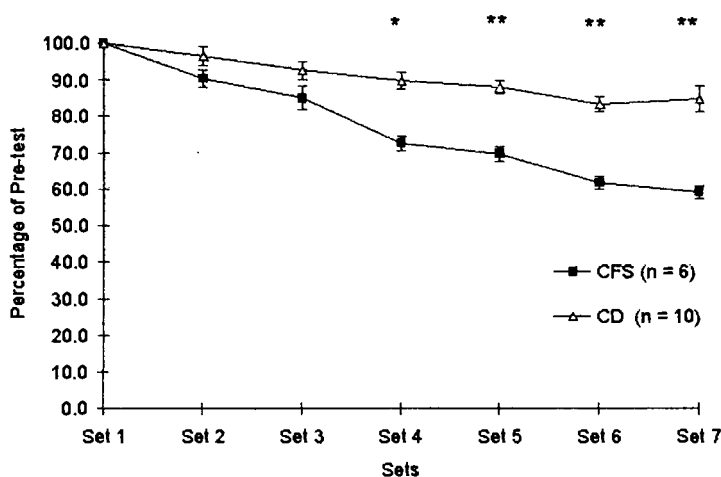
b)
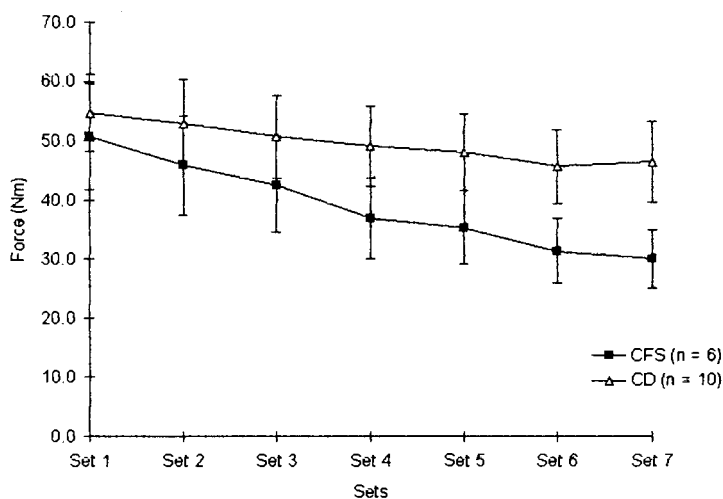
Figure 4.1. a) Isokinetic eccentric torque (normalised to pre-test) produced during damage bout, 7 sets of 5 maximal contractions at $90°/\text{sec}^{-1}$. Values (means ± SEM) are expressed in percentages of pre-test. Significant difference between CFS and CD groups $p < 0.05$ (3rd set), $p < 0.001$ (4-7th sets). b) Isometric eccentric torque (NM) raw data. Values (means ± SEM) are expressed in NM.

* Indicates significant $p < 0.05$
** Indicates significant $P < 0.001$

4.4 Serum Creatine Kinase

Hypothesis 3 proposed that the time course of CK efflux and the concentration of serum CK would be different between the CFS and CD groups. This hypothesis was partially satisfied, in that, the serum CK concentration was significantly different, whilst the time course for CK efflux did not differ. Serum creatine kinase efflux peaked in the CFS & CD groups 4 days post damage with a peak mean of $8388 \pm$ SEM 1224 (UI/L) in the CFS group and a peak mean of $2583 \pm$ SEM 753 (UI/L) in the CD group. As expected the ND group serum CK levels remained constant. Serum CK levels began to diminish after day 4, returning to normal levels in the CFS & CD groups by 12 days post-damage.
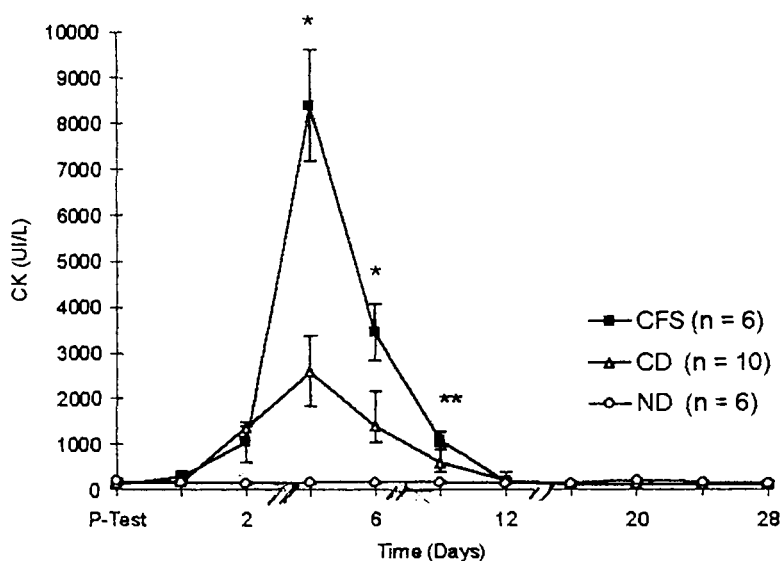
Figure 4.2. Serum creatine kinase values over the time course of the study. Values (means $\pm$ SEM) are expressed in UI/L. Between subjects effects, significant difference between CFS and CD groups $p < 0.01$, CFS and ND groups, $p < 0.001$,

* Indicates a significant difference between CFS and CD, as well as CFS and ND groups.
** Indicates a significant difference between CFS and ND groups.

Following eccentric damage, serum CK was significantly higher in the CFS group (Figure 4.2) when compared to both control groups ($p < 0.001$), with simple comparison showing significant difference between CFS and CD groups ($p < 0.01$), CFS and ND groups ($p < 0.001$). Within subject events with time as main the effect ($p < 0.001$), and interaction ($p < 0.001$). There was no significant difference in the time course of CK efflux between the CFS and CD groups (Figure 4.3).
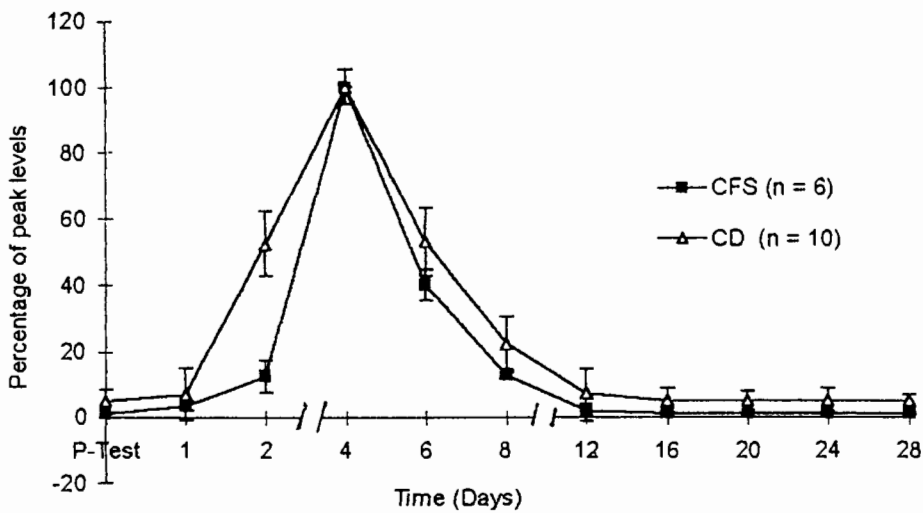
Figure 4.3. Time course of serum CK efflux, following eccentric damage bout, normalised to peak values. Values (means ± SEM) are expressed in percentages of peak values. NS between CFS and CD groups.

4.5 Low Frequency Fatigue (LFF)

Hypothesis 2 which proposed that, after damage, the level of LFF would differ, between the CFS and CD groups, was fully satisfied. The ratio of CFS group (immediately after the damage bout) fell to 25.8% (± 11.8% SEM) of pre-test values compared to 38% (± 9.2% SEM) for CD and 90.6% (± 3.7% SEM) for the ND group (who had only completed the concentric protocols). Refer to Figures 4.4 & 4.5.
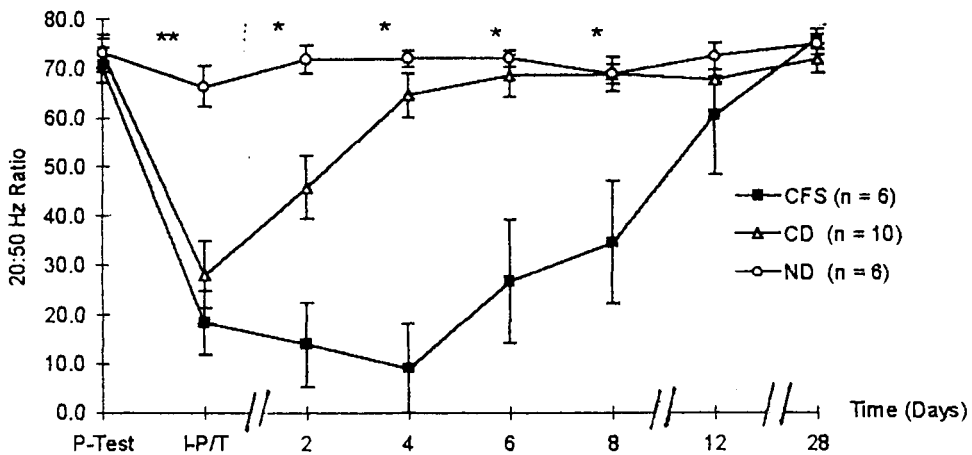
Figure 4.4. Low frequency fatigue, 20 : 50 Hz ratios from biceps brachii. Values (mean ± SEM) are expressed in 20:50 Hz ratios. Between subjects effects, significant difference between CFS and CD groups, $p < 0.001$, CFS and ND groups $p < 0.001$, interaction $p < 0.001$.

* Indicates a significant difference between CFS and CD, as well as CFS and ND groups.
** Indicates a significant difference between CFS and ND groups.
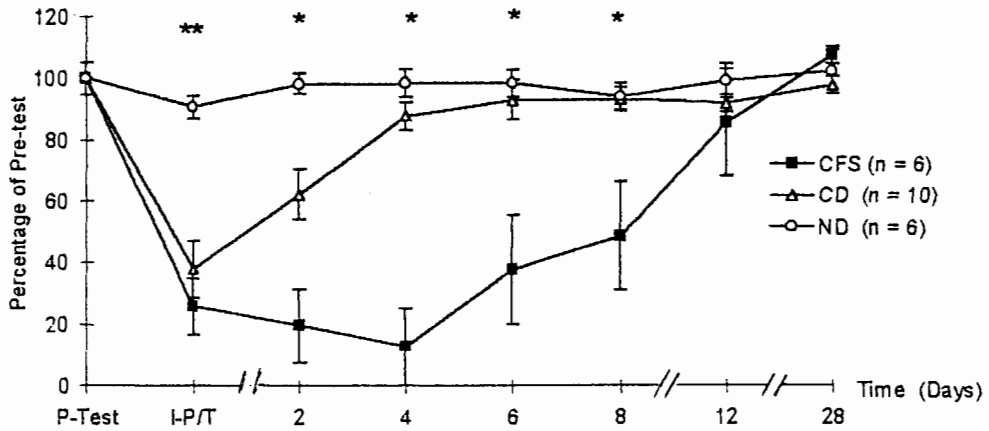
Figure 4.5. Normalised low frequency fatigue, 20 : 50 Hz ratios from biceps brachii. Values (mean ± SEM) are expressed in percentages of initial values. Between subjects effects, significant difference between CFS and CD groups, $p < 0.001$, CFS and ND groups $p < 0.001$, interaction $p < 0.001$.

* Indicates a significant difference between CFS and CD, as well as CFS and ND groups.
** Indicates a significant difference between CFS and ND groups.

The CD group began recovery after 1 day with an increase to 62.3% (± 8.2% SEM) of pre-test values 2 days post damage, which continued to rise to 87.8% (± 4.4% SEM) 4 days post-damage, 93.0% (± 6.4% SEM) 6 days post-damage, from this time the 20 : 50 Hz ratio remained relatively constant during remaining tests (8 & 12 days post damage) with a ratio of 97.8% (± 2.9% SEM) 28 days post damage. Conversely the CFS group ratio continued to fall with 19.5% (± 14.2% SEM) of pre-test values 2 days post-damage,

12.7% (± 17.0% SEM) 4 days post damage, followed then by a gradual rise till a ratio of 85.6% (± 18.8% SEM) of pre-test values being reached 12 days post-damage, increasing to 107.5% (± 3.8% SEM) 28 days post damage. For an illustration of this reduced 20:50 ratio in CFS subjects compared to CD subjects refer to Figures 4.6 & 4.7. Further examples showing 20:50 Hz ratio of 2 x CFS, 2 x CD, 1 x ND subjects, over the time course of the research, are shown in Appendix J.

It was necessary to increase the amperage of some subjects, post-damage, to elicit sufficient contractile response, particularly in the CFS group where 5 of the 6 subjects required increased levels of stimulation compared to 1 of 10 subjects in the CD group.

The LFF ratio (Figure 4.4 & 4.5) was significantly lower in the CFS group when compared to a control group ($p < 0.001$). With a simple comparison showing significant difference between CFS and CD groups ($p < 0.001$), and CFS and ND groups ($p < 0.001$). Within subject analysis whereby time was the main effect ($p < 0.001$), and interaction ($p < 0.001$). Data was analysed on mean figures (Figure 4.4), and normalised for presentation (Figure 4.5).
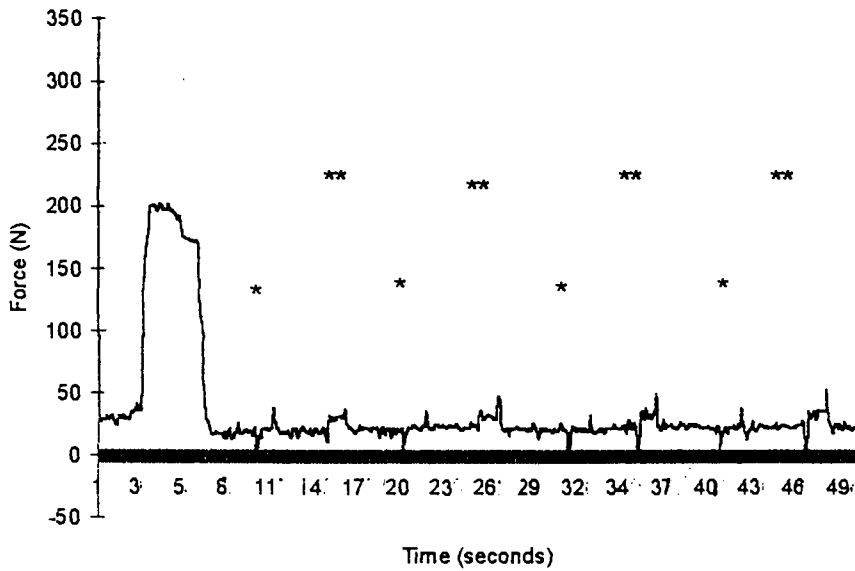
Figure 4.6. Isometric MVC and 20 Hz and 50 Hz percutaneous stimulation trace of CFS subject 8 days post damage, stimulation was given at 400 volts, square wave with 50 ms pulse width, at 0.650 amps.

* indicates 20Hz stimulations
** indicates 50Hz stimulations
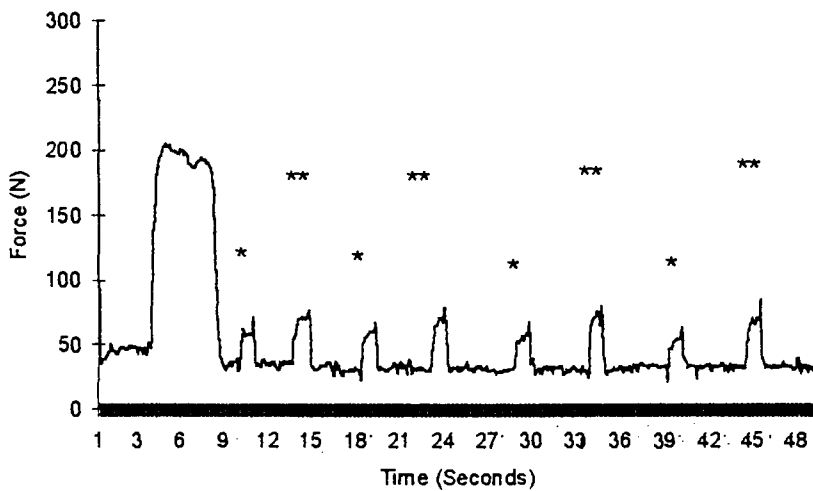
Figure 4.7. Isometric MVC and 20 Hz and 50 Hz percutaneous stimulation trace of CD subject 8 days post damage, stimulation was given at 400 volts, square wave with 50 ms pulse width, at 0.275 amps.

* indicates 20Hz stimulations
** indicates 50Hz stimulations

4.6 Isometric and Isokinetic Concentric Force

Hypothesis 1 which proposed that, following damage, the muscle force characteristics of CFS subjects would differ from the CD group, was tested by isometric and isokinetic concentric force measurements, and was fully supported by the results. Prior to analysis measurements were normalised so as to minimise individual variance and gender differences.

4.6.1 Isometric Force.

Isometric forces in the CFS group fell to 57.7% (± 4.1% SEM) of pre-test values 4 days post-damage compared to 82.4% (± 3.0% SEM) in the CD group and 97.9% (± 4.3% SEM) of the ND group. By 28 days the CFS group had recovered to 86.7% (± 3.7% SEM), the CD group 96.1% (± 2.9% SEM) of pre-test values, and the ND damage group exhibited 104.9% (± 6.3% SEM) of pre-test values (Table 4.4).

Two subjects from the ND group (ND4 & ND6) were at the time of the study undergoing upper body strength training, which in conjunction with any learning curve on the apparatus may account for the increase in isometric force to above pre-test values from 8 days after pre-test. Similarly the strongest subject from the CD group (CD3) in post-test isometric MVC reached 88.5% of pre-test values, after peaking at 96.2% of pre-test values 12 days post-damage. As this subject ceased previously undertaken upper body strength training two weeks after the pre-test damage bout, the resulting decrements in isometric MVC would not be accounted for by the damage bout alone.

The isometric force, following eccentric damage was significantly lower in the CFS group (Figure 4.8), when compared to a control group ($p < 0.001$), with simple comparison showing a significant difference between CFS and CD groups ($p < 0.01$) and CFS and ND groups ($p < 0.001$). Within subject effect with time as major effect ($p < 0.001$), and interaction ($p < 0.001$). The raw data (Appendix H) has been normalised for presentation (Figure 4.8). Refer also to Table 4.4 for a percentage summary of dynamic and isometric force attained over the time course of data collection.
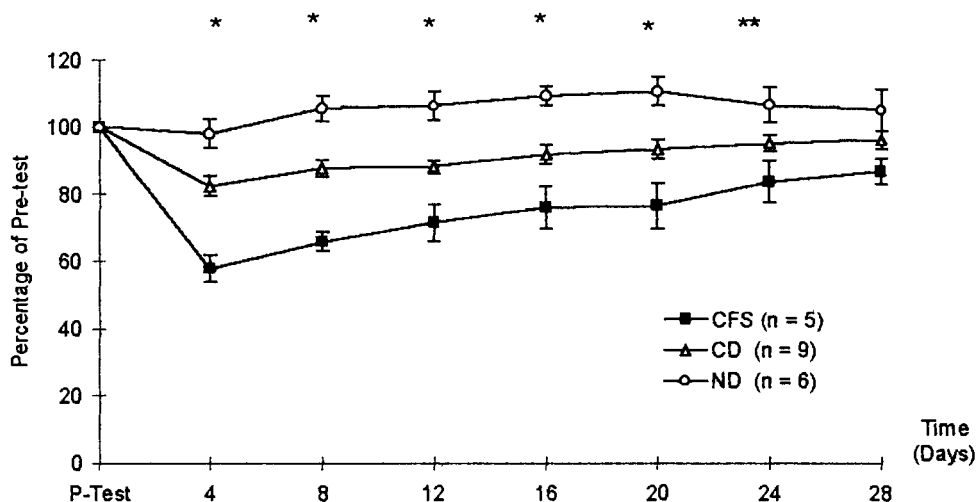
Figure 4.8. Normalised isometric MVC's of forearm flexors at approx 90° elbow flexion, pre-damage and then every 4 days for 28 days following eccentrically induced damage. Values (means ± SEM) are expressed in percentages of pre-test. Between subjects effects, significant difference between CFS and CD groups $p < 0.01$, CFS and ND groups $p < 0.001$. Within subject effects, whereby time was main effect $p < 0.001$, interaction $p < 0.001$.

* Indicates a significant difference between CFS and CD, as well as CFS and ND groups.

** Indicates a significant difference between CFS and ND groups.

4.6.2 Isokinetic Concentric Force

Concentric force measurements, which were determined by using parameters of the non angle specific peak torque (PT) with average torque representing an average of the PT reached in all three sets. Results of these measurements are in the form of normalised pre-test values and individually discussed in sub-sections 4.6.2.1 and 4.6.2.2. The matters raised about subjects ND4, ND6, & CD3 in chapter 4.6.1 should also be considered when interpreting isokinetic concentric force results.

4.6.2.1   Peak Torque (PT).

PT values of the CFS group reduced to 53.9% (± 6.9% SEM) 4 days post-damage, continued to fall to 53.3% (± 7.7% SEM) 8 days post damage with a further drop to 52.1% (± 6.7% SEM) of pre-test values 12 days post-damage. PT slowly recovered after this point to 77.9% (± 6.7% SEM) of pre-test values at the end of data collection 28 days post-damage. On the other hand PT of the CD group reduced to 79.2% (± 3.7% SEM) 4 days post-damage (it is worth noting that CFS group only attained this approximate value at post-test) then slowly recovered to 89.3% (± 1.5% SEM) of pre-test values at post-test 28 days later. PT of the ND group maintained ± 4.2% of pre-test values (Table 4.4 & Figure 4.9).

PT, following eccentric damage was significantly lower in the CFS group (Figure 4.9), when compared to a control group ($p < 0.001$), with simple comparison showing a significant difference between CFS and CD groups ($p < 0.01$) and CFS and ND groups ($p < 0.001$). Within subject effect with time as major effect ($p < 0.001$), and interaction ($p < 0.001$). The raw data (Appendix H) has been

normalised for presentation (Figure 4.9). Refer also to Table 4.4 for a percentage summary of dynamic and isometric force attained over the time course of data collection.
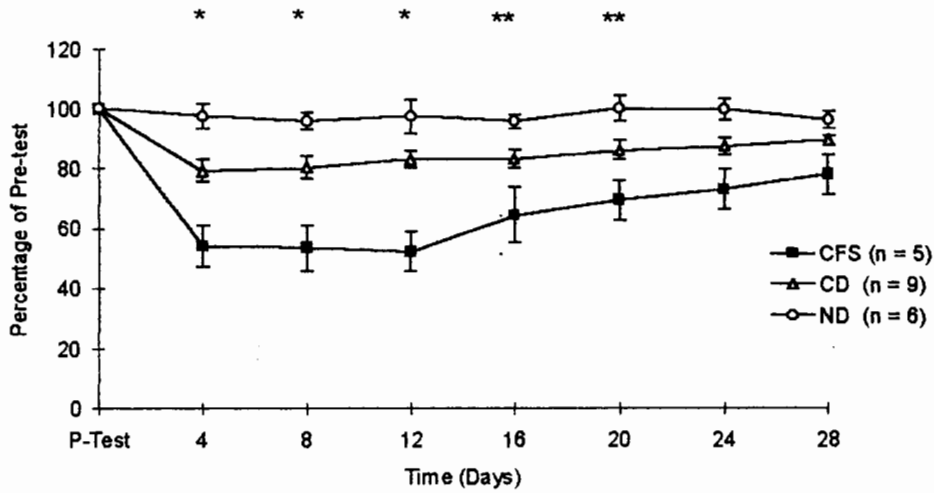
Figure 4.9. Normalised isokinetic concentric peak torque that was attained in the 3x1 contractions at $150°$ /sec $^{-1}$ measured at pre-damage, and then every four days post-damage for 28 days. Values (means ± SEM) are expressed in percentages of pre-test. Between subjects effects, significant difference between CFS and CD groups $p < 0.01$, CFS and ND groups $p < 0.001$. Within subject effects, whereby time was main effect $p < 0.001$, interaction $p < 0.001$.

* Indicates a significant difference between CFS and CD, as well as CFS and ND groups.
** Indicates a significant difference between CFS and ND groups.

4.6.2.2 Average Torque (AT).

AT results were similar to PT with an initial fall to 53.0% (± 6.5% SEM) 4 days post-damage in the CFS group compared to 79.5% (± 4.1% SEM) 4 days post-damage in the CD group. There was a slight recovery of AT in the CFS group 8 days post-damage (54.6% ± 7.3% SEM)) followed by a further drop in AT 12 days post-damage (54.0% ± 6.5% SEM)), followed by a slow recovery of AT peaking at 77.0% (± 5.5% SEM) 28 days post-damage. Which, as with PT, was the same level of force loss attained by the CD group 4 days post-damage. The ND damage group as expected maintained pre-test values (± 5.1%). Refer to Table 4.4 & Figure 4.10.
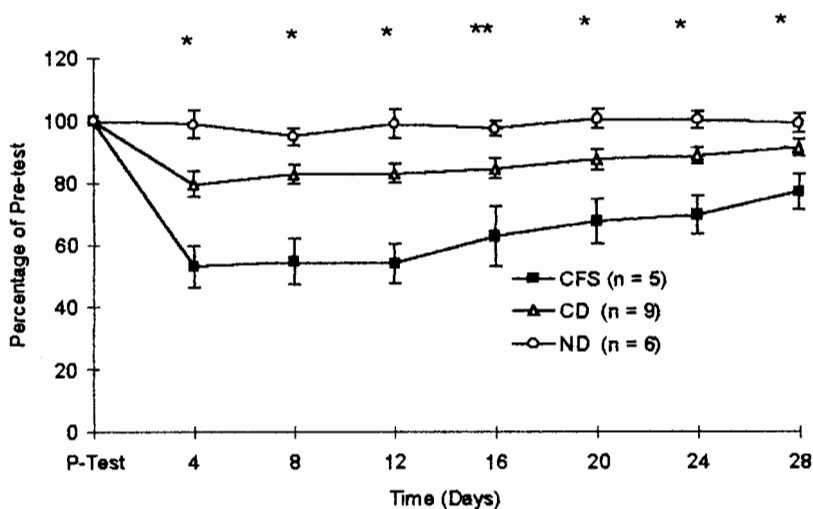
Figure 4.10. Normalised isokinetic concentric average torque, average of the 3x1 contractions at $150°$ /sec^{-1} measured at pre-damage, and then every four days post-damage for 28 days. Values (means ± SEM) are expressed in percentages of pre-test. Between subjects effects, significant difference between CFS and CD groups $p < 0.001$, CFS and ND groups $p < 0.001$. Within subject effects, whereby time was main effect $p < 0.001$, interaction $p < 0.001$.

* Indicates a significant difference between CFS and CD, as well as CFS and ND groups.

** Indicates a significant difference between CFS and ND groups.

AT, following eccentric damage was significantly lower in the CFS group (Figure 4.10), when compared to a control group ($p <$ 0.001), with simple comparison showing a significant difference between CFS and CD groups ($p < 0.001$) and CFS and ND groups ($p < 0.001$). Within subject effect with time as major effect ($p <$ 0.001), and interaction ($p < 0.001$). The raw data (Appendix H) has been normalised for presentation (Figure 4.10). Refer also to Table 4.4 for a percentage summary of dynamic and isometric force attained over the time course of data collection.

Table 4.4.

Summary of isometric (MVC) and concentric results (PT & AT) at pre-test then every four days for 28 days from the CFS (n=5), CD (n=9) & ND (n=6) groups, normalised values ± SEM in brackets.

Test	Isometric			Peak Torque			Average Torque		
	CFS	CD	ND	CFS	CD	ND	CFS	CD	ND
Pre-test	100 (0)	100 (0)	100 (0)	100 (0)	100 (0)	100 (0)	100 (0)	100 (0)	100 (0)
+ 4	57.7 (4.1)	82.4 (3.0)	97.9 (4.3)	53.9 (6.9)	79.2 (3.7)	97.4 (4.1)	53.0 (6.5)	79.5 (4.1)	98.7 (4.4)
+ 8	65.7 (2.9)	87.7 (2.6)	105.6 (3.8)	53.3 (7.7)	80.3 (3.6)	95.8 (2.8)	54.6 (7.3)	82.6 (3.0)	94.9 (2.8)
+ 12	71.4 (5.5)	88.2 (1.9)	106.2 (4.3)	52.1 (6.7)	82.9 (2.7)	97.4 (5.6)	54.0 (6.5)	82.9 (3.1)	99.0 (4.7)
+ 16	76.0 (6.4)	91.8 (2.8)	109.2 (3.0)	64.4 (9.2)	83.2 (3.1)	95.8 (2.3)	62.7 (9.8)	84.5 (3.3)	97.3 (2.3)
+ 20	76.4 (6.7)	93.4 (2.8)	110.6 (4.2)	69.3 (6.3)	86.1 (3.3)	100.0 (4.2)	67.6 (7.3)	87.3 (3.3)	100.4 (3.2)
+ 24	83.6 (6.1)	95.1 (2.2)	106.6 (5.3)	73.0 (6.7)	87.5 (2.9)	99.7 (3.4)	69.5 (6.2)	88.7 (2.6)	100.2 (2.7)
+ 28	86.7 (3.7)	96.1 (2.9)	104.9 (6.3)	77.9 (6.7)	89.3 (1.5)	96.3 (2.9)	77.0 (5.5)	91.3 (2.6)	99.2 (3.1)

4.8 Delayed Onset Muscle Soreness

Hypothesis 4 which proposed that the time course of DOMS would be different between the CFS and CD groups was rejected, for the following reasons. The time course of DOMS, determined by the number of sites, where pain was indicated by the subject during palpation of the damaged biceps brachii (Figure 4.11, see also Appendix E), was similar in both CFS and CD groups. DOMS was felt at a mean of 8.3 ($\pm$ 3.2 SEM) sites in the CFS group and 9.7 ($\pm$ 1.8 SEM) sites in the CD group on after 1 day, with a peak of CFS group 19.5 ($\pm$ 1.6 SEM) and CD group 19.4 ($\pm$ 1.5 SEM) 2 days post-damage. DOMS in terms of location then subsided and was totally gone by day 8 in all subjects. Statistical analysis using Students independent t-test showed that there was no significant difference in the time course of DOMS, between the CFS group and the CD group. This homogeneity of DOMS time course can be clearly seen in Figure 4.11.
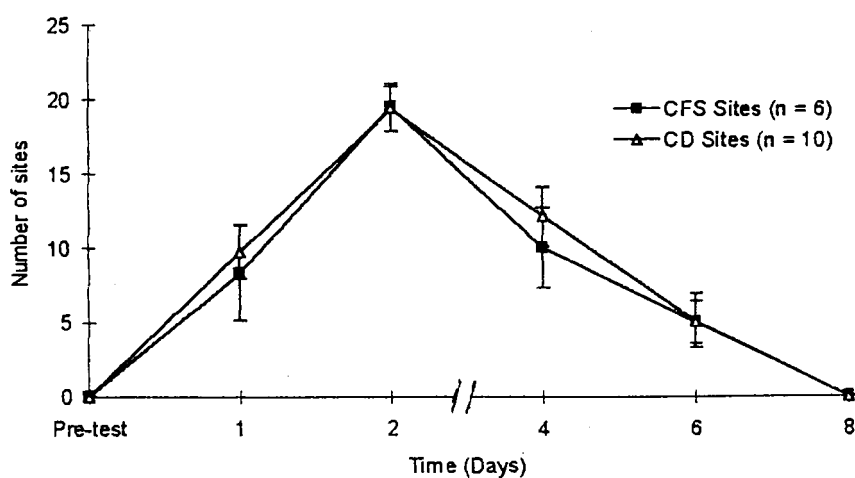
Figure 4.11. Number of indicated sites (maximum 30) of DOMS in the biceps brachii of CFS and CD subjects following eccentric damage bout. Values (means $\pm$ SEM) are expressed in the average number of sites. NS between groups.

The degree of DOMS was represented by the mean score of the intensity, rated between 0 (no pain) and 10 (very, very painful), of pain at the sites as indicated by the subjects during palpation. Figure 4.12 shows that the intensity of DOMS was less in the CFS group with a mean peak of 2.5 ($\pm$ 0.7 SEM) occurring 2 days post-damage in the CFS group, and 4.3 ($\pm$ 0.7 SEM) occurring 4 days post-damage in the CD group. Statistical analysis using independent samples T-test shows that the degree of DOMS was significantly less 6 days post-damage in the CFS group when compared to the CD group ($p < 0.05$). Therefore, the results attained supported hypothesis 5 which proposes that the degree of DOMS following eccentric damage, between the CFS and CD groups would differ.
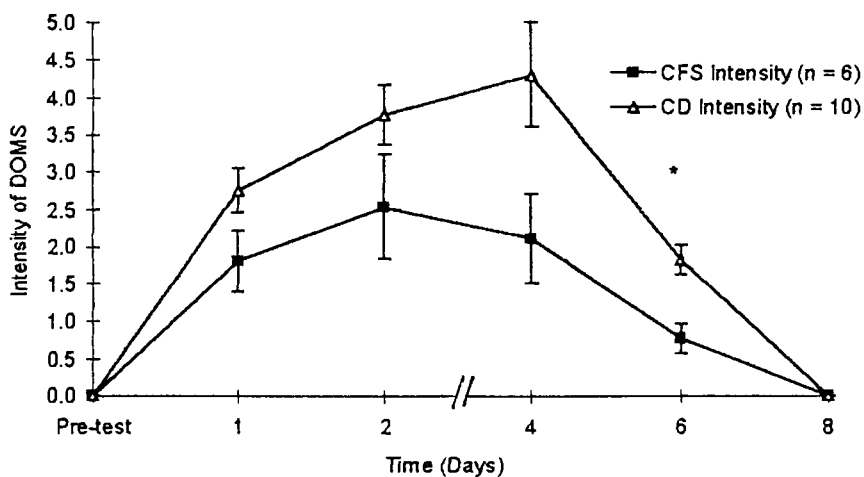
Figure 4.12. Intensity of DOMS as given by the average value from all sites tested, each site attributed a value of between 0 - 10 (0 = no pain, 10 = very, very, painful). Values (means $\pm$ SEM) expressed as an average. Asterisk indicates significant difference between CFS and CD groups at 6 days post-damage, $p < 0.05$.

4.9 Summary

The results gained in this research, as they occurred in a general chronological order showed: a) A significant reduction of isokinetic eccentric torque produced by the CFS group. b) a LFF ratio which was significantly lower, and retained for a longer period in the CFS group. c) DOMS, with the only difference being in the intensity of DOMS in the CFS group, which perhaps surprisingly was significantly lower. d) Serum CK activity, whereby the CFS groups had significantly higher serum concentration as a result of eccentrically induced damage. e) Isometric and isokinetic concentric force measurements (PT & AT) force which were significantly reduced as a result of the damage in the CFS group.

CHAPTER 5

DISCUSSION

5.1 Introduction

The purposes of this study are to establish whether differences exist in muscle force and damage characteristics, in the short term, following eccentrically induced muscle damage, between subjects diagnosed with CFS (inclusive of subjects diagnosed with OTS), and healthy individuals, and to determine the time course of recovery from this damage.

Differences occurring in CFS include; a greater reduction in isometric and isokinetic concentric force output, an increased serum CK activity, a greater decrease 20:50 Hz ratio, and a lower intensity of DOMS.

5.2 Isokinetic Eccentric Torque

The reduction in the amount of eccentric torque absorbed in the CFS group compared to the CD group is of special interest. Previous research (Kent-Braun, et al., 1993; Lloyd, et al., 1988; Stokes et al., 1988) has found that CFS skeletal muscle is no more fatigable than skeletal muscle of healthy controls. This then begs the questions: Is the greater relative reduction in eccentric force absorbed by the CFS group due to eccentrically induced damage? Does this infer that CFS skeletal muscle has a lower "threshold" for damage? Is the reduction due to central and, or peripheral fatigue? Or a combination of fatigue and damage?

Jones & Round (1993) indicate that in healthy fatigued skeletal muscle ATP levels are not significantly reduced, and therefore muscle ATP is not considered to be a major factor in fatigue. On the other hand research by Wong et al., (1992) using 31P NMR spectroscopy found that the level of ATP in skeletal muscle of patients with CFS was significantly lower at peak exercise levels, than that of healthy controls. They inferred that this finding is indicative of some oxidative metabolism defect, and as such glycolysis was accelerated in CFS patients.

In conclusion whether muscle ATP is involved, and to what degree it is involved is a matter for conjecture for the following reasons: a) Eccentric exercise requires less ATP than concentric exercise; b) It is unknown whether the reduced level of ATP that occurred in the Wong et al., (1992) study would occur in the damage protocol adopted in this study. Electromyography (EMG) would have provided some evidence as to whether the reduction in eccentric force absorbed was due to central fatigue, damage at crossbridge attachments, or at the EDF (see Chapter 5.3).

5.3 Low Frequency Fatigue

Low frequency fatigue (LFF) which results from damage occurring at the EDF (Figure 2.5), is not associated with DOMS or serum CK activity (Ebbling & Clarkson, 1989). LFF generally begins to recover 24 to 48 hours post-damage, as was observed with the CD group (Figure 4.4 and 4.5). However, this was not the case with CFS subjects, who appear to have a lower threshold for LFF, in

that, the degree of LFF following the damage is greater, and more prolonged in CFS subjects when compared to healthy controls.

The differences in the 20:50 Hz response may be due to three possible causes. Firstly, whilst most of the subjects from CFS and CD groups were observed to have had a degree of swelling following damage, it is possible that the oedema may disperse from the muscle of CFS subjects more slowly, reducing conductivity during the percutaneous stimulation process. Therefore, a greater proportion of the electric discharge was absorbed by the oedema rather than the muscle. However, the intensity of DOMS observed in the CFS and CD groups does not support this notion, in that, if the oedema was to disperse more slowly it would be reasonable to conclude that the intensity of DOMS would be higher in the CFS group when compared to the CD group (Chapter 5.4) as the level of oedema and serum CK concentration are implicated in the intensity of DOMS (Clarkson, et al., 1992; Jones & Round, 1993). Secondly, practical difficulties in percutaneous stimulation due to the placement of electrodes. However, the range in size of the biceps brachii across the groups was similar, and electrodes and gel were used universally, therefore whilst some practical error may have occurred, it was minimised by careful placement and it is unlikely to account for the marked difference between the groups. Thirdly, there was a greater degree of damage at the EDF. Certainly the absolute forces produced by the 20 : 50 Hz stimulations in the CFS group immediately following eccentric damage, through to day 8, were less than those produced by the corresponding stimulations of the CD group. This reduced absolute force production does support the notion that there is a greater

degree of damage at the EDF. Refer to Figures 4.6 & 4.7 (see also Appendix J).

5.4 Delayed Onset Muscle Soreness

It is apparent from the results that DOMS in subjects with CFS is activated in much the same way as with healthy subjects. This is evidenced by the observation that little difference was noticed in the time course and movement of DOMS within the CFS and the CD groups. Therefore it would seem that the chemical activation of nociceptors, and removal of these chemicals, function normally in subjects with CFS.

More surprisingly perhaps, was the difference in the perceived intensity of DOMS, whereby the intensity of DOMS in CFS subjects was significantly less than with the CD group. This result was in some ways unexpected as the intensity of DOMS is linked to serum CK concentrations whereby low (peak <500 $U.L^{-1}$) CK responders to eccentric damage had significantly less pain than medium (peak 500 - 2000 $U.L^{-1}$) or high (peak $>$ 2000 $U.L^{-1}$) responders (Clarkson et al., 1992). In this study the means of both groups had a peak $>$ 2000 $U.L^{-1}$ and similar pain intensities would have been expected. Furthermore, as hypochondria and histrionics amongst CFS sufferers has been reported (Parker, 1990; Wessely & Thomas, 1990) lower levels of pain may have been described as more severe by these individuals.

However, as previously stated this was not supported by the evidence, which instead supports the notion of a higher threshold of pain as evidenced by a lower intensity of pain for a greater

amount of damage (see Chapter 5.5). What is not clear is whether the myalgia sometimes reported by CFS sufferers is of the same intensity as eccentrically-induced DOMS, and whether the observed lower intensity of DOMS in the CFS subjects was perhaps due the modulation of pain receptors.

5.5 Serum Creatine Kinase

The greater concentration of serum CK in the CFS group following damage when compared to the control groups is of particular interest, indicating a greater degree of eccentrically induced damage. Whilst it is accepted that serum CK activity is "a useful tool for the detection of muscle damage, since it is generally considered to be highly sensitive and relatively specific to muscle" (Dioszeghy & Mechler, 1988, p. 175), doubt remains about the concentration of serum CK being used as a determinant of the amount of damage due to the large inter-subject & gender differences reported in serum CK efflux (Ebbling & Clarkson, 1989). Evans & Gannon, (1991, p. 104) state: "It is likely that postexercise rise in circulating CK activity is a manifestation of skeletal muscle damage but not a direct indicator of it".

Therefore whilst it is interesting that mean peak of serum CK activity was significantly higher in the CFS group than the CD group perhaps of more interest is the possible cause of the higher level, and the ramifications for CFS patients. Research (Clarkson, et al., 1992) has shown that moderate (peak 500 - 2000 $U.L^{-1}$) and high (peak > 2000 $U.L^{-1}$) CK responders to eccentric damage had a significantly greater reduction in isometric force than low responders (peak <500 $U.L^{-1}$). Therefore, the higher serum

concentration of CK that was evident in the CFS group (8388 ± SEM 1224 U.L^{-1}) than the CD group (2583 ± SEM 753 U.L^{-1}) in this study can be linked to the greater loss in isometric force that also occurred in the CFS group. Furthermore, the reduced absolute forces from 20:50 Hz stimulation that were produced in the CFS group when compared to the CD group (Figure 4.4 & 4.5), in conjunction with the increased serum CK concentration may indicate greater muscle damage in the CFS group.

5.6 Isometric Strength and Isokinetic Concentric Force

Both isometric and isokinetic concentric force measurements were shown to be significantly reduced in the CFS group. It is unlikely that peripheral fatigue is an issue with the changes that occurred in isokinetic concentric force following damage, as these tests only involved 3 x 1 MVC's at 150°/sec^{-1} with a rest of 60 seconds between each contraction. Therefore, phospho-creatine regeneration which has a half time of 20 seconds would have been sufficient for maximal ATP usage by the contractile apparatus. Similarly, isometric testing which only contained one 5 second MVC is unlikely to be subject to peripheral fatigue. Therefore it is reasonable to conclude that the reduction in forces in the isometric and isokinetic tests was due to actual muscle damage and possibly an inhibitory effect of pain in conjunction with the perception of effort. This however does not explain the difference between the CD and CFS groups, and in conjunction with the changes that occurred with LFF it is possible that some secondary immune response occurred that resulted in a greater degree of damage to muscle tissue that resulted in a longer lasting force and strength loss in the CFS subjects.

CHAPTER 6

SUMMARY

In the series of events that occurred following eccentric damage, most of the parameters used to measure these events differed between CFS subjects and healthy individuals, with only the degree of DOMS in both damaged CFS and CD groups showing no difference. A summary of the findings of the hypotheses being tested in this research follows.

Hypothesis 1 (after damage, muscle force characteristics of subjects with CFS will be different from the Control Damage (CD) group) was fully proved with isometric muscle force characteristics along with dynamic force differences being significantly different between the groups after the damage. Hypothesis 2 (after damage, the contractile properties of skeletal muscle as determined by the level of low frequency fatigue (LFF), will differ in subjects with CFS when compared to the CD group) was satisfactorily proven by LFF in CFS patients having significantly greater depth, and lasting longer. Hypothesis 3 (the time course of serum CK efflux, and the serum CK concentration in subjects with CFS will be different from the CD group) was partially proved, in so far as the serum concentration of CK was significantly higher in CFS patients following the damage bout, however the time course of the increased serum CK activity was no different from the control group. Hypothesis 4 (the time course of delayed onset muscle soreness (DOMS) during recovery in subjects with CFS will be

different from the CD group) was not proved, in that the time course of DOMS in the two damaged groups did not differ. Lastly, hypothesis 5 (the degree of DOMS in subjects with CFS will be different from the CD group) was proved, in that, the degree of DOMS was significantly less in the CFS group when compared to the other damaged group.

The evidence provided by the combination of higher serum CK activity, greater isometric and dynamic force losses, a longer lasting and greater depth of LFF, and a reduced sensitivity to DOMS, support the notion that CFS patients have a lower threshold of damage. Moreover, these data seems to indicate that a secondary immune response could be implicated in explanation of the possible aetiology of these differences.

Finally, whilst it has been determined that there are differences between the CFS group and the CD group, these findings should be viewed with caution when applying causality, for the following reasons. The CD and ND controls groups by in large came from the Human Movement Department student body, and as such it is likely that they are not representative of the population that the CFS group was drawn from. In that, they are generally younger, weigh less, and by the nature of their studies, probably have a higher cardio-vascular fitness level. Similarly, the greater degree of damage that seems to have occurred in the CFS group could be due to the CFS condition per se, or in some cases it could be due to deconditioning that commonly occurs in CFS.

6.1 Recommendations For Future Research

There is still much to learn in the effort to understand the aetiology, and, in establishing a simple diagnostic protocol for CFS. Firstly, further research is required into the primary and secondary immunological processes that are taking place in CFS subjects over the full damage-recovery time course. This study should also examine CK activity. Secondly, confirmation of the findings of delayed recovery from LFF needs to be examined, with perhaps a study involving direct nerve stimulation, thereby removing any problems associated with electrode positioning or from oedema. Finally, a comparative study between CFS and OTS subjects should be undertaken. All of these studies should wherever possible be age and sex matched.

REFERENCES

Almekinders, L.C., & Almekinders, S.V. (1992). Immune functions in exercise-induced injuries. In Exercise and Disease, Watson, R.R., & Eisinger, M. (Eds.). (pp. 149-158). Boca Raton : CRC Press.

Appell, H. J., Soares, J. M. C., & Duarte, J. A. R. (1992). Exercise, muscle damage and fatigue. Sports Medicine, 13 (2), 108-115.

Armstrong, R. B. (1984). Mechanisms of exercise-induced delayed onset muscular soreness: A brief review. Medicine and Science in Sports and Exercise, 16(6), 529-538.

Armstrong, R. B. (1990). Initial events in exercise-induced muscular injury. Medicine and Science in Sports and Exercise, 22(4), 429-435.

Atwell, A., McNaughton, L., Gorringe, S., & Kaufman, D. (1991). The effects of multiple anaerobic exercise periods on levels of lactate, lactate dehydrogenase, creatine kinase, aspartate transaminase. The Australian Journal of Science and Medicine in Sport, 23(2), 32-36.

Behan, P. O., & Behan, W. M. H. (1993). Chronic fatigue syndrome, what is it? In MacLeod, D. A. D. Maughan, R. J., Williams, C. Madeley, C. R., Sharp, J. C. M., & Nutton, R. W. (Eds.). Intermittent High Intensity Exercise (pp. 227 - 237). London : E. & F., N. Spon.

Braun, H. P., Deneke, U., & Rittersdorf, W. (1987). Test for the quantitative determination of CK (EC 2.7.3.2) in blood, serum or plasma with Reflotron$^{®}$. Clinical Chemistry, 33, 988

Burns, N., & Grove, S. K. (1993). The practice of nursing research conduct, critique & utilization. (2nd ed.). Philadelphia : W. B. Saunders Company.

Buchwald, D., & Komaroff, A.L. (1991). Review of laboratory findings for patients with chronic fatigue syndrome. Reviews of Infectious Diseases, 13(Suppl. 1), S12-S18.

Byrd, S.K. (1992). Alterations in the sarcoplasmic reticulum: A possible link to exercise-induced muscle damage. Medicine and Science in Sport and Exercise, 24(5), 531-536.

Byrne, E. (1991). The chronic fatigue syndrome: A reappraisal and unifying hypothesis. Clinical and Experimental Neurology, 28, 128-138.

Byrnes, W. C., & Clarkson, P. M. (1986). Delayed onset muscle soreness and training. Clinics in Sports Medicine, 5(3), 605-614.

Byrnes, W. C., Clarkson, P. M., & Katch, F.I. (1985).
Muscle soreness following resistance exercise with and without
eccentric contractions. Research Quarterly for Exercise and
Sport, 56(3), 283-285.

Cady, E.B., Jones, D.A., Lynn, J., & Newham, D.J. (1989).
Changes in force and intracellular metabolites during fatigue of
human skeletal muscle. Journal of Physiology, 418, 327-337.

Clarkson, P.M., Nosaka, K., & Braun, B. (1992). Muscle function
after exercise-induced muscle damage and rapid adaptation.
Medicine and Science in Sports and Exercise, 24(5), 512-520.

Committee for the Conduct of Ethical Research, (1994).
Policy for the conduct of ethical research involving human
subjects. Available Edith Cowan University : Perth, Western
Australia.

Dioszeghy, P., & Mechler, F. (1988). The significance of
simultaneous estimation of serum creatine kinase and
myoglobin in neuromuscular disease. Journal of Neurology,
235, 174-176.

Ebbling, C. B., & Clarkson, P. M. (1989). Exercise-induced
muscle damage and adaptation. Sports Medicine, 7(4), 208-
234.

Ebbling, C.B., & Clarkson, P.M. (1990). Muscle adaptation prior to recovery following eccentric exercise. European Journal of Applied Physiology, 60, 26-31.

Edwards, R. H. T., Newham, D. J., & Peters, T. J. (1991). Muscle biochemistry and pathophysiology in postviral fatigue syndrome. British Medical Bulletin, 47(4), 826-837.

Eichner, E.R. (1991). Chronic fatigue and staleness. In Strauss, R.H. (Ed.), Sports Medicine, (2nd ed.), (pp. 207-220). Philadelphia : W. B. Saunders Company.

Evans, W.J., & Gannon, J.G. (1991). The metabolic effects of exercise-induced muscle damage. Exercise and Sport Science Reviews, 19, 99-125.

Fairbanks, V.F., & Klee, G.G. (1994) Biochemical aspects of hemotology. In Burtis, C. A., & Ashwood, E. A. (Eds.). (1994). Tietz textbook of clinical chemistry. (2nd ed.) (pp. 1974-2072). Philadelphia : W. B. Saunders Company.

Fitzgerald, L. (1991). Overtraining increases the susceptibility to infection. International Journal of Sports Medicine, 12(Suppl. 1), S5-S8.

Friden, J., Sjostrom, M., & Ekblom, B. (1981) A morphological study of delayed muscle soreness. Experientia, 37, 306-307.

Friden, J., Sjostrom, M., & Ekblom, B. (1983). Myofibrillar
   damage following intense eccentric exercise in men.
   International Journal of Sports Medicine, 4(3), 170-176

Fry, R. W., Morton, A. R., & Keast, D. (1991a).
   Overtraining in athletes an update. Sports Medicine, 12(1), 32-
   65.

Fry, R. W., Morton, A. R., & Keast, D. (1991b).
   Overtraining syndrome and chronic fatigue syndrome part 1.
   New Zealand Journal of Sports Medicine, 19(3), 48-52.

Fry, R. W., Morton, A. R., & Keast, D. (1991c).
   Overtraining syndrome and chronic fatigue syndrome part 2.
   New Zealand Journal of Sports Medicine, 19(4), 76-77.

Galasso, P.J., Litin, S.C., & O'Brien, J.F. (1993). The
   macroenzymes: A Review. Mayo Clinic Proceedings, 68(4),
   349-354.

Goldenberg, D.L. (1994). Fibromyalgia, chronic fatigue syndrome,
   and myofacial pain syndrome. Current Opinion in
   Rheumatology, 6, 223-233.

Gross, J.B. (1992). Chronic fatigue syndrome and the sports
   performer. Sports Health, 10(3), 25-26.

Horrobin, D.F. (1990). Post-viral fatigue syndrome, viral infections in atopic eczema, and essential fatty acids. <u>Medical Hypotheses,</u> <u>32,</u> 211-217.

Hough, T. (1902). Ergographic studies in muscular soreness. <u>American Journal of Physiology,</u> <u>7,</u> 76-92.

Jessell, T.M., & Kelly, D.D. (1991). Pain and analgesia. In Kandel, E.R., Schwartz, J.H., & Jessell, T. M. (Eds.). <u>Principles of neural science</u> (3rd ed.). New York: Elsevier.

Jones, D. A., Newham, D. J., Round, D.A., & Tolfree, S.E.J. (1986). Experimental human muscle damage: Morphological changes in relation to other indices of damage. <u>Journal of Physiology,</u> <u>375,</u> 435-448.

Jones, D. A., Newham, D. J., & Torgan, C. (1989). Mechanical influences on long-lasting human muscle fatigue and delayed-onset pain. <u>Journal of Physiology,</u> <u>412,</u> 415-427.

Jones, D. A., & Round, J. M. (1993). <u>Skeletal muscle in health and disease.</u> Manchester : Manchester University Press.

Jubrias, S.A., Bennett, R.M., & Klug, G.A. (1994). Increased incidence of a resonance in the phosphodiester region of 31P nuclear magnetic resonance spectra in the skeletal muscle of fibromyalgia patients. <u>Arthritis & Rheumatism,</u> <u>37</u>(6), 801-807.

Kannus, P. (1994). Isokinetic evaluation of muscular performance: Implications for muscle testing and rehabilitation. International Journal of Sports Medicine, 15(Suppl. 1), S11-S18.

Keast, D., & Morton, A.R. (1992). Long-term exercise and immune functions. In Exercise and Disease, Watson, R.R., & Eisinger, M. (Eds.). (pp. 89-120). Boca Raton : CRC Press.

Kent-Braun, J.A., Sharma, K.R., Weiner, M.W., Massie, B., & Miller, R.G. (1993). Central basis of muscle fatigue in chronic fatigue syndrome. Neurology, 43, 125-131.

Kirkendall, D.T. (1990). Mechanisms of peripheral fatigue. Medicine and Science in Sports and Exercise, 22 (4), 444-449

Knochel, J.P. (1993). Mechanisms of rhabdomyolysis. Current Opinions in Rheumatology, 5(6), 725-731.

Krupp, L. B., Mendelson, W. B., & Friedman, R. (1991). An overview of chronic fatigue syndrome. Journal of Clinical Psychiatry, 52(10), 403-410.

LaPerriere, A., Antoni, M.H., Fletcher, M.A., & Schneiderman, N. (1992). Exercise and health maintenance in HIV. In Galantino (Ed.). (pp. 66-75) Clinical assessment and treatment of HIV. New York : McGraw-Hill, Inc.

LaPerriere, A., Ironson, G., Antoni, M.H., Schneiderman, N., Klimas, N., & Fletcher, M.A. (1994). Exercise and psychoneuroimmunology. Medicine and Science in Sports and Exercise, 26(2), 182-190.

Lee, J. (1994). Roots of fatigue. New Scientist, 1926, 21May, 1994, 1-4.

Lehmann, M., Foster, C., & Keul, J. (1993). Overtraining in endurance athletes: A brief review. Medicine and Science in Sports and Exercise, 25(7), 854-862.

Lehmann, M., Schnee, W., Scheu, R., Stockhausen, W., & Bachl, N. (1992). Decreased nocturnal catecholamine excretion: Parameter for an overtraining syndrome in athletes? International Journal of Sports Medicine, 13(3), 236-242.

Lieber, R.L., & Friden, J. (1993). Muscle damage is not a function of muscle force but active muscle strain. Journal of Applied Physiology, 74(2), 520-526.

Lloyd, A.R., Gandevia, S.C., & Hales, J.P. (1991). Muscle performance, voluntary activation, twitch properties and perceived effort in normal subjects and patients with the chronic fatigue syndrome. Brain, 114, 85-98.

Lloyd, A.R., Hales, J.P., & Gandevia, S.C. (1988). Muscle
Strength, endurance, and recovery in the post-infection fatigue
syndrome. Journal of Neurology, Neurosurgery, & Psychiatry,
51, 1316-1322.

MacKinnon, L.T. (1994). Current challenges and future
expectations in exercise immunology: back to the future.
Medicine and Science in Sports and Exercise, 26(2), 191-194.

MacKinnon, L.T., & Hooper, S. (1992). Overtraining: State of the
art review No. 26. Excel, 8, 3-12.

Manfredi, T.G., Fielding, R.A., O'Reilly, K.P., Meredith, C.N., Lee,
H.Y., & Evans, W.J. (1991). Plasma creatine kinase activity
and exercise-induced muscle damage in older men. Medicine
and Science in Sports and Exercise, 23(9), 1028-1034.

Manu, P., Lane, T. J., & Matthews, D. A. (1992). The
pathophysiology of chronic fatigue syndrome : Confirmations,
contradictions, and conjectures. International Journal of
Psychiatry in Medicine, 22(4), 397-408.

Martin, E.A. (Ed.). (1990). Concise Medical Dictionary (3rd ed.).
Oxford : Oxford University Press.

McCluskey, D.R. (1993). Chronic fatigue syndrome and
its effect on exercise capacity. In MacLeod, D. A. D. Maughan,
R. J., Williams, C. Madeley, C. R., Sharp, J. C. M., & Nutton,
R. W. (Eds.). Intermittent High Intensity Exercise (pp. 239-
249). London : E. & F., N. Spon.

McGregor, N., Butt, H.L., Zerbes, M., Dunstan, R.H., Roberts,
T.K., & Klineberg, I.J. (1994, May). Chronic fatigue syndrome:
A urinary biomarker. Paper presented at an international
meeting on Chronic Fatigue Syndrome, Dublin, Ireland.

Minikin, B. (1991). Laboratory standards assistance
scheme- physiology. Requirements and recommended practices
for laboratories conducting physiological and sports
performance testing. Canberra : Australian Sports Commission.

Moss, D.W., & Henderson, A.R. (1994). Enzymes. In
Burtis, C. A., & Ashwood, E. A. (Eds.). (1994). Tietz textbook
of clinical chemistry. (2nd ed.) (pp. 735-896). Philadelphia :
W. B. Saunders Company.

Newham, D. J., Jones, D. A., & Clarkson, P. M. (1987).
Repeated high-force eccentric exercise: effects on muscle pain
and damage. Journal of Applied Physiology, 63(4), 1381-1386.

Newham, D.J., Jones, D.A., Tolfree, S.E.J., & Edwards, R.H.T.
(1986). Skeletal muscle damage: A study of isotope uptake,
enzyme efflux and pain after stepping. European Journal of
Applied Physiology, 55, 106-112.

Newham, D.J., McPhail, G., Mills, K.R., & Edwards, R.H.T. (1983). Ultrastructural changes after concentric and eccentric contractions of human muscle. Journal of Neurological Sciences, 61, 109-122.

Newham, D. J., Mills, K. R., Quigley, B. M., & Edwards, R. H. T. (1983). Pain and fatigue after concentric and eccentric muscle contractions. Clinical Science, 55-62.

Newsholme, E.A., Blomstrand, E., McAndrew, N., & Parry-Billings, M. (1992). Biochemical causes of fatigue and overtraining. In Endurance in sport: The encyclopaedia of sports medicine an IOC medical commission publication (pp. 351-364). Oxford : Blackwell Scientific Publications.

Nosaka, K., & Clarkson, P.M. (1992). Relationship between post-exercise plasma CK elevation and muscle mass involved in the exercise. International Journal of Sports Medicine, 13(6), 471-475.

Nosaka, K., Clarkson, P.M., & Apple, F.S. (1992). Time course of serum protein changes after strenuous exercise of the forearm flexors. Journal of Laboratory and Clinical Medicine, 119(2), 183-188.

O'Brien, M. (1993). Prevention of overtraining. In <u>Sports injuries</u>
<u>basic principles of prevention and care: Volume IV of the</u>
<u>encyclopaedia of sports medicine an IOC medical commission</u>
<u>publication</u> (pp. 291-296). Oxford : Blackwell Scientific
Publications.

Painter, P.C., Cope, J.Y., & Smith, J.L. (1994). Appendix.
In Burtis, C. A., & Ashwood, E. A. (Eds.). (1994). <u>Tietz</u>
<u>textbook of clinical chemistry</u>. (2nd ed.) (pp. 2161-2218).
Philadelphia : W. B. Saunders Company.

Parker, S. (1990). Chronic fatigue syndrome and the athlete. In
<u>Sports Performance Through the Ages</u>: Proceedings of 27th
Annual ASMF Conference, 548-589.

Parker, S., & Brukner, P. (1994). is your sportsperson
suffering from chronic fatigue syndrome. <u>Sport Health, 12</u>(1),
15-17.

Parry-Billings, M., Budgett, R., Koutedakis, Y., Blomstrand,
E., Brooks, S., Williams, C., Calder, S., Pilling, S., Baigrie, R.,
& Newsholme, E. A. (1992). Plasma amino acid concentrations
in the overtraining syndrome: possible effects on the immune
system. <u>Medicine and Science in Sports and Exercise, 24</u>(12),
1353-1358.

Parry-Billings, M., Matthews, V. J., Newsholme, E. A.,
    Budgett, R., & Koutedakis, J. (1993). The overtraining
    syndrome: Some biochemical aspects. In MacLeod, D. A. D.,
    Maughan, R. J. Williams, C., Madeley, C. R., Sharp, J. C. M.,
    & Nutton, R. W. (Eds.). Intermittent High Intensity Exercise
    (pp. 215-225). London : E. & F., N. Spon.

Poels, P.J.E., & Gabreels, F.J.M. (1993). Rhabdomyolysis: A
    review of the literature. Clinical Neurology and Neurosurgery,
    93(3), 175-192.

Powers, S.K. & Howley, E.T. (1994). Exercise physiology: Theory
    and application to fitness and performance (2nd ed.). Dubuque,
    Iowa : WCB Brown & Benchmark.

Rosano, T.G., & Kenny, M.A. (1977). A radioimmunoassay
    for human serum myoglobin. Method development and normal
    values. Clinical Chemistry, 23, 69-75.

Rothwell, J. (1994). Control of human voluntary movement
    (2nd ed.). London : Chapman Hall.

Sale, D. (1991) Testing strength and power. In MacDougall,
    J.D., Wenger, H.A., & Green, H.J. (Eds.). Physiological testing
    of the high-performance athlete (2nd ed.) (pp. 21-106).
    Champaign, Illinois : Human Kinetics Books.

Sapega, A.A., Nicholas, J.A., Sokolow, D., & Saraniti, A. (1982) The nature of torque "overshoot" in Cybex isokinetic dynamometry. Medicine and Science in Sports and Exercise, 14(5), 368-375.

Sharp, C., & Parry-Billings, M. (1992) Can exercise damage your health. New Scientist, 1834, 15 August, 1992, 33-37.

Soares, J.M.C., Duarte, J.A.R., Carvalho, J., & Appell, H.J. (1993). The possible role of intracellular Ca^{2+} accumulation for the development of immobilization atrophy. International Journal of Sports Medicine, 14(8), 437-439.

Stokes, M.J., Cooper, R.G., & Edwards, R.H.T. (1988). Normal muscle strength and fatigability in patients with effort syndromes. British Medical Journal, 297, 1014-1017.

Tabachnick B.G., & Fidell, L.S. (1989). Using multivariate statistics. (2nd ed.). California : Harper Collins Publishers.

Weicker, H., & Werle, E. (1991). Interaction betweeen hormones and the immune system. International Journal of Sports Medicine, 12(Suppl. 1), S30-S37.

Wessely, S., & Thomas, P.K. (1990). The chronic fatigue syndrome-myalgic encephalomyelitis or postviral fatigue. In Keynard, C. (Ed.). Recent Advances in Clinical Neurology, VI. London : Churchill Livingstone.

White, T. A., & Esser, K., A. (1989). Satellite cell and growth factor involvement in skeletal muscle growth. <u>Medicine and Science in Sports and Exercise</u>, <u>21</u>(5 Suppl.), S158-S163.

Wong, R., Lopaschuk, G., Zhu, G., Walker, D., Catellier, D., Burton, D., Teo, K., Collins-Nakai, R., & Montague, T. (1992). Skeletal muscle metabolism in the chronic fatigue syndrome: In vivo assessment by 31P nuclear magnetic resonance spectroscopy. <u>Chest</u>, <u>102</u>, 1716-1722.

Biochemical Test Principles

EC 2.6.1.1 Aspartate transaminase (AST)

It is not possible to directly monitor transaminase reactions, therefore the test principle used to determine AST levels is based upon quantifying the reduction of oxaloacetate (formed by AST reaction) to malate in the presence of malate dehydrogenase (MD)

Aminotransferase reaction (formation of oxaloacetate) Assay reaction	Dehydrogenase reaction (quantification of oxaloacetate) Indicator reaction

Moss & Henderson, (1994, p. 792)
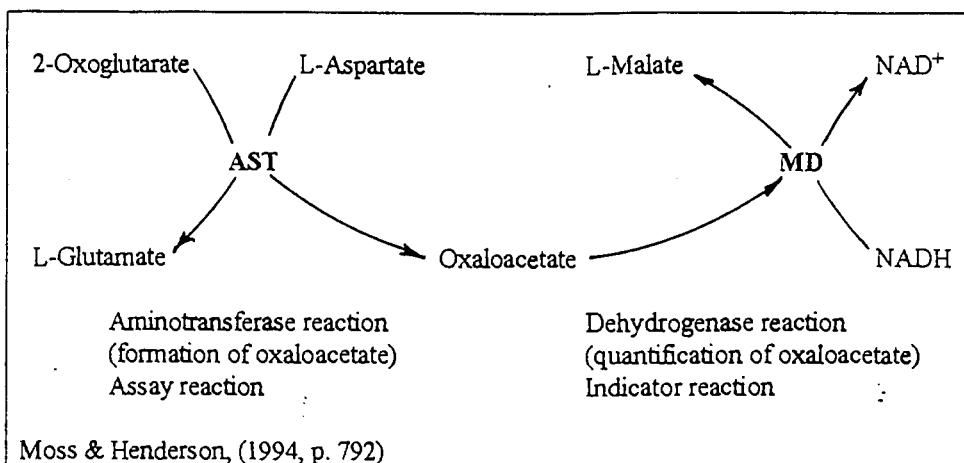
EC 2.7.3.2 Creatine Kinase (CK)

CK activity is determined by the rate of NADPH formation as illustrated below.

a)

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow[\text{pH 6.7}]{\text{CK}} \text{Creatine} + \text{ATP}$$

$$\text{ATP} + \text{glucose} \xrightarrow{\text{HK}} \text{glucose-6-phosphate} + \text{ADP}$$

$$\text{Glucose-6-phosphate} + \text{NADP}^+ \xrightarrow{\text{GPD}} \text{6-phosphogluconate} + \text{NADPH} + \text{H}^+$$

Moss & Henderson, (1994, p. 803)

b)

$$\text{Creatine phosphate} + \text{ADP} \underset{}{\overset{\text{CK}}{\rightleftharpoons}} \text{Creatine} + \text{ATP}$$

$$\text{Glycerol} + \text{ATP} \xrightarrow{\text{GK}} \text{glycerol-3-P} + \text{ADP}$$

$$\text{Glycerol-3-P} + \text{O}_2 \xrightarrow{\text{GPO}} \text{dihydroxyacetone phosphate} + \text{H}_2\text{O}_2$$

$$\text{H}_2\text{O}_2 + \text{indicator (colourless)} \xrightarrow{\text{POD}} \text{dye} + \text{H}_2\text{O}$$

Braun, et al., (1987)
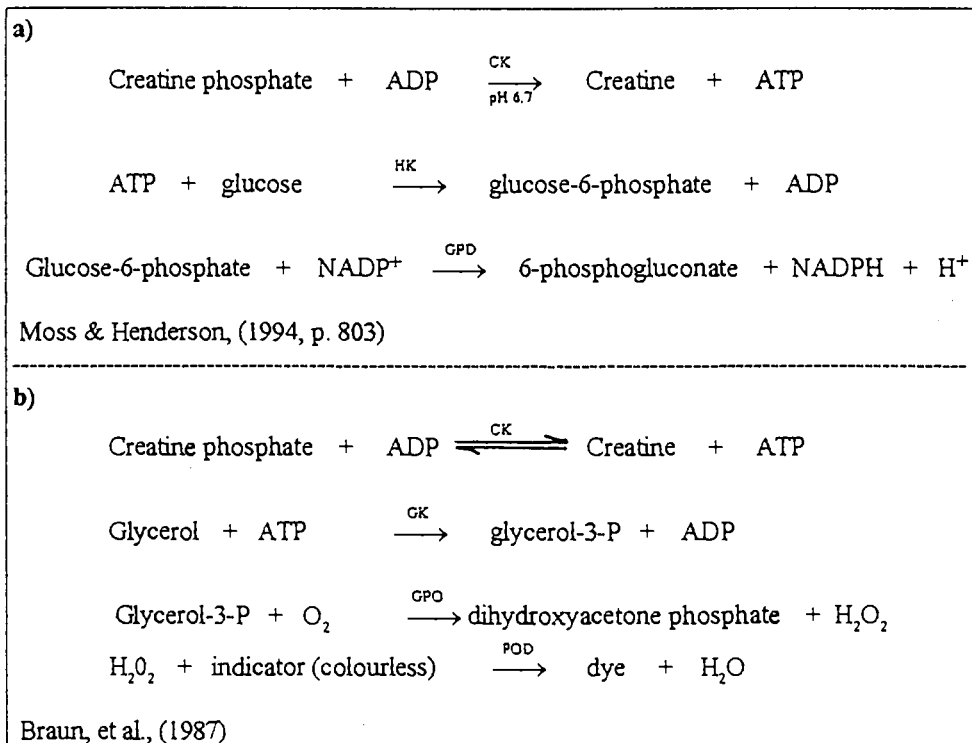
Biochemical Test Principles

Myoglobin

Unable to distinguish between cardiac and skeletal muscle myoglobin, and is generally determined by radioimmunoassay, kits are available from Biomerica Inc. Newport Beach, CA (Fairbanks & Klee, 1994). The method development and normative values for radioimmunoassay for humans is available from Rosano & Kenny, (1977).

EC 1.1.1.27 Lactate Dehydrogenase (LDH)

pyruvate is reduced to lactate in the presence of LDH, with the accompanying oxidation of NADH to NAD^+ measuring the rate of absorption decrease at 339nm by spectrophotometer.

$$
\begin{array}{ccc}
\text{CH3} & & \text{CH3} \\
| & & | \\
\text{H}-\text{C}-\text{O}-\text{H} + \text{NAD}^+ \xrightarrow[\text{pH 7.4 - 7.8}]{\substack{\text{LD}\\ \text{pH 8.8- 9.8}}} & & \text{C}=\text{O} + \text{NADH} + \text{H}^+ \\
| & & | \\
\text{C}=\text{O} & & \text{C}=\text{O} \\
| & & | \\
\text{O}^- & & \text{O}^-
\end{array}
$$

L-Lactate   Pyruvate

Moss & Henderson, (1994, p. 813)
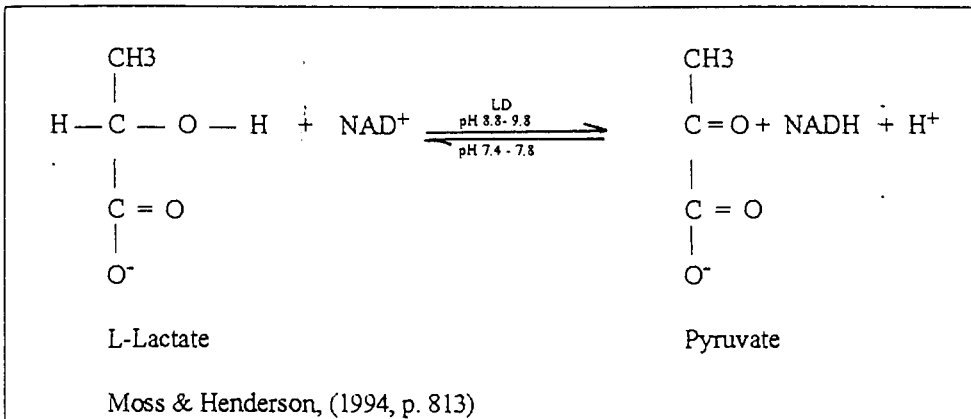
Newspaper Advertisement

VOLUNTEERS WANTED

Exercise physiology postgraduate researcher at Edith Cowan University's Joondalup Campus requires volunteers for a four-week muscle function study. The volunteers need to meet one of the following criteria:

CRITERION 1:
Preferably under 50 years of age and diagnosed with Chronic Fatigue Syndrome (CFS) or Post Viral Fatigue Syndrome

CRITERION 2:
Preferably under 50 years of age and in the opinion of the coach or athlete, has Overtraining Syndrome (OTS) or has been diagnosed as having OTS.

Prospective volunteers would need to be able to attend the Exercise Physiology laboratory at the University's Joondalup Campus on 10 separate occasions over a four-week period to undergo muscle function testing.

Interested parties should contact David Wright on telephone (09) ▮ or after hours on (09) ▮

EDITH COWAN UNIVERSITY
PERTH WESTERN AUSTRALIA

TO BE PUBLISHED: WEST AUSTRALIAN, SATURDAY, OCTOBER 22

JOONDALUP TIMES, OCTOBER 28

Advertising Flyer

Volunteers Wanted

Introduction
Chronic fatigue syndrome (CFS) and Overtraining syndrome (OTS) are separate, complex conditions which are difficult to diagnose that have several similar debilitating effects, one of which is myalgia (muscle pain). This research is aimed at providing a diagnostic protocol for CFS and OTS.

Subjects
We require a total of 40 volunteer subjects for muscle damage-recovery research:
- 10 subjects with CFS or Postviral Fatigue Syndrome (PVFS)
- 10 subjects diagnosed with OTS, or believe they might be overtraining
- 20 subjects without CFS, PVFS or OTS

As a Volunteer Subject You Would:
- Be able to attend the Exercise Physiology laboratory at Edith Cowan University (ECU) Joondalup campus on approximately ten occasions over a 4 week period,
- Undergo one single bout of muscle damaging exercise on your non-dominant arm (biceps) which will **probably** result in some discomfort and reduced mobility in
  this arm for about 1 week,
- Have blood samples taken on each test day,
- Provide one urine sample,
- Undergo strength tests both prior to and after the damaging bout,
- Undergo non-voluntary stimulation of your biceps,
- Undergo tests to determine the level and location of muscle pain,
- As much as possible not change your exercise and diet patterns during this time.

What You Can Expect Of Us
- Be provided with a full briefing prior to, and after any test being undertaken,
- Be treated in a respectful and informed manner.
- Have your confidentiality respected, and
- To respect your right to withdraw from the research at any time without question,

Who To Contact
Any questions or further information can be gained from David Wright on 4055553 or 4781488 (AH)

Appendix D

Confidential

Chronic Fatigue Syndrome (CFS) / Overtraining Syndrome (OTS)

Questionnaire

Name:
Date of Birth:
Sex:
Diagnosis:

How long have you been diagnosed with CFS / OTS?

....

Do you have any Post-Viral infection? if so what infection?

....

If you have CFS has your condition occurred following heavy bouts of exercise? Please describe the level and type of activity undertaken.

....
....
....
....

Do you presently suffer from muscle pain? If so please describe the nature and location of this pain.

....
....
....

Appendix D

Please list any prescription drugs or supplements you are currently taking.

....

....

....

Strain Gauge Calibration Procedures & Schedule.

The aim of the calibration procedure was to convert the voltage response from the Status-30 program into newtons therefore it was necessary to establish the number of newtons per volt.

Calibration of the strain gauge was completed using known weights, which were Cybex 25 lb calibration weights. Mass of these weights were confirmed to be 1) 11.34 kg, 2) 22.49 kg, 3) 34.02 kg by weighing each weight individually and together on high resolution scales.

With the base line voltage set as near as possible to zero, the program was activated at a frequency of 10 Hz for 1024 samples (102 seconds). During this time the known weights were hung from the strain gauge at 10 second intervals (10 sec 11.34 kg, 20 sec 22.49 kg, & 30 sec 34.02 kg), a weight was then removed every ten seconds.

Once the program completed its sampling, the voltage for each phase was measured and recorded, any base line voltage was subtracted from this figure and calculations made as to the number of Newtons per Volt, this conversion factor was entered into the program setup and details saved.

The procedure of calibration was repeated so that the measurements in Newtons could be compared to the number of newtons of the known calibration weights. Calibration was conducted each week.

Mass (kg)	Newtons	Voltage	Baseline	Volts/Newtons
5/10/94				
11.34	111.25	0.2148	0.0061	0.00188
22.68	222.49	0.4236	0.0061	0.00188
34.02	333.74	0.6262	0.0061	0.00186

Conversion factor 531.91 Newtons per volt, error < 1%

Mass (kg)	Newtons	Voltage	Baseline	Volts/Newtons
10/10/94				
11.34	111.25	0.2148	0.0122	0.00182
22.68	222.49	0.4175	0.0122	0.00182
34.02	333.74	0.6201	0.0122	0.00182

Conversion factor 549.45 Newtons per volt, error < 1%

Appendix E

Mass (kg)	Newtons	Voltage	Baseline	Volts/Newtons

17/10/94

11.34	111.25	0.2148	0.0122	0.00182
22.68	222.49	0.4297	0.0122	0.00188
34.02	333.74	0.6323	0.0122	0.00186

Conversion factor 540.54 Newtons per volt, error < 1%

23/10/94

11.34	111.25	0.2026	0.0	0.00182
22.68	222.49	0.4053	0.00	0.00182
34.02	333.74	0.6201	0.00	0.00186

Conversion factor 545.46 Newtons per volt, error < 1%

31/10/94

11.34	111.25	0.2026	0.00	0.00182
22.68	222.49	0.4175	0.00	0.00188
34.02	333.74	0.6201	0.00	0.00186

Conversion factor 540.54 Newtons per volt, error < 1%

10/11/94

11.34	111.25	0.2148	0.00	0.00193
22.68	222.49	0.4175	0.00	0.00188
34.02	333.74	0.6262	0.00	0.00188

Conversion factor 529.1 Newtons per volt, error < 1%

Mass (kg)	Newtons	Voltage	Baseline	Volts/Newtons
19/11/94				
11.34	111.25	0.2148	0.00	0.00193
22.68	222.49	0.4175	0.00	0.00188
34.02	333.74	0.6262	0.00	0.00188

Conversion factor 529.1 Newtons per volt, error < 1%

28/11/94				
11.34	111.25	0.2148	0.0061	0.00193
22.68	222.49	0.4175	0.0061	0.00188
34.02	333.74	0.6262	0.0061	0.00188

Conversion factor 529.1 Newtons per volt, error < 1%

5/12/94				
11.34	111.25	0.2148	0.00	0.00193
22.68	222.49	0.4175	0.00	0.00188
34.02	333.74	0.6262	0.00	0.00188

Conversion factor 529.1 Newtons per volt, error < 1%

12/12/94				
11.34	111.25	0.2026	0.00	0.00182
22.68	222.49	0.4175	0.00	0.00187
34.02	333.74	0.6201	0.00	0.00186

Conversion factor 540.54 Newtons per volt, error < 1%

Test Sheet

General Information

Name: _____   <u>Proximal</u>

DOB: _____

Height: _____

Sex: _____

Mass: _____
                                          <u>Distal</u>
Race: _____

Cybex Arm: _____   Cybex Height: _____

Cybex X: _____   Cybex O: _____

Preacher Bench Height: _____   Iso MVC Angle: _____

Digitimer AMPS: _____   Files: _____

Test Data

CK: _____

MVC Iso:
Baseline _____

20 Hz:
Baseline _____

50 Hz:
Baseline☐ _____

20 : 50 _____

Pain: _____

Concentric: _____

Eccentric: _____

Pain Proforma

0	=	No pain
10	=	Extremely painful

Proximal

X	X	X	X	X
X	X	X	X	X
X	X	X	X	X
X	X	X	X	X
X	X	X	X	X
X	X	X	X	X

Distal

Appendix H

Raw Data

Physiological Data

	CF1	CF2	CF3	CF4	CF5	CF6	CF7	CF8	CF9	CF10	Mean	SD
Age	29.5	48.6	48.2	41.8	36.8	16.4	45.1	24.0			36.3	11.9
Mass (kg)	63.9	65.6	130.0	89.0	48.7	62.0	59.6	79.0			74.7	25.5
Height (cm)	169	168	155	179	157	166	161	192.5			168.4	12.3
Sex (Male=2)	2	2	1	2	1	1	1	2				
Race	cauc	cauc	cauc	cauc	cauc	cauc	cauc	cauc				
Cy Arm	10	5	3	8	3	4	4	11				
Cybex Ht	13.75	6.00	10.00	6.00	10.00	8.00	8.00	16.00				
Cybex O	30	35	34	33	33	34	34	34				
Cybex X	65	71	69	69	71	1	0	69				
PB Height	2	2	1	2	2	2	2	4				
Iso Angle	66	90	88	90	80	88	83	85			83.8	8.0
Stimulation	225	325	275	300	275	200	275	375				
	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10	Mean	SD
Age	21.3	26.3	29.8	27.3	24.8	19.4	31.8	19.0	37.3	35.3	27.2	6.4
Mass (kg)	58.7	82.2	81.6	60.7	56.2	61.3	71.6	95.0	57.8	83.3	70.8	13.8
Height (cm)	162	188	184	163	159	170	176	185	166	171	172.4	10.4
Sex (Male=2)	1	2	2	1	1	1	2	2	1	2		
Race	cauc	cauc	cauc	cauc	cauc	cauc	cauc	cauc	cauc	cauc		
Cy Arm	5	8	8	1	3	3	5	8	5	7		
Cybex Ht	6.00	6.00	8.25	6.00	13.75	6.50	6.00	18.00	9.00	10.00		
Cybex O	32	32	4	33	6	0	33	33	34	33		
Cybex X	69	70	39	0	36	35	71	70	70	70		
PB Height	1	2	2	1	2	1	1	4	2	2		
Iso Angle	65	82	89	80	86	88	75	89	80	80	81.4	7.4
Stimulation	250	400	300	275	250	250	275	325	300	250		
	ND1	ND2	ND3	ND4	ND5	ND6	ND7	ND8	ND9	ND10	Mean	SD
Age	35.4	26	30.6	22.3	22.2	23.5	25.5				26.5	4.9
Mass (kg)	52.8	65.4	66.5	67.3	53.7	81.6	73.3				65.8	10.2
Height (cm)	163	178	170	177	162	185	176				173.0	8.4
Sex (Male=2)	1	1	2	2	1	2	2					
Race	cauc	cauc	cauc	cauc	asian	cauc	asian					
Cy Arm	5	7	7	8	3	8	4					
Cybex Ht	8.00	12.00	6.00	13.75	14.75	13.50	14.00					
Cybex O	33	33	34	33	34	33	32					
Cybex X	68	1	69	70	69	69	71					
PB Height	1	3	2	3	3	3	3					
Iso Angle	73	87	89	82	87	90	84				84.6	5.8
Stimulation	250	275	350	500	225	250	275					

Raw Data

Conc, Ecc 90

Concentric	CF1	CF2	CF3	CF4	CF5	CF6	CF7	CF8	CF9	CF10	Mean	Max	Min	SD
Peak Torque	49	43	31	54	16	24	19	38			34	54	16	14
Ave Torque	44	41	29	51	15	23	17	36			32	51	15	13
Ave Power	49	41	34	53	17	26	18	40			35	53	17	13
Total Work	74	59	51	86	23	33	24	60			51	86	23	23
Eccentric	CF1	CF2	CF3	CF4	CF5	CF6	CF7	CF8	CF9	CF10	Mean	Max	Min	SD
Peak Torque	57	65	42	83	28	34	34	60			50	83	28	19
Ave Torque	56	48	40	65	21	28	24	48			41	65	21	16
Ave Power	58	48	44	68	19	30	26	50			43	68	19	17
Total Work	89	72	67	102	26	39	35	78			63	102	26	27
Concentric	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10	Mean	Max	Min	SD
Peak Torque	30	50	71	33	23	28	37	54	41	50	42	71	23	15
Ave Torque	29	47	71	31	23	25	36	53	38	49	40	71	23	15
Ave Power	15	59	90	39	24	23	45	64	44	57	46	90	15	23
Total Work	32	78	126	48	42	33	60	86	61	77	64	126	32	29
Eccentric	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10	Mean	Max	Min	SD
Peak Torque	37	69	106	46	35	28	50	71	49	69	56	106	28	23
Ave Torque	32	61	96	40	28	24	48	62	43	62	50	96	24	21
Ave Power	32	68	105	43	26	23	54	69	46	66	53	105	23	25
Total Work	46	97	158	57	49	36	76	99	64	94	78	158	36	36
Concentric	ND1	ND2	ND3	ND4	ND5	ND6	ND7	ND8	ND9	ND10	Mean	Max	Min	SD
Peak Torque	27	45	61	64	27	72	41				48	72	27	18
Ave Torque	25	42	58	62	27	70	41				46	70	25	17
Ave Power	42	49	63	74	22	79	46				54	79	22	20
Total Work	29	41	91	104	34	113	61				68	113	29	35

Raw Data

Eccentric Sets Data

	CF2	CF4	CF5	CF6	CF7	CF8	Mean	Max	Min	SD				
Set 1	65	83	28	34	34	60	50.7	83	28	22				
Set 2	56	77	24	33	28	57	45.8	77	24	21				
Set 3	53	71	20	31	26.0	54	42.5	71	20	20				
Set 4	46	62	19	27	22	45	36.8	62	19	17				
Set 5	41	60	19	26	23	43	35.3	60	19	16				
Set 6	37	52	18	23	19	39	31.3	52	18	14				
Set 7	35	49	18	22	19	37	30.0	49	18	12				
	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10	Mean	Max	Min	SD
Set 1	35	69	95	46	35	28	50	71	49	69	54.7	95	28	21
Set 2	37	65	106	45	31	24	50	66	42	62	52.8	106	24	24
Set 3	31	61	100	38	28	27	49	61	46	66	50.7	100	27	22
Set 4	31	61	96	41	28	23	49	57	43	62	49.1	96	23	21
Set 5	30	60	91	38	27	23	47	62	42	61	48.1	91	23	21
Set 6	28	57	89	35	26	24	45	57	42	53	45.6	89	24	20
Set 7	30	53	96	39	23	22	49	57	35	60	46.4	96	22	22

	CFS (n	CD (n	CF SE	CD SE			CFS (	CD (r	CF SE	CD SE
Set 1	50.7	54.7	8.9	6.5		Set 1	100.0	100.0	17.5	11.8
Set 2	45.8	52.8	8.4	7.4		Set 2	90.3	96.5	16.5	13.5
Set 3	42.5	50.7	8.0	7.0		Set 3	85.0	92.6	15.7	12.7
Set 4	36.8	49.1	6.8	6.7		Set 4	72.5	89.7	13.4	12.2
Set 5	35.3	48.1	6.3	6.5		Set 5	69.6	87.9	12.4	11.8
Set 6	31.3	45.6	5.5	6.2		Set 6	61.7	83.3	10.8	11.3
Set 7	30.0	46.4	5.0	6.9		Set 7	59.1	84.8	9.8	12.6

	CF2	CF4	CF5	CF6	CF7	CF8	sem				
Set 1	100	100	100	100	100	100	0.0				
Set 2	86.1	92.8	85.7	97.1	82.4	95.0	2.4				
Set 3	81.5	85.5	71.4	91.2	76.5	90.0	3.2				
Set 4	70.8	74.7	67.9	79.4	64.7	75.0	2.2				
Set 5	63.1	72.3	67.9	76.5	67.6	71.7	1.9				
Set 6	56.9	62.7	64.3	67.6	55.9	65.0	1.9				
Set 7	53.8	59.0	64.3	64.7	55.9	61.7	1.8				
	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10	sem
Set 1	100	100	100	100	100	100	100	100	100	100	0
Set 2	105.7	94.2	111.6	97.8	88.6	85.7	100.0	93.0	85.7	89.9	2.7
Set 3	88.6	88.4	105.3	82.6	80.0	96.4	98.0	85.9	93.9	95.7	2.5
Set 4	88.6	88.4	101.1	89.1	80.0	82.1	98.0	80.3	87.8	89.9	2.2
Set 5	85.7	87.0	95.8	82.6	77.1	82.1	94.0	87.3	85.7	88.4	1.7
Set 6	80.0	82.6	93.7	76.1	74.3	85.7	90.0	80.3	85.7	76.8	2
Set 7	85.7	76.8	101.1	84.8	65.7	78.6	98.0	80.3	71.4	87.0	3.5

Appendix H

Raw Data

Creatine Kinase Raw Data

	CF2	CF4	CF5	CF6	CF7	CF8	Mean	Max	Min	SD
P-Test	98	111	79	83	53	106	88	111	53	21
1	863	284	132	112	129	168	281	863	112	292
2	2544	2228	354	249	160	685	1037	2544	160	1065
4	9240	12720	9520	5560	4400	8890	8388	12720	4400	2998
6	5201	4680	3560	2180	1230	3768	3437	5201	1230	1499
8	1286	902	1020	602	650.0	1926	1064	1926	602	491
12	177	122	424	106	80	151	177	424	80	128
16	133	97	100.0	76	63	68	89	133	63	26
20	129	136	100.0	67	63	84	97	136	63	31
24	95	99	100.0	53	44	121	85	121	44	30
28	189	68	100.0	66	38	86	91	189	38	52

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10	Mean	Max	Min	SD
P-Test	101	292	159	171	79	55	97	278	64	132	143	292	55	84
1	110	204	245	222	129	67	129	240	97	294	174	294	67	76
2	270	2260	174	8150	475.00	1110	332	132	443	179	1353	8150	132	2476
4	2780	3870.0	490.0	7800	599	1548	4960	1040	2280	459	2583	7800	459	2379
6	1300	3870	490	2040	862	366	2456	497	1000.0	884	1377	3870	366	1108
8	733	2157	388	523	533	115	763	135	92	283	572	2157	92	608
12	102	345	368	120	66	127	131	177	144	291	187	368	66	107
16	86	223	168	185	87	69	97	87	37	256	129	256	37	73
20	197	275	151	196	108	55	98	83	60.0	178	140	275	55	71
24	81	225.0	192	159	65	69	63	54	60.0	123	109	225	54	62
28	453	169	105	273	88	44	84	61	60.0	103	144	453	44	128

	ND1	ND3	ND4	ND5	ND6	ND7	Mean	Max	Min	SD
P-Test	321	159	129	66	369	158	200	369	66	118
1	204	133	167	80	238	165	165	238	80	55
2	224	121	197	113	70	102	138	224	70	60
4	196	126	261	82	166	108	156	261	82	65
6	196.0	96	251	70	189	107	152	251	70	71
8	195	121	266	61	188	83	152	266	61	78
12	196	120	156	50	163	188	145	196	50	54
16	124	115	210.0	52	160.0	141	134	210	52	52
20	172	206	266	50	154	368	203	368	50	108
24	180.0	109	247	52.5	175.0	200.0	161	247	53	69
28	190	96	245	55	193	53	139	245	53	81

	CFS (n	CD (n	ND (n	se	se	se		CFS (n	CD (n	cfse	cdse
P-Test	88	143	200	8.7	26.5	48.1	P-Test	1	5	0.12	3.45
1	281	174	165	119.0	24.1	22.4	1	3	7	1.46	8.13
2	1037	1353	138	434.7	782.8	24.3	2	12	52	4.92	9.87
4	8388	2583	156	1223.7	752.8	26.7	4	100	100	0.00	5.35
6	3437	1377	152	611.8	350.5	28.8	6	40	53	4.62	10.27
8	1064	572	152	200.4	192.2	31.7	8	13	22	1.36	8.40
12	177	187	145	51.3	33.9	22.0	12	2	7	3.42	7.14
16	89	129	134	10.6	23.1	21.3	16	1	5	0.13	3.72
20	97	140	203	12.6	22.5	43.9	20	1	5	0.08	2.94
24	85	109	161	12.2	19.6	28.2	24	1	5	0.05	3.60
28	91	144	139	21.3	40.3	33.1	28	1	5	0.25	2.11

	CF2	CF4	CF5	CF6	CF7	CF8		CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10
P-Test	1.06	0.87	0.83	1.49	1.20	1.19	P-Test	3.63	7.54	32.45	2.10	9.16	3.55	1.96	26.73	2.80	14.93
1	9.33	2.23	1.39	2.01	2.93	1.89	1	3.96	5.27	50.00	2.72	14.97	4.33	2.60	23.08	4.25	33.26
2	27.53	17.51	3.72	4.48	3.64	7.71	2	9.71	58.40	35.50	100.00	55.10	71.71	6.69	12.69	19.43	20.25
4	100.00	100.00	100.00	100.00	100.00	100.00	4	100.00	100.00	100.00	95.71	69.49	100.00	100.00	100.00	100.00	51.92
6	56.28	36.79	37.40	39.20	27.95	42.38	6	46.76	100.00	100.00	25.03	100.00	23.64	49.52	47.79	43.86	100.00
8	13.91	7.09	10.71	10.83	14.77	21.66	8	26.37	55.74	79.18	6.42	61.83	7.43	15.38	12.98	4.04	32.01
12	19.15	0.96	4.45	1.91	1.82	1.70	12	3.67	8.91	75.10	1.47	7.66	8.20	2.64	17.02	6.32	32.92
16	1.43	0.76	1.05	1.37	1.43	0.76	16	3.09	5.76	34.29	2.27	10.09	4.46	1.96	8.37	1.62	28.96
20	1.39	1.07	1.05	1.21	1.43	0.95	20	7.09	7.11	30.82	2.40	12.53	3.55	1.98	8.00	2.63	20.14
24	1.02	0.78	1.05	0.95	1.00	1.36	24	2.91	5.81	39.18	1.95	7.54	4.46	1.27	5.19	2.63	13.91
28	2.04	0.53	1.05	1.18	0.86	0.97	28	16.29	4.37	21.42	3.35	10.21	2.84	1.69	5.87	2.63	11.65

Appendix H

Raw Data

Low Frequency Fatigue Raw Data

	CF2	CF4	CF5	CF6	CF7	CF8	Mean	Max	Min	SD
Pre-test	74.6	70.0	77.0	73.0	76.0	52.6	70.5	77	53	9
Immed P/T	26.3	25.0	0.0	0.0	17.0	40.8	18.2	41	0	16
2	41.7	0.0	0.0	0.0	0.0	40.8	13.8	42	0	21
4	0.0	0.0	0.0	0.0	0.0	53.7	9.0	54	0	22
6	0.0	39.7	0.0	72.1	0.0	48.0	26.6	72	0	31
8	35.8	0.0	0.0	75.0	34.40	61.4	34.4	75	0	31
12	0.0	71.9	63.8	81.2	76.5	69.2	60.4	81	0	30
16	82.0	84.5					83.3	85	82	2
20	80.6						80.6	81	81	#####
28	76.6	74.5	77.00	77.1	82.9	66.5	75.8	83	67	5

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10	Mean	Max	Min	SD
Pre-test	83.5	69.6	79.4	77.6	77.4	77.3	58.8	65.5	74.5	71.5	73.5	84	59	7
Immed P/T	35.1	50.00	57.1	36.0	47.0	0.0	34.0	21.0	0.0	0.0	28.0	57	0	22
2	55.00	55.2	71.8	50.0	57.00	46.0	0.0	22.0	49.2	51.7	45.8	72	0	20
4	76.8	65.00	75.00	70.6	66.5	82.8	33.7	60.3	65.00	50.0	64.6	83	34	14
6	77.00	76.0	79.1	43.5	72.3	82.00	72.7	66.0	70.00	45.3	68.4	82	44	13
8	68.00	68.00	68.00	65.0	68.00	80.9	72.2	55.8	74.0	67.0	68.7	81	56	6
12	67.00	67.00	67.00	67.00	67.00	67.00	67.00	74.3	67.00	65.0	67.5	74	65	2
28	74.5	53.0	77.4	77.6	76.8	84.0	60.3	64.8	75.00	75.3	71.9	84	53	9

	ND1	ND3	ND4	ND5	ND6	ND7	Mean	Max	Min	SD
Pre-test	79.5	83.5	80.0	68.0	62.0	64.7	73.0	84	62	9
Immed P/T	80.00	74.8	62.0	69.0	53.0	58.5	66.2	80	53	10
2	81.4	73.9	73.1	75.0	63.0	64.0	71.7	81	63	7
4	69.9	79.8	71.2	69.1	73.3	68.1	71.9	80	68	4
6	71.2	79.5	72.8	67.0	72.2	68.6	71.9	80	67	4
8	77.2	67.9	73.5	69.4	53.0	71.8	68.8	77	53	8
12	73.50	72.00	73.2	81.0	60.0	74.6	72.4	81	60	7
28	71.0	76.5	67.7	81.9	77.8	73.5	74.7	82	68	5

				CFS	CD	ND					CFS	CD	ND	
	CFS (n	CD (n =	ND (n =	se	se	se		CFS (n	CD (n	ND (n =	se	se	se	
P-Test	70.5	73.5	73.0	3.7	2.3	3.7	P-Test	100	100	100	5.2	3.1	5.0	
I-P/T	18.2	28.0	66.2	6.5	6.8	4.1	I-P/T	25.8	38.0	90.6	9.2	9.2	5.6	
2	13.8	45.8	71.7	8.6	6.4	2.8	2	19.5	62.3	98.2	12.1	8.7	3.8	
4	9.0	64.6	71.9	8.9	4.4	1.7	4	12.7	87.8	98.4	12.6	5.9	2.3	
6	26.6	68.4	71.9	12.6	4.2	1.7	6	37.7	93.0	98.4	17.8	5.7	2.3	
8	34.4	68.7	68.8	12.5	2.0	3.4	8	48.7	93.4	94.2	17.7	2.7	4.6	
12	60.4	67.5	72.4	12.3	0.7	2.7	12	85.6	91.8	99.1	17.4	0.1	3.6	
28	75.8	71.9	74.7	2.1	2.9	2.0	28	107.5	97.8	102.3	2.9	3.9	2.7	

	CF2	CF4	CF5	CF6	CF7	CF8	sem
Pre-test	100.0	100.0	100.0	100.0	100.0	100.0	0
Immed P/T	35.3	35.7	0.0	0.0	22.4	77.6	11.8
2	55.9	0.0	0.0	0.0	0.0	77.6	14.3
4	0.0	0.0	0.0	0.0	0.0	102.1	17
6	0.0	56.7	0.0	98.8	0.0	91.2	19.3
8	48.0	0.0	0.0	102.7	45.3	116.7	20.2
12	0.0	102.7	82.6	111.2	100.8	131.6	18.8
28	102.7	106.4	100.0	106.4	109.8	126.4	3.8

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD9	CD10	sem
Pre-test	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	0.0
Immed P/T	42.0	71.8	71.9	46.4	60.7	0.0	57.8	32.1	0.0	0.0	9.2
2	65.9	79.3	90.4	64.4	73.6	59.5	0.0	33.6	66.0	72.3	8.2
4	92.0	93.4	94.5	91.0	85.9	107.1	57.3	92.1	87.2	69.9	4.4
6	90.7	109.2	99.6	56.1	93.4	106.1	123.6	100.8	94.0	63.4	6.4
8	90.7	97.7	98.6	83.8	96.0	104.7	122.8	85.2	99.3	93.7	3.5
12	90.7	96.3	98.6	86.3	96.0	106.0	112.0	113.4	99.0	90.9	2.9
28	89.2	76.1	97.5	100.0	99.2	108.7	102.6	98.9	99.0	105.3	2.9

	ND1	ND3	ND4	ND5	ND6	ND7	sem		CFS (n	CD (n =	ND (n = 6)
Pre-test	100.0	100.0	100.0	100.0	100.0	100.0	0.0	P-Test	100.0	100.0	100
Immed P/T	100.60	89.6	77.5	101.5	85.5	90.4	3.7	I-P/T	28.5	38.3	91
2	102.4	88.5	91.4	110.3	101.6	98.9	3.2	2	22.3	60.5	99
4	87.9	95.6	89.0	101.6	118.2	105.3	4.6	4	17.0	87.0	100
6	89.6	95.2	91.0	98.5	116.5	106.0	4.2	6	41.1	93.7	99
8	97.1	81.3	91.9	102.1	85.5	111.0	4.5	8	52.1	97.3	95
12	92.30	86.20	91.5	119.1	96.8	115.3	5.6	12	88.2	98.9	100
28	89.3	91.6	84.6	120.4	125.5	113.6	7.2	28	108.6	97.7	104

Appendix H

Raw Data

Pain

Day	1					2						4					6						8						Day	1					2
	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
CD1 A						A						A						A						A						A	CF1 A						A
B					1	B	2	2	2	2	2	B						B						B						B		B						B
C						C						C						C						C		0				C		C						C
D						D	5	6	6	5	5	D						D						D						D		D						D
E						E				5	5	E	8	8	8	8	8	E						E						E		E						E
F					4	F				6	6	F	8	8	8	8	8	F				2		F						F		F						F
CD2	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A						A						A						A						A						A	CF2 A	2					A
B						B		4	5	4		B					6	B						B						B		B	1					B
C						C			5	5		C				6	6	C						C		0				C		C						C
D						D			4	4		D				6	6	D						D						D		D						D
E					3	E	5	4	4	5	5	E			6	6	6	E				2	2	E						E		E						E
F			3	3	3	F	4	5	5	4	4	F	6	6	6	6	6	F				2	2	F						F		F						F
CD3	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A						A	2	3	3	2	2	A						A			2			A						A	CF3 A		4	4	4		A
B						B						B						B						B						B		B		1	1	1		B
C						C	3	4	4	3	3	C						C						C		0				C		C						C
D						D	5	5	5	5	5	D				8	8	D						D						D		D		2	2	2		D
E						E	5	5	5	5	5	E			8	8	8	E						E						E		E	2	2	2	4	2	E
F		3	2	2	3	F	4	4	4	5	5	F			8	9	8	F						F						F		F	2	3	3	3	3	F
CD4	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A						A	3	3	4	4	8	A	2					A		2	3	3		A						A	CF4 A						A
B					2	B					8	B						B		3	2	2		B						B		B						B
C			3			C			4	5	8	C		2	2	3		C		2	2	2		C		0				C		C						C
D	3	3	3	3	3	D		5	5	4	8	D						D		2	2			D						D		D						D
E	4	4	4	4	4	E		4	5		8	E		2	2	2	2	E		3	3			E						E		E					2	E
F	4	4	4	4	4	F	4	4	3	3	8	F	4	3	3		5	F		3	3		2	F						F		F					1	F
CD6	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A						A						A						A						A						A	CF5 A			1			A
B			3	3		B	1	1	1	1		B	1	1	1	1		B						B						B		B	1	1	1		B
C			2			C		2	2			C		2	2			C		2	2			C		0				C		C						C
D			2			D	5	4	4	5	5	D	5	4	4	4	5	D						D						D		D		1	1			D
E	2	2	2	2	2	E	4	6	6	6	5	E	4	5	5	5	5	E						E						E		E						E
F	2	2	2	2	2	F	2	8	8	8	5	F	2	8	8	8	5	F						F						F		F		1		2		F
CD6	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A						A	1					A						A						A						A	CF6 A	2					A
B		1				B	1					B						B	1	1	1			B						B		B	1					B
C		3				C	1					C						C	1	1	1			C		0				C		C						C
D						D	1	1	1	1	2	D		1	1			D	1	1	1			D						D		D						D
E						E						E		1	1			E	1	1	1			E						E		E						E
F						F	3				3	F	1					F						F						F		F						F
CD7	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A						A						A						A						A						A	CF7 A						A
B		5	5	5		B	5	6	6	6		B						B						B						B		B		1	1	1		B
C			6			C	5	7	7	7	5	C						C						C		0				C		C		1	1	1		C
D			6			D	5	7	7	7	5	D				4		D		3	3			D						D		D		1	1	1		D
E	5	5	5	5	5	E	5	5	5	5	7	E						E		3				E						E		E		2	2	2	2	E
F	6	6	6	6	6	F	6	6	4	4	8	F					5	F						F						F		F		2	2	2	2	F
CD8	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A						A	2	2	2	2		A						A						A						A	CF8 A		2	3	2	1	A
B			2	2		B	3	3	3	3		B						B						B						B		B						B
C			2	2		C			3	3	2	C		1				C						C		0				C		C		5	6	5		C
D			3	3	2	D			4	4	1	D		1				D						D						D		D		5	4	5		D
E		4	4	4	2	E			4	4	2	E		2	2	2	2	E						E						E		E		7	6	7	2	E
F	2				2	F	4	4	3	3	2	F		2	2		3	F						F						F		F	3	3	2	3	1	F
CD9	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A	1				1	A	2	2	3	3	2	A						A						A						A	CF9 A						A
B					1	B	3	3	4	4	4	B	2	2	3	2	2	B						B						B		B						B
C					2	C	3	3	4	4	4	C	3	3	4	4	5	C		2	1	1		C		0				C		C						C
D		1			2	D			3	3	7	D	4	4	6	6	7	D		2	2	4	3	D						D		D						D
E		1			3	E		4	4	4	8	E	6	6	8	8	8	E		3		4	4	E						E		E						E
F			3	3	3	F					7	F					9	F					5	F						F		F						F
CD10	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5
A			1	1		A						A						A						A						A	CF10 A						A
B			1	1		B	1	2	2	2		B		2	2	2		B						B						B		B						B
C			2	2		C	2	2	2	2	3	C		3	3	3	1	C						C		0				C		C						C
D			2	2	1	D	3	2	2	2	3	D		3	3	3	2	D						D						D		D						D
E			2	2	1	E	4	1	1	1	4	E	2	4	4	4	3	E						E						E		E						E
F				4	4	F			3	3	4	F	1				5	F					1	F						F		F						F
	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5			1	2	3	4	5

	CF2	CF4	CF5	CF6	CF7	CF8	mean		CD	CD	CD	CD	CD	CD	CD	CD	CD	CD	mean		CF2	CF4	CF5	CF6	CF7	CF8	mean				CD1	CD	CD	CD	CD	CD5	CD6	CD7
p-tes	0	0	0	0	0	0	0	p-te	0	0	0	0	0	0	0	0	0	0	0	p-tes	0.0	0.0	0.0	0.0	0.0	0.0	0.0			p-tes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	2	2	8	2	17	19	8	1	2	4	5	17	14	2	15	13	11	14	#	1	1.5	1.5	1.1	1.5	1.4	3.8	1.8			1	2.5	3.0	2.6	3.4	2.1	2.0	5.5
2	24	18	15	16	19	25	20	2	14	17	25	16	21	10	24	22	23	22	#	2	1.3	2.6	2.3	1.9	1.0	6.1	2.5			2	4.1	3.5	4.0	5.4	4.2	1.5	6.0
4	16	15	8	16	0	5	10	4	10	16	8	11	21	5	2	9	21	18	#	4	1.9	4.0	1.0	3.7	0.0	2.0	2.1			4	8.0	6.0	8.0	2.7	3.7	1.0	4.5
6	9	9	2	5	0	5	5	6	1	4	1	16	2	12	3	0	11	1	5	6	1.0	1.2	1.0	1.4	0.0	0.0	0.8			6	2.0	2.0	2.0	2.4	2.0	1.0	3.0
8	0	0	0	0	0	0	0	8	0	0	0	0	0	0	0	0	0	0	8	0.0	0.0	0.0	0.0	0.0	0.0	0.0			8	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Appendix H

Raw Data

Pain

				4					6					8					
1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
				A					A					A					A
				B					B					B					B
				C					C					C					C
				D					D					D					D
				E					E					E					E
				F					F					F					F

CDE	CD9	CD10	mean		CF	CD			CF	CD									
0.0	0.0	0.0	0.0		Site	Sites (n = 1)		inter	intensity	se	se	se	se						
2.6	1.9	1.9	2.8	Pre	0	0		Pre	0.0	0.0	0.0	0.0	0.0						
2.9	3.8	2.3	3.8	1	8	10		1	1.8	2.8	3.2	1.8	0.4	0.3						
1.9	4.5	2.7	4.3	2	20	19		2	2.5	3.8	1.6	1.5	0.7	0.4						
0.0	2.3	1.0	1.8	4	10	12		4	2.1	4.3	7	2.0	0.6	0.7						
0.0	0.0	0.0	0.0	6	5	5		6	0.8	1.8		1.8	0.2	0.2						
				8	0	0		8	0.0	0.0	0.0	0.0	0.0	0.0						

Appendix H

Raw Data

Isometric Force Raw Data

	CF2	CF4	CF6	CF7	CF8	Mean	Max	Min	SD
P-Test	214	329	175	189	237	228.7	329	175	61
4	137	145	107	110	161	132.0	161	107	23
8	147	184	127.0	130.0	164	150.3	184	127	24
12	153	178	147	140	199	163.4	199	140	25
16	152	199	171	145	204	174.0	204	145	26
20	167	206	171	122	208	174.8	208	122	35
24	192	234	183	139	208	191.3	234	139	35
28	193	262	171	149	218	198.4	262	149	44

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD10	Mean	Max	Min	SD
P-Test	220	282	368	229	210	146	243	305	302	256.1	368	146	65
4	168	232.0	358	174	170	121	191	283	205	211.2	358	121	71
8	187	232	367	169	189	117	221	260	280	224.6	367	117	72
12	188	217	354	200	196	130	214	257	278	226.0	354	130	64
16	201	215	332	187	215	143	233	293	297	235.1	332	143	61
20	228	226	352	193	223	134	235	287	277	239.4	352	134	61
24	220	236.0	339	208	233	142	227	306	281	243.6	339	142	58
28	204	246	326	204	227	148	256	328	278	246.1	328	148	59

	ND1	ND3	ND4	ND5	ND6	ND7	Mean	Max	Min	SD
P-Test	187	312	361	207	329	287	280.6	361	187	69
4	219	270	368	193	330	268	274.7	368	193	66
8	200	312	406	203	389	269	296.5	406	200	89
12	201	346	386	177	382	297	298.2	386	177	91
16	205	333	390.0	205	400.0	306	306.5	400	205	86
20	222	316	392	218	419	296	310.4	419	218	84
24	200.0	294	391	210.0	425.0	275.0	299.2	425	200	92
28	189	291	395	202	435	257	294.6	435	189	101

	CFS (n	CD (n	ND (n	CFS SE	CD SE	ND SE	CFS SEM	CD SEM	ND SEM
P-Test	228.7	256.1	280.6	27.1	21.7	28.2	0	0	0.0
4	132.0	211.2	274.7	10.3	23.7	26.8	4.1	3	4.3
8	150.3	224.6	296.5	10.7	24.1	36.3	2.9	2.6	3.8
12	163.4	226.0	298.2	10.9	21.2	37.0	5.5	1.9	4.3
16	174.0	235.1	306.5	11.8	20.1	35.0	6.4	2.8	3
20	174.8	239.4	310.4	15.7	20.4	34.2	6.7	2.8	4.2
24	191.3	243.6	299.2	15.6	19.3	37.7	6.1	2.2	5.3
28	198.4	246.1	294.6	19.6	19.6	41.2	3.7	2.9	6.3

	CFS (n	CD (n	ND (n =
P-Test	100	100	100
4	57.7	82.4	97.9
8	65.7	87.7	105.6
12	71.4	88.2	106.2
16	76.0	91.8	109.2
20	76.4	93.4	110.6
24	83.6	95.1	106.6
28	86.7	96.1	104.9

	CF2	CF4	CF6	CF7	CF8		ND1	ND3	ND4	ND5	ND6	ND7
P-Test	100.0	100.0	100.0	100.0	100.0	P-Test	100.0	100.0	100.0	100.0	100.0	100.0
4	64.0	44.1	61.1	58.2	67.9	4	117.1	86.5	101.9	93.2	100.3	93.4
8	68.7	55.9	72.6	68.8	69.2	8	107.0	100.0	112.5	98.1	118.2	93.7
12	71.5	54.1	84.0	74.1	84.0	12	107.5	110.9	106.9	85.5	116.1	103.5
16	71.0	60.5	97.7	76.7	86.1	16	109.6	106.7	108.0	99.0	121.6	106.6
20	78.0	62.6	97.7	64.6	87.8	20	118.7	101.3	108.6	105.3	127.4	103.1
24	89.7	71.1	104.6	73.5	87.8	24	107.0	93.3	108.3	101.4	129.2	95.6
28	90.2	79.6	97.7	78.8	92.0	28	101.1	93.3	109.4	97.6	132.2	89.5

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD10
P-Test	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
4	76.4	82.3	97.3	76.0	81.0	82.9	78.6	92.8	67.9
8	85.0	82.3	99.8	73.8	90.0	80.1	90.9	85.2	92.7
12	85.5	77.0	96.2	87.3	93.3	89.0	88.1	84.3	92.1
16	91.4	76.2	90.2	81.7	102.4	97.9	95.9	96.1	98.3
20	103.6	80.1	95.7	84.3	106.2	91.8	96.7	94.1	91.7
24	100.0	83.7	92.1	90.8	106.2	97.3	93.4	100.3	93.0
28	92.7	87.2	88.6	89.1	108.1	101.4	105.3	107.5	92.1

											mean	sd
cfs	165	214	222	329	174	175	189	237			213	53
cd	220	282	368	229	210	146	243	305	236	302	254	62
nd	187	207	312	367	207	329	287				271	70

Appendix H

Raw Data

Peak Torque (PT) Raw Data

	CF2	CF4	CF6	CF7	CF8	Mean	Max	Min	SD
P-Test	37	50	22	19	35	32.6	50	19	13
4	27	18	12	8.0	23	17.6	27	8	8
8	18	19.0	14	8.0	28	17.4	28	8	7
12	17.0	20	14	8	26	17.0	26	8	7
16	16	27	16	12	34	21.0	34	12	9
20	23	27	18	14	31	22.6	31	14	7
24	26	31	18	11	33	23.8	33	11	9
28	30	34	18	11	34	25.4	34	11	10

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD10	Mean	Max	Min	SD
P-Test	27	42	64	31	22	23	34	50	45	37.6	64	22	14
4	20	34.0	61	18	19	16	27	42	31	29.8	61	16	15
8	23	34	60	20	16	14	28	38	39	30.2	60	14	14
12	23	30	58	23	19	20	28	37	43	31.2	58	19	13
16	24	30	56	22	18	18	30.0	39.0	45	31.3	56	18	13
20	24	31	56	24.0	18.0	18.0	33	41	47	32.4	56	18	13
24	24.0	34.0	52	26	18	19	35	42	46	32.9	52	18	12
28	24	38	52	27	20	22	33	45	41	33.6	52	20	11

	ND1	ND3	ND4	ND5	ND6	ND7	Mean	Max	Min	SD
P-Test	23	53	57	24	65	38	43.3	65	23	18
4	24	46	61	23	57	42	42.2	61	23	16
8	22	45	59.0	23	61	39	41.5	61	22	17
12	23	45.0	57	24	57	47	42.2	57	23	15
16	22	45.0	57.0	24	64.0	37	41.5	64	22	17
20	20	46	57	24	71	42	43.3	71	20	19
24	21.0	46	61	25.0	66.0	40.0	43.2	66	21	18
28	22	46	57	26	61	38	41.7	61	22	16

	CFS	CD	ND	CFS SE	CD SE	ND SE		CFS (n	CD (n	ND (n =	CFS SE	CD SE	ND SE
P-Test	32.6	37.6	43.3	5.5	4.6	7.2	P-Test	100	100	100	16.8	12.2	16.6
4	17.6	29.8	42.2	3.4	4.8	6.5	4	53.9	79.2	97.4	10.4	12.7	15.0
8	17.4	30.2	41.5	3.7	4.8	6.8	8	53.3	80.3	95.8	11.3	12.7	15.7
12	17.0	31.2	42.2	3.1	4.2	6.2	12	52.1	82.9	97.4	9.5	11.1	14.3
16	21.0	31.3	41.5	4.0	4.3	6.9	16	64.4	83.2	95.8	12.2	11.4	15.9
20	22.6	32.4	43.3	3.0	4.4	7.9	20	69.3	86.1	100.0	9.2	11.7	18.2
24	23.8	32.9	43.2	4.1	4.0	7.4	24	73.0	87.5	99.7	12.5	10.6	17.0
28	25.4	33.6	41.7	4.6	3.7	6.5	28	77.9	89.3	96.3	14.1	9.8	15.0

	CF2	CF4	CF6	CF7	CF8	sem		ND1	ND3	ND4	ND5	ND6	ND7	sem
P-Test	100.0	100.0	100.0	100.0	100.0	0.0	P-Test	100.0	100.0	100.0	100.0	100.0	100.0	0
4	73.0	36.0	54.5	42.1	65.7	6.9	4	104.3	86.8	107.0	95.8	87.7	110.5	4.1
8	48.6	38.0	63.6	42.1	80.0	7.7	8	95.7	84.9	103.5	95.8	93.8	102.6	2.8
12	45.9	40.0	63.6	42.1	74.3	6.7	12	100.0	84.9	100.0	100.0	87.7	123.7	5.6
16	43.2	54.0	72.7	63.2	97.1	9.2	16	95.7	84.9	100.0	100.0	98.5	97.4	2.3
20	62.2	54.0	81.8	73.7	88.6	6.3	20	87.0	86.8	100.0	100.0	109.2	110.5	4.2
24	70.3	62.0	81.8	57.9	94.3	6.7	24	91.3	86.8	107.0	104.2	101.5	105.3	3.4
28	81.1	68.0	81.8	57.9	97.1	6.7	28	95.7	86.8	100.0	108.3	93.8	100.0	2.9

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD10	sem
P-Test	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	0
4	74.1	81.0	95.3	58.1	86.4	69.6	79.4	84.0	68.9	3.7
8	85.2	81.0	93.8	64.5	72.7	60.9	82.4	76.0	86.7	3.6
12	85.2	71.4	90.6	74.2	86.4	87.0	82.4	74.0	95.6	2.7
16	88.9	71.4	87.5	71.0	81.8	78.3	88.2	78.0	100.0	3.1
20	88.9	73.8	87.5	77.4	81.8	78.3	97.1	82.0	104.4	3.3
24	88.9	81.0	81.3	83.9	81.8	82.6	102.9	84.0	102.2	2.9
28	88.9	90.5	81.3	87.1	90.9	95.7	97.1	90.0	91.1	1.5

Appendix H

Raw Data

Average Peak Torque (AT) Data

	CF2	CF4	CF6	CF7	CF8	Mean	Max	Min	SD
P-Test	36.0	48.0	20.0	16.0	34.3	30.9	48	16	13
4	25.7	15.7	11.3	8.00	21.3	16.4	26	8	7
8	18.0	18.00	13.3	8.00	27.3	16.9	27	8	7
12	17.00	19.5	14.0	8.0	25.0	16.7	25	8	6
16	15.3	24.0	15.3	9.3	33.0	19.4	33	9	9
20	20.3	25.7	17.0	10.7	30.7	20.9	31	11	8
24	22.0	29.0	16.7	9.7	30.3	21.5	30	10	9
28	28.0	32.0	16.0	10.3	32.7	23.8	33	10	10

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD10	Mean	Max	Min	SD
P-Test	25.0	41.0	61.7	30.0	20.3	19.0	33.3	47.0	43.7	35.7	62	19	14
4	17.0	33.3	60.0	17.0	16.7	14.0	26.7	41.5	29.0	28.4	60	14	15
8	23.0	33.3	57.7	19.7	16.0	14.0	26.7	36.3	38.7	29.5	58	14	14
12	21.7	28.3	56.7	21.7	17.7	16.3	26.3	35.7	42.3	29.6	57	16	13
16	23.0	29.3	54.0	21.0	16.3	17.0	29.0	38.0	44.3	30.2	54	16	13
20	23.0	31.0	54.0	23.0	16.0	17.0	32.0	40.0	45.0	31.2	54	16	13
24	23.0	33.0	50.3	24.7	17.2	17.0	32.7	41.7	45.3	31.7	50	17	12
28	23.0	36.3	50.7	26.3	19.5	21.0	32.3	43.0	41.0	32.6	51	20	11

	ND1	ND3	ND4	ND5	ND6	ND7	Mean	Max	Min	SD
P-Test	21.0	51.7	54.3	23.3	61.3	35.7	41.2	61	21	17
4	23.0	45.3	56.0	22.7	56.0	41.3	40.7	56	23	15
8	20.3	43.7	56.0	22.7	55.7	36.3	39.1	56	20	16
12	22.3	45.0	56.3	23.7	55.3	42.3	40.8	56	22	15
16	20.3	45.0	56.0	23.7	60.0	35.3	40.1	60	20	16
20	19.7	45.5	55.7	23.3	65.3	39.0	41.4	65	20	18
24	21.0	46.0	56.0	24.0	62.0	39.0	41.3	62	21	17
28	22.0	45.3	55.0	25.3	60.0	37.7	40.9	60	22	15

				CFS	CD	ND					CFS	CD	ND
	CFS	CD	ND	SE	SE	SE		CFS (n	CD (n	ND (n =	SE	SE	SE
P-Test	30.9	35.7	41.2	5.7	4.6	6.9	P-Test	100	100	100	18.4	12.8	16.7
4	16.4	28.4	40.7	3.2	5.0	6.1	4	53.0	79.5	98.7	10.3	14.0	14.8
8	16.9	29.5	39.1	3.1	4.5	6.3	8	54.6	82.6	94.9	10.0	12.6	15.2
12	16.7	29.6	40.8	2.8	4.3	6.0	12	54.0	82.9	99.0	9.0	12.0	14.5
16	19.4	30.2	40.1	4.1	4.3	6.7	16	62.7	84.5	97.3	13.2	12.0	16.2
20	20.9	31.2	41.4	3.4	4.3	7.2	20	67.6	87.3	100.4	11.0	12.0	17.4
24	21.5	31.7	41.3	3.8	4.0	6.7	24	69.5	88.7	100.2	12.2	11.2	16.2
28	23.8	32.6	40.9	4.5	3.6	6.3	28	77.0	91.3	99.2	14.5	10.0	15.2

	CF2	CF4	CF6	CF7	CF8	sem		ND1	ND3	ND4	ND5	ND6	ND7	sem
P-Test	100.0	100.0	100.0	100.0	100.0	0.0	P-Test	100.0	100.0	100.0	100.0	100.0	100.0	0.0
4	71.4	32.7	56.5	50.0	62.1	6.5	4	109.5	87.6	103.1	97.4	91.4	115.7	4.4
8	50.0	37.5	66.5	50.0	79.6	7.3	8	96.7	84.5	103.1	97.4	90.9	101.7	2.8
12	47.2	40.6	70.0	50.0	72.9	6.5	12	106.2	87.0	103.7	101.7	90.2	118.5	4.7
16	42.5	50.0	76.5	58.1	96.8	9.8	16	96.7	87.0	103.1	101.7	97.9	98.9	2.3
20	56.4	53.5	85.0	66.9	89.5	7.3	20	93.8	88.0	102.6	100.0	106.5	109.2	3.2
24	61.1	60.4	83.5	60.6	88.3	6.2	24	100.0	89.0	103.1	103.0	101.1	109.2	2.7
28	77.8	66.7	80.0	64.4	95.3	5.5	28	104.8	87.6	101.3	108.6	97.9	105.6	3.1

	CD1	CD2	CD3	CD4	CD5	CD6	CD7	CD8	CD10	sem
P-Test	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	0
4	68.0	81.2	97.2	56.7	82.3	73.7	80.2	88.3	66.4	4.1
8	92.0	81.2	93.5	65.7	78.8	73.7	80.2	77.2	88.6	3
12	86.8	69.0	91.9	72.3	87.2	85.8	79.0	76.0	96.8	3.1
16	92.0	71.5	87.5	70.0	80.3	89.5	87.1	80.9	101.4	3.3
20	92.0	75.6	87.5	76.7	78.8	89.5	96.1	85.1	103.0	3.1
24	92.0	80.5	81.5	82.3	84.7	89.5	98.2	88.7	103.7	2.6
28	92.0	88.5	82.2	87.7	96.1	110.5	97.0	91.5	93.8	2.6

Appendix I

INFORMED CONSENT FORM

The aim of this research is to establish the time course of recovery in muscle damage following a maximal eccentric contraction in persons diagnosed as having Chronic Fatigue Syndrome (CFS) or Overtraining Syndrome (OTS), and whether this time course of recovery differs to persons asymptomatic to CFS or OTS. The results of this research has the potential to improve rehabilitation from OTS or CFS.

The study will be conducted over a five week period at the Exercise Physiology Laboratory at the Joondalup campus of Edith Cowan University. As a subject you will required to perform thirty five (7 x 5) maximal eccentric contractions in the biceps of your non-dominant arm on one occasion to elicit damage. Testing will entail six maximal concentric contractions, one maximal isometric contraction and eight contractions activated by tetanic stimulation on the same arm after performing the eccentric contractions. Initially there may be localised tenderness in the biceps muscle following the eccentric contractions and as part of the research, the level of muscle pain will be determined by myometer. A 30 µl blood sample will be taken for analysis on every test day of the study, and will be taken from your finger following pin prick. Testing will take place at pre-test and +1, +2, +4, +6, +8, +12, from then on every four days till the conclusion of the study. All testing information is confidential and will only be used for the purpose of this study. Information will be kept under lock and key, and your data only identifiable through a number coding system held by the principal researchers. Data used in analysis will not include any names. During the period of research we request that you make no major changes to your exercise and nutritional habits. Participation in this study is purely voluntary, and you may withdraw at any time, for any reason.

Any questions about this study can be directed to:

David Wright
Principal Investigator.

Dr Colin James
Exercise Physiologist, Human Movement Dept., Edith Cowan University.

I   have read the informed consent above, and any questions have been answered to my satisfaction. I agree to participate in this study realising that I may withdraw at any time.

I agree that the research data obtained from this study may be published, provided I am not identifiable.

I understand and agree that the Edith Cowan University Human Movement Department will not be held responsible for any injury or permanent damage sustained.

_____   _____
Participant   Date

_____
Investigator

Appendix J

Examples of isometric MVC & 20 : 50 Ratio Traces

Figure 1. CFS2 pre-test isometric MVC and 20:50 Hz trace, 400v, 50ms, square wave, 0.325 amp.
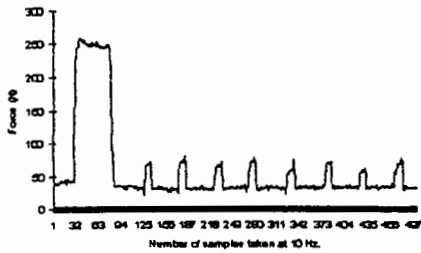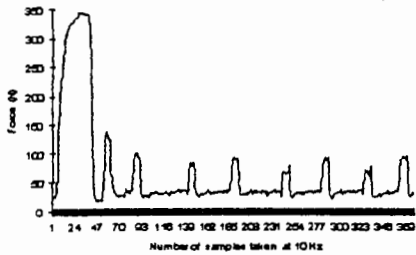
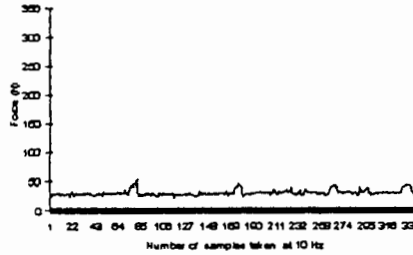Figure 2. CFS2 20:50 ratio immediately post-damage, 400v, 50ms, square wave, 0.450 amp.
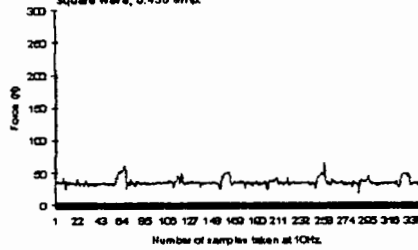
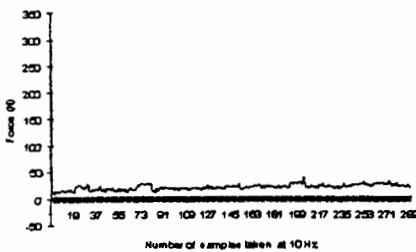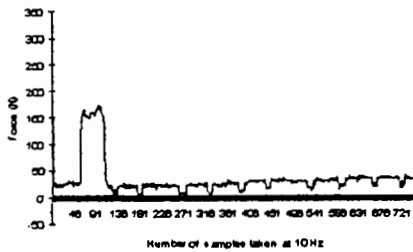Figure 3. CFS2 20:50 Hz ratio 2 days post-damage, 400v, 50ms, square wave, 0.450 amp.
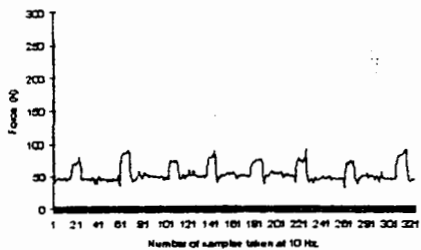
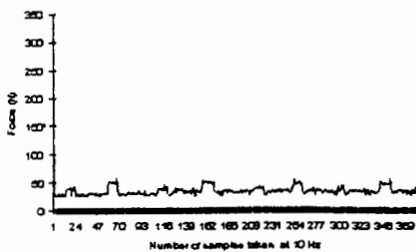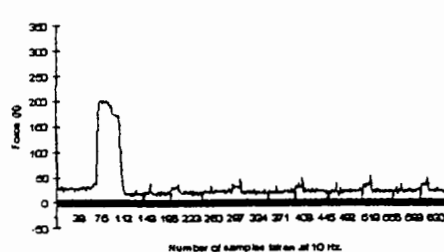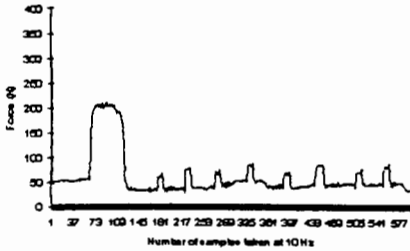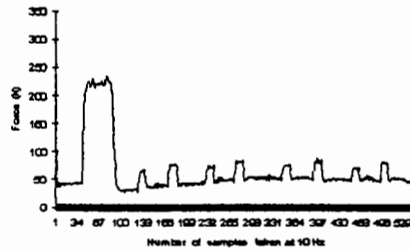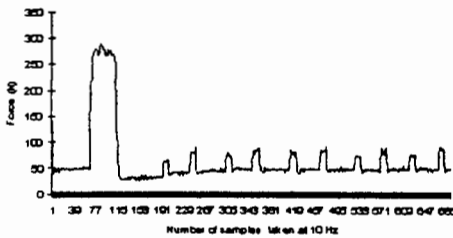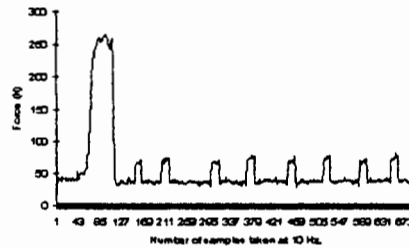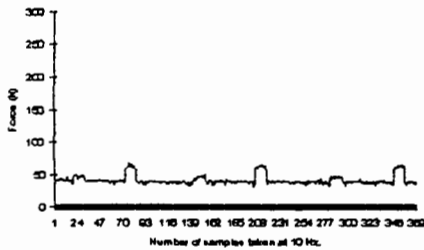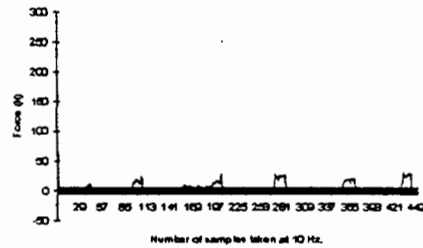Figure 4. CFS2 20:50 Hz ratio 4 days post-damage, 400v, 50ms, square wave, 0.475 amp.
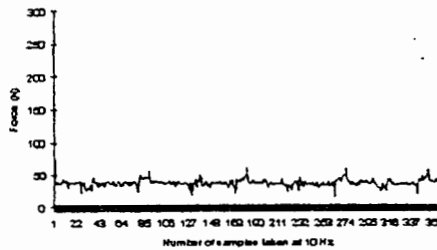
Figure 5. CFS2 20:50 Hz ratio 6 days post-damage, 400v, 50ms, square wave, 0.475 amp.
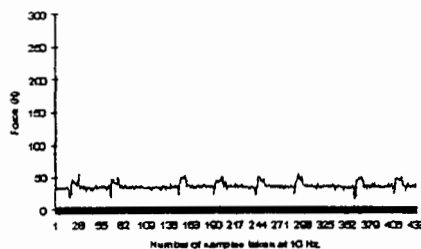
Figure 6. CF2 20:50 Hz ratio 8 days post-damage, 400v, 50ms, square wave, 0.500 amp.
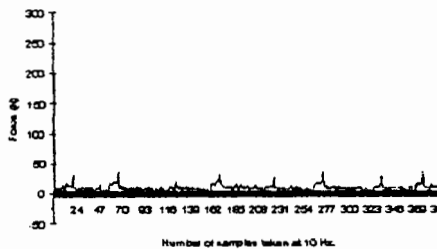
Figure 7. CFS2 20:50 Hz ratio 12 days post-damage, 400v, 50ms, square wave, 0.500 amp.
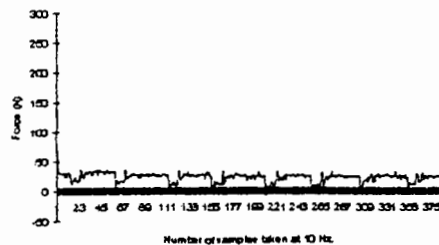
Figure 8. CFS2 20:50 Hz ratio 16 days post-damage, 400v, 50ms, square wave, 0.400 amp.
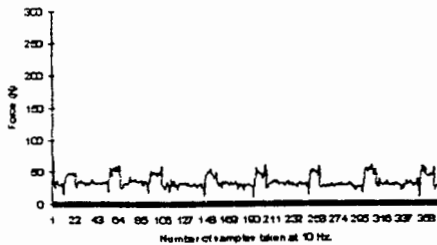
Appendix J

Examples of isometric MVC & 20 : 50 Ratio Traces

Figure 9. CFS2 isometric MVC and 20:50 Hz ratio 20 days post-damage, 400v, 50ms, square wave, 0.450 amp.
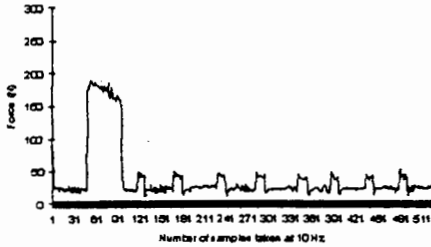
Figure 10. CFS2 isometric MVC and 20:50 Hz ratio at post-test 28 days after damage bout, 400v, 50ms, square wave, 0.325 amp.
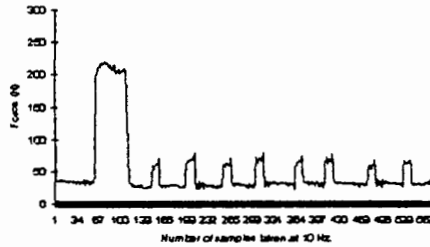
Figure 11. CFS4 isometric MVC, and 20:50 Hz ratio at pre-test, 400v, 50ms, square wave, 0.300 amp.

Figure 12. CFS4 20:50 Hz ratio immediately post damage bout, 400v, 50ms, square wave, 0.300 amp.

Figure 13. CFS4 20:50 Hz ratio 2 days post-damage, 400v, 50ms, square wave, 0.450amp.

Figure 14. CFS4 isometric MVC and 20:50 Hz ratio 4 days post-damage, 400v, 50ms, square wave, 0.550 amp.
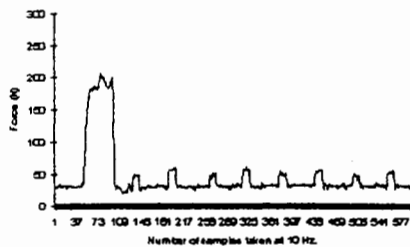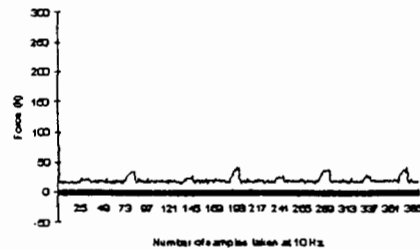
Figure 15. CFS4 20:50 Hz ratio 6 days post-damage, 400v, 50ms, square wave, 0.500 amp.

Figure 16. CFS4 isometric MVC and 20:50 Hz ratio 8 days post-damage, 400v, 50ms, square wave, 0.650 amp.

Appendix J

Examples of isometric MVC & 20 : 50 Ratio Traces

Figure 17. CFS4 Isometric MVC and 20:50 Hz ratio 12 days post-damage, 400v, 50ms, square wave, 0.475 amp.
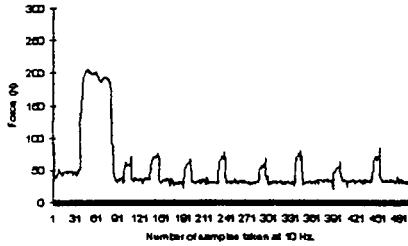
Figure 18. CFS4 Isometric MVC and 20:50 Hz ratio 18 days post-damage, 400v, 50ms, square wave, 0.375 amp.

Figure 19. CFS4 Isometric MVC and 20:50 Hz ratio at post-test 28days post damage, 400v, 50ms, square wave, 0.300 amp.

Figure 20. CD4 Isometric MVC and 20:50 Hz ratio at pre-test, 400v, 50ms, square wave, 0.275 amp.

Figure 21. CD4 20:50 Hz ratio immediately post-damage, 400v, 50ms, square wave, 0.275 amp.

Figure 22. CD4 20:50 Hz ratio 2 days post damage, 400v, 50ms, square wave, 0.275 amp.

Figure 23. CD4 Isometric MVC and 20:50 Hz ratio 4 days post-damage, 400v, 50ms, square wave, 0.275amp.

Figure 24. CD4 20:50 Hz ratio 6 days post-damage, 400v, 50ms, square wave, 0.275 amp.

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Examples of isometric MVC & 20 : 50 Ratio Traces

Figure 25. CD4 isometric MVC and 20:50 Hz ratio 8 days post damage, 400v, 50ms, square wave, 0.275 amp.

Figure 26. CD4 isometric MVC and 20:50 Hz ratio at post-test 28 days after damage, 400v, 50ms, square wave, 0.275 amp.
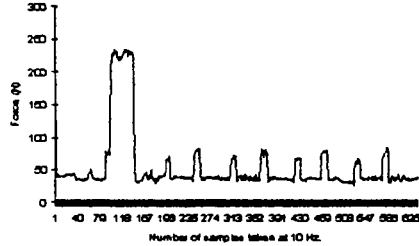

Figure 27. CD8 isometric MVC and 20:50 Hz ratio at pre-test, 400v, 50ms, square wave, 0.325 amp.
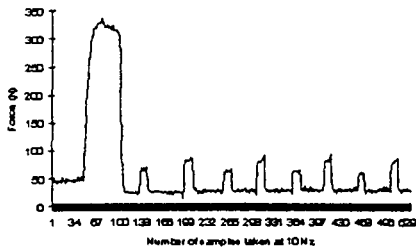

Figure 28. CD8 20:50 Hz ratio immediately post-damage, 400v, 50ms, square wave, 0.325 amp.

Figure 29. CD8 20:50 Hz ratio 2 days post-damage, 400v, 50ms, square wave, 0.325 amp.

Figure 30. CD8 isometric MVC and 20:50 Hz ratio 4 days post-damage, 400v, 50ms, square wave, 0.325 amp.
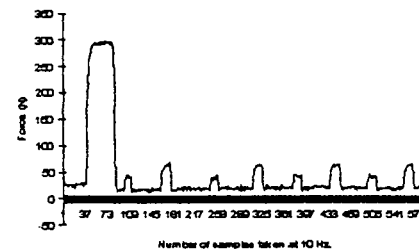

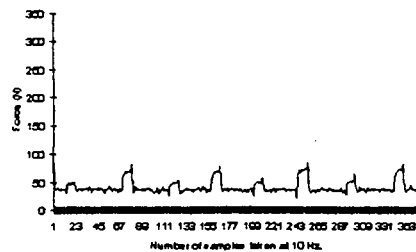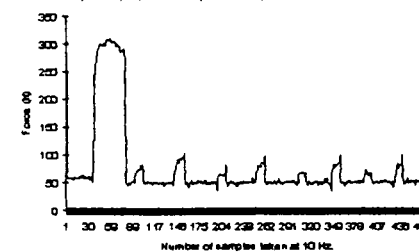Figure 31. CD8 20:50 Hz ratio 6 days post-damage, 400v, 50ms, square wave, 0.325 amp.

Figure 32. CD8 isometric MVC and 20:50 Hz ratio 8 days post damage, 400v, 50ms, square wave, 0.325 amp.

Examples of isometric MVC & 20 : 50 Ratio Traces

Figure 41. ND7 isometric MVC and 20:50 Hz ratio 12 days after pre-test, 400v, 50ms, square wave, 0.275 amp.
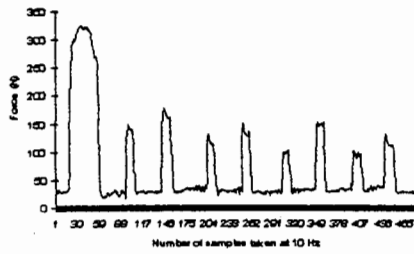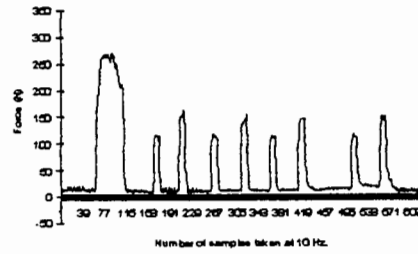

Figure 42. ND7 isometric MVC and 20:50 Hz ratio at post-test 28 days after pre-test, 400v, 50ms, square wave, 0.275 amp.

F Values and Full Statistical Findings

Repeated Measures 2 way ANOVA			
Test Parameter	D.F	F	p
Creatine Kinase			
Between Subjects	(19,2)	10.62	< 0.001
Within Subjects	(190,10)	33.70	< 0.001
Interaction	(190,20)	14.22	< 0.001
Low Frequency Fatigue			
Between Subjects	(19,2)	30.68	< 0.001
Within Subjects	(133,7)	18.10	< 0.001
Interaction	(133,14)	6.86	< 0.001
Isometric Force			
Between Subjects	(17,2)	18.99	< 0.001
Within Subjects	(119,7)	18.76	< 0.001
Interaction	(119,14)	5.84	< 0.001
Peak Torque (PT)			
Between Subjects	(17,2)	19.20	< 0.001
Within Subjects	(119,7)	20.91	< 0.001
Interaction	(119,14)	5.83	< 0.001
Average Peak Torque (AT)			
Between Subjects	(17,2)	21.47	< 0.001
Within Subjects	(119,7)	20.10	< 0.001
Interaction	(119,14)	5.70	< 0.001

F Values and Full Statistical Findings

Students Independent t-test			
Test Parameter	Mean	D.F	p

Delayed Onset Muscle Soreness (time course)

Not significant

Delayed Onset Muscle Soreness (intensity)

		Mean	D.F	p
6 days post-	CFS	0.80		
damage	CD	1.80	14	< 0.05

Eccentric Damage Bout

		Mean	D.F	p
3rd set	CFS	82.70		
	CD	91.50	14	< 0.05
4th set	CFS	72.10		
	CD	88.50	14	< 0.001
5th set	CFS	69.90		
	CD	86.60	14	< 0.001
6th set	CFS	62.10		
	CD	82.50	14	< 0.001
7th set	CFS	59.90		
	CD	82.90	14	< 0.001