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Neuromuscular fatigue in people with chronic stroke

Nada Signal

A thesis submitted for the degree of
Masters in Health Science
At the Auckland University of Technology,
Auckland, New Zealand

Abstract

Aim:

The aim of this study was to examine and compare the contribution of central neuromuscular fatigue and peripheral neuromuscular fatigue to total neuromuscular fatigue in the hemiplegic leg of people with stroke, with that of a matched control group.

Study Design:

This experimental study utilised a repeated measures block design.

Participants:

Fifteen people with chronic stroke who had mild to moderate physical disability and fifteen age, height and weight matched controls were compared.

Main outcome measures

Participants physical function was evaluated using the 30s Chair Stand Test, Comfortable Paced Walking Speed and Fast Paced Walking Speed. Neuromuscular function was measured using maximal voluntary isometric contraction force and voluntary activation. Total neuromuscular fatigue, central neuromuscular fatigue and peripheral neuromuscular fatigue was measured during a 90 second sustained maximal voluntary isometric contraction of the quadriceps muscle.

Results:

The fatigue profile of stroke participants differed from that of control participants. Stroke participants demonstrated less total neuromuscular fatigue ($U=41.00$, $p=.026$) and less peripheral neuromuscular fatigue ($U=14.00$, $p=.000$) than the control participants. While stroke participants did demonstrate greater

central neuromuscular fatigue than control participants, this finding was not statistically significant (U=80.00, p=.817).

Conclusions:

Statistically significant differences were found in the performance of people with mild to moderate physical disability following stroke on measures of neuromuscular fatigue when compared to age, weight and height matched healthy adults.

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I am indebted to all the people who gave up their time to participate in this study, I know it wasn't exactly comfortable, and I am in awe of your generosity and fortitude.

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Contents

List of Figures

List of Tables

Attestation of Authorship

I hereby declare that this submission is my own work and that to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.

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Nada E.J. Signal

15th February 2007

1. Introduction

The ability to sustain physical activity over a period of time is a fundamental component of everyday living, whether it be to maintain a sitting position, climb a set of stairs or walk to the shops. Neuromuscular fatigue is defined as an activity induced impairment in the ability to exert force, and is quantified by the reduction in force that a muscle or muscles can exert following or during an activity (Gandevia, Enoka, McComas, Stuart, & Thomas, 1995). Without the ability to maintain force over time, physical activity is limited.

Neuromuscular fatigue has been attributed to all aspects of the neuromuscular system including the central nervous system, peripheral nervous system and muscle. For clarity, the different levels of the system are usually referred to as peripheral, including neuromuscular junction and muscle fibre deficits and central, including brain, spinal cord and peripheral nerve deficits. Peripheral neuromuscular fatigue may result from the accumulation of metabolites, depletion of substrates, effects on excitation-contraction coupling and deficits in the transmission of impulses at the neuromuscular junction (Paul & Wood, 2002). Central neuromuscular fatigue is identified as depletion in the voluntary activation of the motor neuron pool by the nervous system (Herbert & Gandevia, 1999). Researchers suggest that deficits in voluntary activation may occur due to a reduction in motor evoked potentials, alteration in cortical excitability, increased inhibition from afferents and alterations in motor unit firing rates ((Paul & Wood, 2002, Gandevia, Allen, & McKenzie, 1995).

While neuromuscular fatigue is a normal phenomenon, seen in people without pathology, the degree to which it affects an individual during a given task

may determine whether or not it is considered pathological (Paul & Wood, 2002). Abnormally high levels of neuromuscular fatigue have the potential to limit physical activity and result in a loss of physical independence. Increased neuromuscular fatigue may be concomitant with muscle weakness, or an independent phenomenon, and is identified as of particular relevance in people with neurological pathologies, such as stroke (McComas, Miller, & Gandevia, 1995).

Stroke affects approximately 223 people per 100,000, per year in New Zealand, and is similarly prevalent in other developed countries (Anderson et al., 2005). Stroke causes significant disability and potentially impacts on a person's ability to participate in society. Of those people who have a stroke, approximately eighty eight percent are expected to experience some impairment in neuromuscular function (Bonita & Beaglehole, 1988). This indicates that the neuromuscular impairments associated with stroke are significant, and alterations in both the neural and muscular components of the neuromuscular system have been identified following stroke (Gemperline, Allen, Walk, & Rymer, 1995; Metoki, Sato, Satoh, Okumura, & Iwamoto, 2003; Newham & Hsiao, 2001; Sunnerhagen, Svantesson, Lonn, Krotiewski, & Grimby, 1999; Thickbroom, Byrnes, Archer, & Mastaglia, 2002). Based on what is known about the mechanisms of neuromuscular fatigue development in people without pathology, it may be assumed that these neuromuscular changes are likely to have a significant impact on the development of neuromuscular fatigue following stroke. However, research into neuromuscular fatigue following stroke is scarce. Few studies describe the scope of neuromuscular fatigue, or the contribution of peripheral and central processes to the development of neuromuscular fatigue following stroke.

Both anecdotal and research evidence suggests that neuromuscular fatigue is a problem following stroke (Morley, Jackson, & Mead, 2005; Riley & Bilodeau, 2002; Sunnerhagen et al., 1999). However, studies are generally restricted to people with minimal levels of neuromuscular impairment following stroke (Lindstrom, Gerdle, & Forsgren, 1998; Sunnerhagen et al., 1999; Svantesson, Osterberg, Grimby, & Sunnerhagen, 1998; Svantesson, Sunnerhagen, Carlsson, & Grimby, 1999). A better understanding of the scope of the problem in people with moderate stroke, and its relevance to physical function might assist researchers and clinicians to determine whether neuromuscular fatigue is worthy of greater attention following stroke.

In addition, little is known about the mechanism of neuromuscular fatigue development following stroke, in particular whether it is a phenomenon of central or peripheral origin. Previous studies evaluating neuromuscular fatigue following stroke have had small sample sizes and have relied on measures which fail to elucidate the contribution of central neuromuscular fatigue versus peripheral neuromuscular fatigue to the total fatigue developed (Lindstrom et al., 1998; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999). Although preliminary findings have suggested that central neuromuscular fatigue may be an important contributor, this has not been fully evaluated (Riley & Bilodeau, 2002). A greater understanding of the relative contributions of central and peripheral processes to neuromuscular fatigue following stroke might aid in its management and treatment, and provide direction for future research into its physiological mechanisms.

1.1. Outline of the study

The purpose of this study was to examine and compare the contribution of central neuromuscular fatigue and peripheral neuromuscular fatigue to total neuromuscular fatigue during a sustained maximal voluntary isometric contraction of the quadriceps muscle in the hemiplegic leg of people with stroke, with that of age, height and weight matched controls. Other aims of the study were to consider the association between neuromuscular fatigue, voluntary activation, strength and physical function following stroke and to consider whether measures of maximal voluntary contraction (MVC), voluntary activation and neuromuscular fatigue were reliable in both control and stroke populations.

1.2. Hypotheses

The following general hypotheses were adopted for this study:

1. In people with stroke and control participants, measures of neuromuscular function and neuromuscular fatigue will demonstrate test-retest reliability.
2. Performance of people with stroke will differ from control participants during a sustained maximal voluntary isometric contraction of the quadriceps muscle in measures of neuromuscular fatigue.
    a. Stroke participants will demonstrate greater total neuromuscular fatigue, when compared to control participants
    b. Stroke participants will demonstrate greater central neuromuscular fatigue, when compared to control participants
    c. Stroke participants will demonstrate less peripheral neuromuscular fatigue, when compared to control participants
3. In participants with stroke measures of neuromuscular function, physical function and neuromuscular fatigue will be correlated.

1.3. Delimitations

The following delimitations apply to this study:

1. Fatigue was measured during a sustained 90-second maximal isometric task of the quadriceps muscle. No information on how people with stroke perform during other motor tasks or the participant's perception of fatigue was collected.
2. Measurement of central neuromuscular fatigue and peripheral neuromuscular fatigue was limited to twitch interpolation amplitude measures. No information about the underlying physiological processes which cause neuromuscular fatigue was considered.
3. Extrapolation of the results for the participants with stroke is limited to those people with stroke who have had a single stroke resulting in hemiplegia; are able to walk independently indoors; have mild to moderate hypertonia; and who are at least six months post-stroke.

1.4. Limitations

The following limitations apply to this study:

1. Clinical judgement was used to exclude people with non-hemispheric stroke, as brain imaging of participants with stroke was not available.

1.5. Operational Definitions

Stroke: clinical signs of focal disturbance of cerebral function lasting greater than 24 hours with no apparent cause other than that of vascular origin (Anderson et al., 2005)

Total neuromuscular fatigue: an exercise or activity induced reduction in force that a muscle or muscles can exert

Central neuromuscular fatigue: an exercise or activity induced reduction in voluntary activation of the muscle

Peripheral neuromuscular fatigue: an exercise or activity induced reduction in the force generating capacity of the muscle

Voluntary activation: the level of motoneuronal drive to the muscle during a voluntary contraction

Maximal voluntary contraction: a voluntary contraction which the subject believes to be maximal

2. Literature Review

2.1. Introduction

The purpose of this study was to examine and compare the contribution of central neuromuscular fatigue and peripheral neuromuscular fatigue to total neuromuscular fatigue during a sustained isometric MVC of the quadriceps muscle in the hemiplegic leg of people with stroke, with that of age, height and weight matched controls. This chapter presents a context for the study by providing an overview of neuromuscular fatigue, the neuromuscular changes which are likely to occur following stroke and their potential relationship to the development of neuromuscular fatigue. The evidence for alterations in the neuromuscular fatigue profile in people with stroke, and in younger and older people without pathology, is then considered. Finally, the chapter focuses on the measurement of neuromuscular fatigue, with particular reference to the measurement of central neuromuscular fatigue.

2.2. Neuromuscular Fatigue

Neuromuscular fatigue is defined as an, "acute impairment in the ability to exert force or power" (Allman & Rice, 2002, p. 785) and is quantified by the resultant reduction in force that a muscle or muscles can exert following or during activity. This has particular relevance to the ability to carry out physical functions and to maintain physical activity throughout the day.

Neuromuscular fatigue has been attributed to all aspects of the neuromuscular system including the central nervous system, peripheral nervous system and muscle. Fatigue related changes have been identified at muscle fibre,

muscle fibre membrane, neuromuscular junction, motor neuron and both the segmental and supraspinal circuit levels of the neuromuscular system (Taylor & Gandevia, 2001). For clarity, the different levels of the system are usually referred to as peripheral, including neuromuscular junction and muscle fibre deficits and central, including brain, spinal cord and peripheral nerve deficits.

Peripheral neuromuscular fatigue may result from the accumulation of metabolites, depletion of substrates such as glycogen, effects on excitation-contraction coupling and deficits in the transmission of impulses at the neuromuscular junction (Paul & Wood, 2002). Central neuromuscular fatigue is identified as depletion in the voluntary activation of the motor neuron pool by the nervous system (Herbert & Gandevia, 1999). Deficits in voluntary activation may occur as a result of changes at any level of the nervous system including; the frontal and pre-frontal areas, the motor cortex and sub cortical structures and the spinal networks. Researchers suggest that deficits in voluntary activation may occur due to a decrease in motor evoked potentials, increased cortical excitability threshold, increased intracortical inhibition, increased inhibition from afferents and reduced motor unit firing rates (Gandevia, Allen et al., 1995).

Prior to considering the evidence for neuromuscular fatigue following stroke it is important to gain an understanding of the physiological impact of stroke on the neuromuscular system, in order to be able to reflect on the possible impact of changes in the neuromuscular system on the development of both peripheral and central neuromuscular fatigue.

2.3. Neuromuscular changes following Stroke

Stroke is a central nervous system (CNS) pathology which occurs as a result of compromise to the circulation of the brain, leading to permanent tissue damage through anoxia and ischemia (Carr & Shepherd, 1998). Injury to the cortical and/or sub cortical structures of the brain may affect the sensory, perceptual, cognitive and motor systems. However, damage to any of these systems has the potential to influence motor control, and therefore motor output. Stroke is likely to influence motor output in two ways; through the primary effects of the central nervous system lesion on neuromuscular output, and through the development of secondary changes in the neuromuscular system as a result of the events which occur following the stroke, such as immobilisation and physical inactivity.

Neuromuscular impairments occur in up to eighty eight percent of all people with stroke (Bonita & Beaglehole, 1988). Commonly identified primary neuromuscular impairments include muscle weakness, inco-ordination and hypertonicity (Carr & Shepherd, 1998; Gracies, 2005a; Lum, Burgar, & Shor, 2003; Shumway-Cook & Woollacott, 2001). Frequently acknowledged secondary neuromuscular impairments include muscle contracture and atrophy (Ada, Canning, & Dwyer, 2000; Carr & Shepherd, 1998; Gracies, 2005a; Shumway-Cook & Woollacott, 2001). There is a growing body of evidence regarding the importance of neuromuscular impairments in determining outcome after stroke (Bohannon, 1986; Bohannon & Andrews, 1990; Hamrin et al., 1982; Hsu, Tang, & Jan, 2003; Kim, C. & Eng, 2003; Nakamura, Watanabe, Handa, & Morohashi, 1988; Pohl et al., 2002). However, there has been limited research into the presence, cause and effect of neuromuscular fatigue in people following stroke. This section focuses on the physiological effects of stroke on the neuromuscular system and the potential for

these changes to influence the development of neuromuscular fatigue in people after stroke.

2.3.1. Neural changes

As noted earlier, disruption of the sensory, perceptual, cognitive and motor systems has the potential to influence motor output. The neuromuscular impairments which result from stroke are dependent on both the site and size of the brain lesion. Extensive research using neuroimaging and transcranial magnetic stimulation techniques to map areas of the brain continues to evaluate the impact of the site and size of the brain lesion on motor output (Liepert, 2003; Nudo, Plautz, & Frost, 2001; Schneider & Gautier, 1994). However it is clear that the degree of neuromuscular impairment is influenced by a variety of other factors, not only the site and size of the brain lesion, and that significant interindividual variation is common following stroke (Hendricks, vanLimbeek, Geurts, & Zwarts, 2002) There has been little consideration of the role of lesion location or size in the development of neuromuscular fatigue following stroke. Some authors have considered the influence of lesion location on the person's perception of fatigue, no relationship was identified (Choi-Kwon, Han, Kwon, & Kim, 2004; Ingles, Eskes, & Phillips, 1999; van der Werf, van den Broek, & Anten, 2001).

Recent advances in transcranial magnetic stimulation and other cortical investigative techniques have allowed researchers to consider changes in cortical neural circuitry through interpretation of electrophysiological responses following stroke, and the relationship among these changes, neuromuscular impairments and outcome following stroke (Kobayashi & Pascual-Leone, 2003). Researchers have clearly identified differences in the response to transcranial magnetic stimulation in

people with stroke, when compared to people without neurological pathology (Delvaux et al., 2003; Escudero, Sancho, Bautista, Escudero, & Lopez-Trigo, 1998; Thickbroom et al., 2002; Thickbroom, Byrnes, Archer, & Mastaglia, 2004). Of particular note are changes in the excitability of the motor cortex and the cortex - muscle pathway. These include elevated motor thresholds, reduced amplitude of motor evoked potentials, alterations in intracortical inhibition and a lengthening of motor conduction time (Escudero et al., 1998; Liepert, 2003; Thickbroom et al., 2002, 2004). These alterations are presumed to reflect the neuronal damage caused by the brain lesion and secondary disuse, and are thought to be related to the neuromuscular impairments seen following stroke (Butler, A. J. & Wolf, 2003; Liepert, 2003). Studies suggest a role for transcranial magnetic stimulation in the gross prediction of stroke outcome, as measured by disability (Liepert, 2003). However, the exact relationship between the changes identified using transcranial magnetic stimulation and specific neuromuscular impairments have been poorly investigated. A moderate relationship between electrophysiological measures and strength does appear to exist (Stulin et al., 2003; Thickbroom et al., 2002, 2004), however this may be dependent on the type and severity of stroke, the length of time since stroke and the method used to assess strength. No studies were identified which considered the relationship between electrophysiological changes and the impairment of neuromuscular fatigue.

Studies of brain activity during sustained maximal and submaximal fatiguing contractions in normal participants highlights the role of increasing brain activity in response to a fatiguing motor task (Korotkov et al., 2005; Liu et al., 2003). Neuroimaging studies indicate that increases in brain activity occur in response to sustained motor activity. These increases in levels of brain activity include increase

in the level of activity in currently active areas of the brain and the recruitment of areas of the brain not previously active. What is not clear from these studies is how much of the activity increase represents an attempt to augment the voluntary activation of the muscle and how much reflects processing of afferent input (Korotkov et al., 2005; Liu et al., 2003). During sustained muscle contraction, transcranial magnetic stimulation studies show that the amplitude and area of the motor evoked potential enlarges and the silent period is lengthened, indicating an increase in motor cortex excitability in response to activity in normal participants (Gandevia, Herbert, & Leeper, 1998; Loscher & Nordlund, 2002; Sacco, Thickbroom, Thompson, & Mastaglia, 1997; Todd, Taylor, & Gandevia, 2003). The capacity of the brain to increase activity, recruit additional cortical areas and alter electrophysiological parameters in response to sustained activity following stroke is unclear. Changes in available cortical area and electrophysiological responses following stroke presumably are likely to alter the CNS response to a sustained motor task and therefore increase the potential for central neuromuscular fatigue to develop.

The impact of neural changes following stroke on neuromuscular output may be more grossly quantified using measures of voluntary activation. Voluntary activation refers to the extent that the CNS is driving the muscle at the time of muscle contraction. During an MVC, voluntary activation in people without pathology is between 95 and 100% of the muscles peripheral capacity, dependent on the muscle being investigated. Four studies have identified marked deficits in voluntary activation following stroke (Harris, Polkey, Bath, & Moxham, 2001; Newham & Hsiao, 2001; Newham, Mayston, & Davies, 1996; Riley & Bilodeau, 2002). Based on these studies voluntary activation in people with stroke has been

identified as between 59-66.4% in the more affected side (contralesional) and between 59.3-88.5% on the less affected side (ipsilesional). These findings suggest that the CNS fails to maximally drive muscles on both the more affected and less affected sides following stroke. The extent to which this relates to changes in strength, co-ordination, hypertonicity and neuromuscular fatigue is unclear. It is thought that deficits in voluntary activation reflect the primary effects of the brain lesion (Newham & Hsiao, 2001). It may be hypothesised that reductions in voluntary activation, and the potential inability to maintain voluntary activation during sustained activity, is likely to increase the amount of central neuromuscular fatigue developed following stroke.

Muscle force is graded and sustained through both the recruitment of motor units and the modulation of the rate of recruitment of motor units (Gemperline et al., 1995). Recruitment of motor units is influenced by the amount of voluntary activation from the CNS and potentially also through intraspinal and afferent inputs. Alterations in motor unit recruitment have been identified following stroke (Dietz, Ketelsen, Berger, & Quintern, 1986; Frontera, Grimby, & Larsson, 1997; Gemperline et al., 1995; Jakobsson, Grimby, & Edstrom, 1992; Rosenfalck & Andeassen, 1980).

A number of researchers have acknowledged a reduction in the firing rate of motor units following stroke, when compared to control participants, in a variety of muscles including muscles of the arm, forearm and lower leg (Frontera et al., 1997; Gemperline et al., 1995; Jakobsson et al., 1992; Rosenfalck & Andeassen, 1980). In addition modulation of the firing rate, which is an essential component of force grading and the ability to sustain force during continued contraction, has been recognized as being disturbed following stroke. It has been shown that people with

stroke are unable to increase the firing rate of motor units, or to vary the rate to meet altering task demands (Dietz et al., 1986; Frontera et al., 1997; Gemperline et al., 1995). Rosenflack and colleagues in 1980 reported that poor motor unit firing rate modulation in stroke participants was associated with force fluctuations.

What is not clear from studies of motor unit recruitment following stroke is whether these changes are the result of primary changes in the central nervous system (Gemperline et al., 1995; Jakobsson et al., 1992), secondary transsynaptic degeneration at the segmental level due to a reduction in voluntary activation (Gemperline et al., 1995; McComas, Sica, Upton, & Aguilera, 1973), a response to alterations in the peripheral properties of the motor unit, including motor unit size and fibre type composition (Dietz et al., 1986; McComas et al., 1973; Rosenfalck & Andeassen, 1980), or a response to reduced afferent feedback (Rosenfalck & Andeassen, 1980). Nor is it clear how disordered motor unit recruitment is associated with neuromuscular impairment following stroke. No studies were identified which specifically investigated motor unit recruitment changes and impairments such as weakness, inco-ordination or fatigue. However, some authors highlight the possible role of disturbances in motor unit firing in the development of weakness, the efficiency of force generation, and the development of fatigue following stroke (Gemperline et al., 1995). On the other hand, Thomas and colleagues (2002) hypothesise that some changes in motor unit recruitment seen following stroke may in fact be a secondary strategy to increase overall muscle activation.

Motor unit recruitment alterations following stroke including; the inability to increase the rate of motor unit recruitment and to vary the rate of motor unit recruitment to meet force requirements may result in inefficiencies in force

generation and thereby result in earlier peripheral neuromuscular fatigue through the inappropriate recruitment of type II muscle fibres, and earlier central neuromuscular fatigue through increased effort.

Alterations in neural circuitry following stroke are evidenced by changes in cortical representation, electrophysiological properties, voluntary activation and motor unit recruitment. The relationship between these neural changes and neuromuscular impairments has been established for some electrophysiological properties and muscle strength but not for fatigue. The relationship between deficits in cortical representation, voluntary activation and alterations in motor unit firing and neuromuscular fatigue is not well understood. Based on what is known about neural responses to sustained activity during fatiguing motor tasks in normal participants, it maybe asserted that the effects of stroke on neural processes are likely to cause alterations in the fatigue profile of people following stroke.

2.3.2. Muscular changes

Muscular or peripheral changes including; muscle atrophy, muscle structure changes and fibre type alterations have been identified as potential causes or contributors to neuromuscular impairment following stroke (Datolla et al., 1993; Dietz et al., 1986; Edstrom, 1970; Frontera et al., 1997; Hachisuka, Umezu, & Ogata, 1997; Jakobsson et al., 1992; Jorgensen & Jacobsen, 2001; Metoki et al., 2003; Ramnemark, Nyberg, Lorentzon, Olsson, & Gustafson, 1999; Ryan, Dobrovolny, Smith, & Silver, 2002; Slager, Hsu, & Jordan, 1985; Sunnerhagen et al., 1999). Muscle size, structure and composition are known to influence the ability to generate and sustain force in people without neurological pathology; it is assumed

that these changes would also influence the development of neuromuscular fatigue in people with stroke.

Muscle atrophy in the more affected leg following stroke has been recognized in a number of studies (Jorgensen & Jacobsen, 2001; Metoki et al., 2003; Ryan et al., 2002), while two studies have found no differences between the more affected and less affected legs in relation to muscle atrophy (Ramnemark et al., 1999; Sunnerhagen et al., 1999). It is difficult to distinguish from these studies how sample differences, such as the time since stroke and the severity of impairment and disability, might impact on the disparity of these results. Nevertheless, the use of the less affected leg as a comparison may not be appropriate given the potential influence of ipsilateral voluntary activation deficits and physical inactivity on muscle bulk in the less affected side.

In general it is likely that muscle atrophy does occur in both the less and more affected lower limbs acutely following stroke and that atrophy in the less affected leg resolves as a person becomes physically active (Jorgensen & Jacobsen, 2001). It is unclear whether muscle atrophy in the more affected limb is an independent phenomenon, the result of reduced voluntary activation of the muscle or reduced over all physical activity (Jorgensen & Jacobsen, 2001; Metoki et al., 2003; Sunnerhagen et al., 1999). Nor is it clear how muscle atrophy relates to neuromuscular impairments and particularly to neuromuscular fatigue in people following stroke. Reductions in the muscle mass available to generate and sustain force are likely to result in increased peripheral neuromuscular fatigue.

There is little information available regarding changes to muscle architecture and structure following stroke, including potential changes in cross-sectional area and pennation angle (Patten, Lexell, & Brown, 2004). These factors could also

reduce the ability to generate and sustain force and therefore result in increased peripheral neuromuscular fatigue.

Evidence of changes in muscle composition following stroke is provided by studies using histochemical techniques to investigate fibre type changes and the proportions of different fibre types within muscles. Many studies indicate a relative reduction in the proportion of Type II fibres and an increase in the proportion of Type I fibres in muscles following stroke (Datolla et al., 1993; Dietz et al., 1986; Edstrom, 1970; Hachisuka et al., 1997). However, other studies report contradictory findings, suggesting a relative increase in Type II fibres (deDeyne, Hafer-Macko, Ivey, Ryan, & Macko, 2004; Frontera et al., 1997; Slager et al., 1985). In addition to alterations in the proportion of muscle fibre types, an overall reduction in the number and size of both Type I and II muscle fibres has been reported (Datolla et al., 1993; Frontera et al., 1997). Fronterra and colleagues (1997) suggested that the reduction in size of Type I fibres influenced their ability to generate maximal tension and that there was potentially a reduction in the number of cross-bridges available to generate tension within individual fibres.

Two studies have investigated the relationship between fibre type changes and different variables following stroke, including neuromuscular impairments (Hachisuka et al., 1997; Slager et al., 1985). Both report no correlation between fibre type changes and age, sex, time since onset of stroke, severity of paralysis and disability level. However, Hachisuka and colleagues (1997) demonstrated a relationship between muscle fibre size, fibre type changes and daily physical activity, as measured by a pedometer. This suggests that muscle composition maybe more influenced by actual physical activity than the degree of neuromuscular impairment or disability.

Alterations in the proportion of Type I and Type II fibres may directly impact the development of neuromuscular fatigue, particularly peripheral neuromuscular fatigue in people following stroke. A relative increase in the proportion of Type I fibres may suggest that following stroke people are less likely to exhibit peripheral neuromuscular fatigue, given the fatigue resistant nature of these muscle fibres. Nevertheless, consideration also needs to be given to the effect of alterations in the total number of muscle fibres, reductions in muscle fibre size and ability to generate maximal tension, all of which are likely to increase the potential for peripheral neuromuscular fatigue to develop.

Alterations in muscular properties following stroke are evidenced by research demonstrating muscle atrophy, alterations in fibre type proportions, fibre size and ability to generate tension. It is not known whether changes in muscle architecture are common following stroke. Whether muscular properties relate to the development of neuromuscular fatigue has not been rigorously established, although many researchers assert that fibre type changes are likely to be related to neuromuscular fatigue in people following stroke.

2.3.3. Section Summary

In summary, at first glance it might be assumed that people with stroke are likely to experience predominately central neuromuscular fatigue given that stroke is primarily a pathology of the CNS. However, considering the evidence for changes at multiple levels of the neuromuscular system, including supraspinal, spinal, motor unit, muscle and muscle fibre levels, the development of neuromuscular fatigue in this population is likely to be more complex, potentially affecting the development of both central neuromuscular fatigue and peripheral neuromuscular fatigue.

2.4. Neuromuscular Fatigue following Stroke

Reports of abnormal fatigue following stroke can be divided into two bodies of evidence; studies which evaluate the participants perception of fatigue (subjective fatigue) and studies which objectively measure neuromuscular fatigue during motor tasks. The relationship between subjective fatigue and neuromuscular fatigue is poorly understood in both the normal population and people with neurological pathologies. The concept of subjective fatigue is considered beyond the scope of this paper, therefore, this section focuses specifically on the evidence for altered neuromuscular fatigue in people following stroke.

Given the evidence for muscle weakness and other neuromuscular impairments following stroke (Ada et al., 2000; Andrews & Bohannon, 2000, 2003; Bohannon, 1987, 1997; Bohannon & Andrews, 1990; Brown & Kautz, 1999; Canning, Ada, & O'Dwyer, 1999; Eng, Kim, & MacIntyre, 2002; Harris et al., 2001; Hsu, Tang, & Jan, 2002; Landau & Sahrmann, 2002; Newham, Davies, & Mayston, 1995; Newham & Hsiao, 2001; Newham et al., 1996) there is a surprising dearth of research regarding neuromuscular fatigue following stroke. The few studies which do specifically investigate neuromuscular fatigue following stroke, tend to focus on people with mild physical disability and to use measures of neuromuscular fatigue which make identification of the source of the fatigue difficult to interpret (Lindstrom et al., 1998; Riley & Bilodeau, 2002; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999).

Lindstrom and colleagues (1998) investigated the development of fatigue in stroke participants with minimal or no residual motor deficits. Ten stroke participants were compared with twenty-two healthy participants. Participants

performed ten continuous maximal knee flexion/extension concentric actions at a speed of 90 degrees per second. Peak torque, root mean square (RMS) of electromyography (EMG) and mean frequency of the power density spectrum (MPF) of EMG were recorded. Total neuromuscular fatigue, as measured by decline in peak torque, was demonstrated in the control group and in the unaffected limb of the stroke participants; however total neuromuscular fatigue was only evident in the flexion action of the affected limb of the stroke participants. Differences in total neuromuscular fatigue between control and stroke participants were not statistically analysed and review of the mean values suggest that the difference between the two groups is not likely to have been statistically significant. In control participants and in the less affected limb of stroke participants the MPF of EMG demonstrated significant changes, while no changes were observed in the more affected limb. This failure to alter MPF of EMG during the fatigue task was interpreted as evidence for an increase in Type I muscles fibres and a relative decrease in Type II fibres, although the authors acknowledged that other factors might also influence MPF. RMS values demonstrated no statistically significant changes across the task in the stroke participants for either limb or muscle, although there was large variability in the stroke group in this measure. Whereas, control participants demonstrated marked increases in RMS values.

The results of this study suggest that during a maximal concentric task of alternating flexion and extension of the knee, the more affected limb in participants with mild hemiplegia demonstrate total neuromuscular fatigue in the flexors but not the extensors, and that neither muscle group demonstrates neuromuscular fatigue as measured by EMG parameters. The authors suggest that the failure to develop peripheral neuromuscular fatigue, as determined by MPF, is likely due to a failure to

voluntarily activate the muscle sufficiently to cause peripheral neuromuscular fatigue. It is asserted that increased variability seen in RMS values with fatigue may be due to impairment in the regulation of central drive in stroke participants.

A series of three further studies investigating fatigue in people with stroke were carried out by a research group in Sweden (Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999). The first study considered the development of fatigue during the standing heel-rise test (Svantesson et al., 1998). Eight male participants with mild hemiplegia due to stroke were compared to eight age matched males without pathology. Participants performed repeated concentric and eccentric plantarflexion in a weightbearing position at a set angular velocity until exhaustion. Percentage decline in Work was used as a measure of total neuromuscular fatigue, while MPF and RMS were evaluated. There were no statistically significant differences between the stroke participants and control participants in terms of the amount of total neuromuscular fatigue. There were no significant differences between the participants in terms of either MPF or RMS values. In this study, despite differences in clinical measures of strength and walking speed, no statistically significant differences were noted between control and stroke participants with mild hemiplegia on measures of total neuromuscular fatigue or EMG profile during a weight bearing task.

In a second study, sixteen participants with mild hemiplegia following stroke were compared to age matched control participants (Sunnerhagen et al., 1999). Fatigue of the quadriceps muscle was evaluated during an isometric sustained submaximal (40% MVC) contraction and during fifty continuously performed concentric knee extensions. Total neuromuscular fatigue was evaluated using the time till task failure (endurance time) for the isometric task and torque decline for

the concentric task. Endurance time for the isometric task was not different from the control participants, however the authors state that there was a large amount of individual variation within the stroke group. It was reported that there were no significant differences between the more affected and less affected legs of the stroke participants in torque decline during the concentric task, however no results were presented. The presentation of the results severely limited analysis of the findings of this study, as the results were subdivided into male and female groups and left and rights legs, giving subgroups with as few as two participants. The results provided were generally in graph format, and the data for some key aspects of the study were not presented, it is therefore not possible to comment on group differences or total neuromuscular fatigue during a concentric task. Based on the results available it may be asserted that in people with mild hemiplegia endurance time during an isometric submaximal task of the knee extensors is not different between the less and more affected legs.

In a final study by the same group of researchers the development of fatigue of the plantarflexors was evaluated (Svantesson et al., 1999). Seven male participants with chronic stroke, were compared with seven healthy male controls. The authors did not describe the stroke severity or level of disability of the stroke participants, however, comparison of data relating to peak torque, age of participants, lesion location and time since stroke with that presented in the early study (Svantesson et al., 1998) suggested that the same participants were used for both studies. This would indicate that the participants had mild hemiplegia. Participants performed repeated concentric and eccentric contractions on a KinKom dynamometer until exhaustion. Total neuromuscular fatigue was evaluated using the number of repeated cycles, the percentage decrease in peak torque during both the

concentric and eccentric phases of the task and the percentage decrease in Work (Joules). RMS and MPF were used to evaluate EMG profiles.

There were no statistically significant differences between the more affected leg and either, the less affected leg or the control group in terms of number of repetitions, the decline in peak torque or the percentage decline in Work done across the task, indicating no differences in the total neuromuscular fatigue. The MPF decreased significantly in the both the control group and the less affected leg across the task, but did not decrease in the more affected leg. This finding suggests that during the task both control participants and less affected limb displayed evidence of peripheral neuromuscular fatigue, while the more affected limb of stroke participants did not. The authors do not present statistical analysis of group differences in MPF; however review of difference between the means and standard deviations would suggest that the difference is likely to be significant. Statistical analysis of RMS differences between the groups are also not presented or discussed. The authors suggest that peripheral fatigue factors are not reflected in EMG changes in patients with altered supraspinal control. An alternative explanation may be that following stroke a failure to voluntarily activate the muscle results in reduced peripheral neuromuscular fatigue, and that the net equity of total neuromuscular fatigue between participants with stroke and control participants is due to a relative increase in central neuromuscular fatigue in stroke participants.

One small study by supports this alternative explanation, Riley & Bilodeau (2002) evaluated torque and EMG changes during a sustained maximal isometric task of the elbow flexors in a group of people with stroke. Ten participants, who were more than three months post-stroke, were evaluated, and comparisons made between the more affected and less affected limbs. Participants had variable motor

deficits, with scores of 24-65/66 on the upper limb section of the Fugl-Meyer Motor Assessment, and high levels of functional ability as measured by the Barthel Index (range = 90-100/100). Eight of the ten participants performed a sustained maximal isometric contraction of the elbow flexors until torque decreased below 50% of MVC. The researchers evaluated endurance time, torque forces about the shoulder, elbow and radio-ulnar joint, MPF and RMS of the biceps and brachioradialis muscles and m-wave amplitude of the brachioradialis muscle during this task. The endurance times were similar across limbs. During the fatigue task m-wave amplitude did not decrease in either limb, suggesting that neuromuscular junction propagation failure was not a significant issue. MPF decreased in the less affected limb and not in the more affected limb, this difference was statistically significant. RMS values decreased across the task and were not different between limbs. These results suggest that the peripheral capacity of the more affected limb remained unchanged during the fatigue task, despite the development of total neuromuscular fatigue. Either the peripheral neuromuscular fatigue measurement methods (MPF, m-wave) were inappropriate for evaluating peripheral neuromuscular fatigue in stroke participants, or fatigue was developing at other sites of the neuromuscular system.

In the remaining two participants in Riley & Bilodeau's (2002) study were evaluated using a different methodology. Voluntary activation was determined every ten seconds during a 60 second sustained maximal isometric contraction of the elbow flexors. The results for the more affected limb of both participants qualitatively demonstrated a decrease in the level of voluntary activation as the fatigue task progressed, indicating the development of central neuromuscular fatigue. In contrast the less affected side demonstrated minimal change in voluntary

activation, suggesting that little central neuromuscular fatigue developed. Results from these two participants indicate that in participants with stroke, the central nervous system maybe a key factor in the development of fatigue. This study is a key pointer that central neuromuscular fatigue may have a role in the development of total neuromuscular fatigue in participants with stroke. However, it is limited by the small number of participants tested, by the method used to measure change in voluntary activation and that central neuromuscular fatigue and peripheral neuromuscular fatigue were not measured concurrently in participants. The reliance on the less affected side to act as a control may also fail to highlight the magnitude of the difference between the more affected limb and normal participants. There is strong evidence to show that the strength and voluntary activation of the less affected side is influenced by stroke (Bohannon, 1997; Davies, Mayston, & Newham, 1996; Harris et al., 2001) and that during neuromuscular fatigue tasks there is a centrally mediated fatigue response which affects both limbs (Rattey, Martin, Kay, Cannon, & Marino, 2005; Todd, Petersen, Taylor, & Gandevia, 2003). Therefore, the fatigue profile of the less affected limb is likely to be influenced by ipsilateral central nervous system changes.

Of the five studies that evaluate neuromuscular fatigue following stroke (Lindstrom et al., 1998; Riley & Bilodeau, 2002; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999), four are limited to participants with minimal physical disability (Lindstrom et al., 1998; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999). The use of participants with minimal physical impairment may provide a poor representation of the stroke population, particularly of participants with moderate to severe physical deficits who make up approximately fifty percent of the population at twelve months post-stroke

(Baskett, 1996). All of the studies reviewed are limited by small sample sizes which increase the risk of type two error, this is especially valid in such a heterogeneous population, as is evidenced by the large standard deviations seen in some of the fatigue measures in stroke participants. Finally, studies which rely on EMG measures to quantify peripheral neuromuscular fatigue maybe jeopardised by the fact that EMG does not reflect clearly differences between central and peripheral mechanisms of fatigue.

Based on the findings of the above studies it is concluded that although there is evidence that people with stroke fatigue differently from control participants during motor tasks, the exact mechanism of these differences remains unclear. There is some indication that there is a reduction in the amount of peripheral neuromuscular fatigue developed by people with stroke, potentially due to a failure to voluntarily activate the muscle fully. While increased central neuromuscular fatigue has been noted in one small study (Riley & Bilodeau, 2002) and suggested by a number of researchers (Lindstrom et al., 1998; Riley & Bilodeau, 2002). Therefore, the contribution of central neuromuscular fatigue and peripheral neuromuscular fatigue to total neuromuscular fatigue in people with stroke warrants further investigation.

2.5. Central Neuromuscular Fatigue in Normal Participants

Given the assertion that neuromuscular fatigue following stroke is likely to be primarily caused by central neuromuscular fatigue it is important to consider the evidence for development of central neuromuscular fatigue in people without pathology. Extensive research in normal younger participants shows that task parameters influence the source and degree of fatigue developed in the

neuromuscular system during a motor task. In normal younger participants these differences have been demonstrated based upon; contraction intensity, contraction duration, type of contraction, whether work is intermittent or sustained and the muscle group being investigated (Babault, Desbrosses, Fabre, Michaut, & Pousson, 2005; Behm & St-Pierre, 1997; Bigland-Ritchie, Rice, Garland, & Walsh, 1995; Loscher & Nordlund, 2002; Nordlund, Thorstensson, & Cresswell, 2004; Oskouei, vanMazijk, Schuiling, & Herzog, 2003; Todd, Petersen et al., 2003). Review of the research evaluating central neuromuscular fatigue during sustained isometric tasks indicates the variability in the degree of central neuromuscular fatigue developed (Bigland-Ritchie, Jones, Hosking, & Edwards, 1978; Bilodeau, Erb, Nichols, Joiner, & Weeks, 2001a; Butler, J. E., Taylor, & Gandevia, 2003; Chan, Raja, Strohschein, & Lechelt, 2000; Taylor, Butler, & Gandevia, 1999; Todd, Petersen et al., 2003; Todd, Taylor et al., 2003; Williams, Sharma, & Bilodeau, 2002).

2.5.1. Central Neuromuscular Fatigue during isometric tasks

Four studies were identified which look specifically at the quadriceps muscle during a sustained isometric task (Babault et al., 2005; Bigland-Ritchie et al., 1978; Place, 2005; Rattey et al., 2005) A paper by Bigland-Ritchie and colleagues (1978), considered the development of central neuromuscular fatigue and peripheral neuromuscular fatigue in the quadriceps muscle during a maximal isometric task. This seminal paper was one of the early studies which used a twitch interpolation method to evaluate the development of central neuromuscular fatigue. Nine participants were evaluated during a 60 second sustained task, which was interrupted at 15 second intervals to provide percutaneous electrical stimulation. Central neuromuscular fatigue was determined by comparing the fall in voluntary force with the fall in electrically stimulated force during the task. If electrically stimulated force

was maintained relative to voluntary force, the authors assumed that this was evidence of central neuromuscular fatigue. Of the nine participants tested, four demonstrated little or no evidence of central neuromuscular fatigue. In the other five participants the authors estimated that central neuromuscular fatigue represented between 10 and 30% of the force loss during the contraction. Although the method of measurement and quantification of central neuromuscular fatigue had significant limitations, this study demonstrated the development of central neuromuscular fatigue in some healthy participants.

Another study by Place and colleagues (2005) evaluated the development of central neuromuscular fatigue and peripheral neuromuscular fatigue in the quadriceps muscle during a sustained task at 20% MVC. Eleven participants were evaluated during an MVC prior to and immediately following the fatigue task, using the twitch interpolation method. Results identified that central neuromuscular fatigue accounted for a 14% - 19% decline in voluntary activation. The results of this study maybe limited by the method of stimulation used and the use of a separate task (i.e. a 100% MVC not a 20% MVC contraction) to measure central neuromuscular fatigue. The development of central neuromuscular fatigue is thought to be task specific and evidence exists to suggest that cortical excitability is significantly altered during higher intensity muscle contractions (Taylor & Gandevia, 2001; Todd, Taylor et al., 2003). In addition, the delay between task completion and central neuromuscular fatigue measurement may also be a problem, as some researchers suggest that central neuromuscular fatigue recovers very rapidly (Kufel, Pineda, & Mador, 2002; Suter & Herzog, 2001).

A study which aimed to consider the evidence for contralateral neuromuscular fatigue in normal younger participants was carried out by Rattey and

colleagues (2005). The study investigated a sustained (100 second) maximal isometric contraction of the quadriceps, resulting in an average force decline of 77% MVC. Central neuromuscular fatigue was calculated as the decline in voluntary activation during the task, where the superimposed twitch was referenced to an unpotentiated control twitch. Central neuromuscular fatigue was on average 17% (i.e. a decline in voluntary activation of 17%) in the exercised leg following the fatigue task.

Another study by Babault and colleagues (2005) aimed to compare the development of central neuromuscular fatigue and peripheral neuromuscular fatigue during concentric and isometric tasks at similar levels of total neuromuscular fatigue. Central neuromuscular fatigue was calculated as the decline in voluntary activation during the task, where the superimposed twitch was referenced to a potentiated control twitch. Each sustained maximal isometric contraction was, on average 48 seconds long, resulting in an average force decline of 37.8% MVC. Central neuromuscular fatigue was on average 27.5% (±6.6).

These four studies demonstrate that in young normal participants central neuromuscular fatigue is seen to develop during sustained isometric contractions of the quadriceps. However, the exact amount of central neuromuscular fatigue can only be broadly classified as a decline in voluntary activation of less than 30%. The parameters of the fatigue task and the method of assessment vary across studies, limiting comparison between studies.

Assessment of central neuromuscular fatigue during sustained isometric tasks in other muscle groups has considered the elbow flexors, dorsiflexors and thumb adductors (Bilodeau et al., 2001a; Butler, J. E. et al., 2003; Chan et al., 2000; Kent-Braun, 1999; Kent-Braun & LeBlanc, 1996; Taylor et al., 1999; Todd,

Petersen et al., 2003; Todd, Taylor et al., 2003). Four studies which consider the development of central neuromuscular fatigue in the elbow flexors have been completed by a group of researchers in Australia (Butler, J. E. et al., 2003; Taylor et al., 1999; Todd, Petersen et al., 2003; Todd, Taylor et al., 2003). These studies appear to suggest lower levels of central neuromuscular fatigue than those identified in the quadriceps studies, with a range of between 7-15 %. Differences across the four studies are likely due to variations in the task and central neuromuscular fatigue measurement method. The difference in results between studies of the elbow flexors and those of the quadriceps muscle may be due to two factors; firstly transcranial magnetic stimulation was the primary measure of central neuromuscular fatigue in these studies, which is an indication of central neuromuscular fatigue in the structures upstream of the motor cortex and therefore does not account for central neuromuscular fatigue in the motor cortex, subcortical structures and the spinal networks. Secondly, the elbow flexors include the biceps, brachioradialis and brachialis muscles, the contribution of synergists may alter the fatigue profile of individual muscles, this may be reflected in measures of central neuromuscular fatigue.

Studies of sustained isometric tasks in the quadriceps and other muscle groups provide some support to the concept that during sustained isometric tasks central neuromuscular fatigue is less than 30% in normal younger participants. This indicates that central neuromuscular fatigue has a limited contribution to total neuromuscular fatigue during sustained maximal isometric tasks in normal subjects, and that the majority of force decline is attributed to peripheral mechanisms. The variation seen in the above studies highlights the importance of clear definition of the task parameters and measurement method when evaluating central

neuromuscular fatigue. It is essential that the parameters of the task used to test central neuromuscular fatigue in different populations be clearly defined and controlled to allow comparison between participants and across studies.

2.5.2. Central Neuromuscular Fatigue in older participants

The influence of age is a key issue when considering central neuromuscular fatigue in the stroke population, as this pathology is likely to affect predominately older people (Baskett, 1996). Other age related changes in neuromuscular function have been well identified, including; loss of muscle mass, reductions in motor unit and fibre numbers, remodelling of motor units and alterations to fibre type composition within muscle, with a proportionally greater loss of type II muscle fibres (Allman & Rice, 2002). To date it is unclear whether central neuromuscular fatigue contributes significantly to deficits in neuromuscular function in older adults. If neuromuscular fatigue in older participants is in large part due to central neuromuscular fatigue this would be an important consideration when measuring central neuromuscular fatigue in people with stroke.

There have been two main approaches to measuring central neuromuscular fatigue in older adults; studies using intermittent tasks and those using sustained tasks. The assertion that central neuromuscular fatigue recovers promptly following task completion suggests that central neuromuscular fatigue is less likely to develop during intermittent exercise protocols. Despite this assertion, the majority of research investigating the development of central neuromuscular fatigue in older people has been carried out using intermittent exercise protocols, with five of the eight studies evaluated using an intermittent protocol.

The results of studies using intermittent exercise protocols are contradictory. Three studies demonstrated no difference in central neuromuscular fatigue between older and younger participants (Allman & Rice, 2001, 2003; Kent-Braun, Ng, Doyle, & Towse, 2002), one study demonstrated more central neuromuscular fatigue in younger participants (Ditor & Hicks, 2000) and one study more central neuromuscular fatigue in older participants (Stackhouse et al., 2001). It could be argued that central neuromuscular fatigue was more likely to develop during protocols that had a higher exercise to rest ratio. However, comparison of studies based on exercise to rest ratio provides a confusing picture, with the two studies that have higher exercise to rest ratio demonstrating polar results (Ditor & Hicks, 2000; Stackhouse et al., 2001). Marked problems with measurement method, statistical analysis and sample size limit the validity of results and comparison between studies. No conclusions regarding the development of central neuromuscular fatigue during intermittent exercise protocols can be made from the five studies reviewed.

Like the research evaluating intermittent tasks, the three articles evaluating central neuromuscular fatigue during sustained tasks present conflicting results. Two studies identify increased central neuromuscular fatigue in older participants, with a sustained maximal task (Bilodeau et al., 2001a) and with a sustained sub-maximal task (Bilodeau, Henderson, Nolta, Pursley, & Sandfort, 2001b). These results were found when using the CAR calculation method during the task, and not when voluntary activation was calculated using twitch measures taken during MVC and referenced to a control twitch (refer to Section 2.6.3. for an explanation of the two calculation methods). These findings may therefore represent differences attributable to the calculation method, the timing of measurement or true differences between the groups. In research by Chan and colleagues (2000), the task was in essence

intermittent due to the two rest periods provided. All three studies were limited by methodological problems and small sample size.

The disparity of results found in the eight studies investigating central neuromuscular fatigue in older adults means that no conclusions could be made. Based on two studies, with significant methodological and design flaws, it maybe asserted that central neuromuscular fatigue is more likely to develop in older adults to a greater degree during sustained tasks, when compared to younger adults. The disparity of results investigating central neuromuscular fatigue in older adults highlights the importance of providing an age matched control group when evaluating the development of central neuromuscular fatigue in a stroke population. If the development of central neuromuscular fatigue is influenced by age this will be a key factor to control.

2.5.3. Section Summary

Research in normal younger participants during sustained isometric tasks illustrates how the task parameters influence the amount of central neuromuscular fatigue developed. Studies of central neuromuscular fatigue during isometric sustained activity of the quadriceps muscle suggest that central neuromuscular fatigue accounts for a less than 30% decline in voluntary activation during these tasks in normal younger participants. Based on the studies reviewed no conclusions regarding the influence of age on the development of central neuromuscular fatigue could be made.

2.6. Measurement of Neuromuscular Fatigue

As noted earlier, in the review of studies of neuromuscular fatigue following stroke, the method used to quantify neuromuscular fatigue is a fundamental issue.

Therefore, the focus of this section is the measurement of neuromuscular fatigue. The measurement methods which are selected to quantify fatigue are usually determined by the task being carried out and the information which is sought about the physiological response to the task (Cairns, Knicker, Thompson, & Sjogaard, 2005). In the current study, information is sought about the contribution of peripheral and central processes to neuromuscular fatigue, hence, review of methods to quantify total neuromuscular fatigue, peripheral neuromuscular fatigue and central neuromuscular fatigue is undertaken. However, given the potential relevance of central mechanisms in the development of neuromuscular fatigue in people with stroke, particular attention is given to the measurement of central neuromuscular fatigue.

2.6.1. Measurement of Total Neuromuscular Fatigue

Neuromuscular fatigue is an acute, activity induced, impairment in the ability to exert force and is normally quantified by the resultant reduction in force that a muscle or muscles can exert following or during activity. The most common measure of total neuromuscular fatigue is decline in force across the task, often measured as change in percentage of MVC (Vollestad, 1997). The use of decline in MVC as a measure of total neuromuscular fatigue allows relative ease of quantification, comparison across individuals and consideration of physiological processes (Gandevia, 2001).

The reliability of decline in MVC as a measure of total neuromuscular fatigue is not frequently discussed in the literature, either in relation to normal or pathological populations (Schwid et al., 1999; Surakka et al., 2004). Nevertheless, some researchers make recommendations regarding methodology, with the aim of

improving the reliability of the measurement. Much of this advice is based on work carried out in studies of MVC measurement in normal subjects (Gandevia, 2001).

Using change in percentage MVC as a measure of total neuromuscular fatigue has been criticised for a failure to demonstrate other fatigue induced changes, a failure to mimic real life muscle activity, and the potential to underestimate fatigue changes (Cairns et al., 2005). Alternative measures of total neuromuscular fatigue tend to consider other aspects of performance and may include measurement of power, work, force variability, number of repetitions of an activity performed till failure and endurance time. While these measurement methods may provide alternative information about fatigue related changes, they also potentially add complexity to the analysis of the contribution of peripheral and central processes to neuromuscular fatigue. These measurement methods have, therefore, not been considered.

2.6.2. Measurement of Peripheral Neuromuscular Fatigue

Peripheral neuromuscular fatigue describes fatigue induced changes which occur, 'at or distal to the neuromuscular junction' (Gandevia, 2001, pg1733). Peripheral neuromuscular fatigue therefore reflects alterations in the capacity of the muscle to generate force at a given level of activation (Paul & Wood, 2002). While sophisticated techniques including; nuclear magnetic resonance spectroscopy, muscle biopsy analysis, low-frequency fatigue and high frequency fatigue measures, have been developed to attempt to quantify the physiological processes associated with peripheral neuromuscular fatigue, (Kent-Braun, 1997; Vollestad, 1997), the focus of this study was to quantify the amount of peripheral neuromuscular fatigue, rather than to consider it physiological cause. Therefore, relatively gross measures of peripheral neuromuscular fatigue were considered.

One method of evaluating neuromuscular fatigue is surface EMG. Measures such as signal amplitude and power spectrum have been utilised in studies of fatigue, and notably in studies of neuromuscular fatigue in stroke (Lindstrom et al., 1998; Riley & Bilodeau, 2002; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999). However this method presents a number of challenges, given that EMG may reflect changes at both a central and peripheral level. Mean power frequency of EMG signal, which is regularly used to quantify peripheral fatigue, may reflect alterations in the conduction velocity of muscle fibres (a peripheral process) or a change in the recruitment of motor units (a central process) (Mathur, Eng, & MacIntyre, 2005; Rau, Schulte, & Disselhorst-Klug, 2004). Therefore EMG may not represent a good measure of peripheral neuromuscular fatigue in subjects with impaired voluntary activation and alterations in motor unit recruitment, such as people with stroke.

As peripheral neuromuscular fatigue occurs in response to changes at, or peripheral to, the neuromuscular junction, measures which directly assess the contractile capacity of the muscle are of value. One method of detecting change in contractile capacity of the muscle is to measure the change in twitch amplitude at rest when an external electrical stimulus is provided (Bulow, Norregaard, Danneskiold, & Mehlsen, 1993; Kufel et al., 2002; Polkey et al., 1996; Schillings et al., 2003; Schillings, Stegeman, & Zwarts, 2005; Todd, Taylor et al., 2003). Using the resting twitch amplitude enables the researcher to consider the development of peripheral neuromuscular fatigue irrespective of the level of voluntary activation of the muscle (Kufel et al., 2002). This is valuable when comparing populations who have different levels of voluntary activation, such as participants with and without stroke. Twitches are normally expressed as a percentage of the control twitch taken

following MVC to allow comparison between individuals. High test-retest reliability and low levels of error in resting twitch measures has been established in twitches following MVC (Allen, Gandevia, & McKenzie, 1995; Kufel et al., 2002; Polkey et al., 1996; Todd, Taylor, & Gandevia, 2004) but the reliability of change in resting twitch amplitude following fatigue has not been well investigated. Kufel and colleagues (2002) have reported that potentiated resting twitch amplitude is sensitive to the changes which occur in fatigued muscle.

2.6.3. Measurement of Central Neuromuscular Fatigue

Given that stroke is primarily a CNS pathology a key issue in investigation of influence of central and peripheral processes to the development of neuromuscular fatigue in people with stroke is the methodology used to measure and quantify central neuromuscular fatigue. Central neuromuscular fatigue is a change in the voluntary activation of a muscle in response to a fatiguing exercise. The establishment of central neuromuscular fatigue occurs through the comparison of voluntary activation before a fatiguing task to voluntary activation during or after the task. Therefore comparison of measures of voluntary activation is utilized as a measure central neuromuscular fatigue.

The basic premise of methods used to assess voluntary activation is that if a muscle can be further stimulated peripherally then the central nervous system is failing to drive the muscle maximally. Measurement of voluntary activation provides a snapshot picture of the extent that the central nervous is driving the muscle at that time. Two techniques have been established to measure voluntary activation; the transcranial magnetic stimulation and interpolated twitch methods.

2.6.3.1. Transcranial Magnetic Stimulation

Transcranial magnetic stimulation involves application of an electromagnetic field and hence perpendicular electrical stimulation directly to the motor cortex, which elicits a short latency excitatory response in the target muscle (Taylor & Gandevia, 2001). The size of motor evoked potential elicited during transcranial magnetic stimulation is normalized to the average area of the maximal M-wave to account for activity related changes in the muscle fibre action potential (Todd, Taylor et al., 2003). It is not possible to normalize motor evoked potentials taken during fatiguing tasks with motor evoked potential taken at rest, as the motor cortex output during muscle activity is affected by activity dependent excitatory influences which are not present at rest. However, recent advances in the use of this technique have attempted to quantify the extent of the central neuromuscular fatigue as measured by transcranial magnetic stimulation by extrapolating a 'control twitch' from submaximal testing of voluntary activation (Todd, Taylor et al., 2003). This calculation method has not been tested fully and the validity of this extrapolation requires further discussion from a theoretical perspective. The location of the transcranial magnetic stimulation stimulus means that this method does not evaluate the voluntary activation of the whole CNS but of the structures upstream of the motor cortex, such as the pre-frontal cortex and the frontal cortex. This method does not evaluate fatigue occurring in the motor cortex, sub cortical structures and spinal networks. Therefore the technique is not appropriate to gain an appreciation of the central neuromuscular fatigue through out the entire CNS, but is useful in determining the location of reductions in voluntary activation within the central nervous system (Taylor & Gandevia, 2001; Todd, Taylor et al., 2003). Therefore, while the usefulness of transcranial magnetic stimulation in elucidating aspects of central neuromuscular fatigue is acknowledged, as this paper focuses on exploring

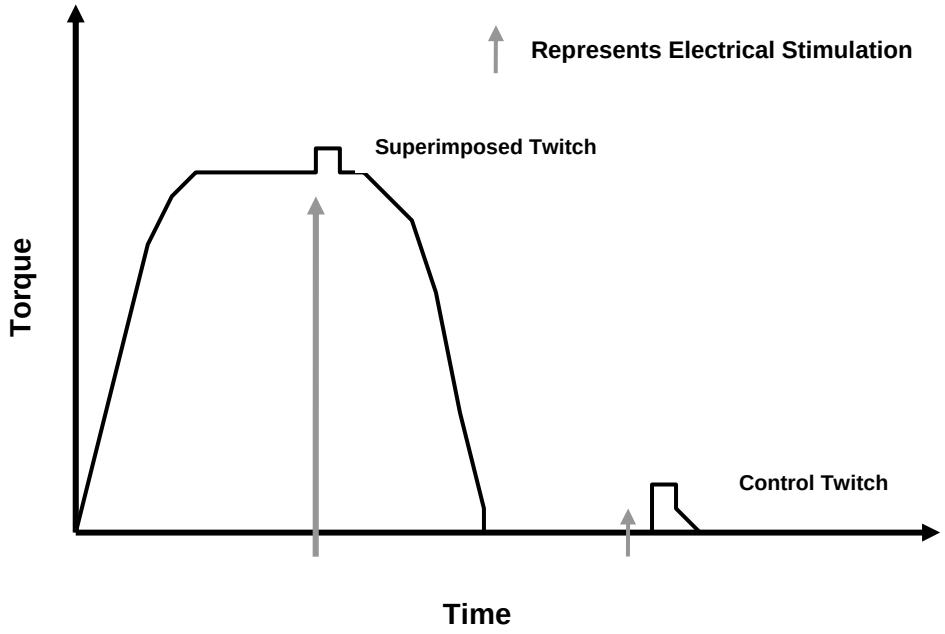
the contribution of central neuromuscular fatigue to total neuromuscular fatigue in people with stroke, the twitch interpolation method of measurement is the focus of discussion related to methodology.

2.6.3.2. Twitch Interpolation

The other method utilized to test voluntary activation is the interpolated twitch technique; this method involves application of an electrical stimulus to the muscle or electromagnetic stimulus to the peripheral motor nerve to stimulate the muscle. The interpolated twitch method has been widely utilized to measure voluntary activation and central neuromuscular fatigue in both normal participants and participants with pathologies such as chronic fatigue syndrome, multiple sclerosis and amyotrophic lateral sclerosis (Kent-Braun & Miller, 2000; Riley & Bilodeau, 2002; Sharma et al., 1995; Sheean, Murray, Rothwell, Miller, & Thompson, 1997).

The basic methodology of interpolated twitch involves measurement of torque generated by the target muscle using a strain gauge. Participants voluntarily generate a contraction to a specific level of MVC, an electrical stimulus is then applied to the muscle. If the motor neurons have not been recruited fully or have not been recruited at a sufficient rate the stimulus will elicit a further increase in torque. The development of additional torque suggests that the muscle has further peripheral capacity that is not being voluntarily activated. If more force is generated by stimulation during the muscle contraction then it is assumed that the nervous system is failing to drive the muscle to its maximum capacity. Depending on the method used to calculate voluntary activation, another twitch may be applied to the muscle immediately following the contraction (see Figure 2.1).

Figure 2.1: Schematic representation of interpolated twitch technique application



Note: Twitch interpolation involves the application of an electrical stimulus (superimposed twitch) during muscle contraction. The amplitude of the additional torque generated through electrical stimulation is usually normalised to a control or resting twitch which is delivered immediately following the contraction

The most commonly used method of calculating voluntary activation from interpolated twitch measures involves 'normalising' the twitch superimposed during contraction to the twitch at rest (Behm, Power, & Drinkwater, 2001), where;

$$\text{Voluntary activation} = 1 - \left(\frac{\text{superimposed twitch}}{\text{control twitch}} \right) \times 100$$

This method assumes a linear relationship between the superimposed and control twitches, where a twitch made at an MVC and a twitch made at rest are assumed to have a linearly scaled relationship.

The second method is called the Central Activation Ratio (CAR), this method normalizes the total force generated during twitch or maximal evocable

contraction (MEC) to the MVC (Behm et al., 2001). This method assumes a linear relationship between the level of MVC and the MEC, where;

$$\text{Central Activation Ratio} = \frac{\text{MVC}}{\text{MEC (twitch)}}$$

A concern with both of these methods of calculating voluntary activation is that researchers have identified that the relationship between MVC and twitch size is sometimes curvilinear rather than linear (Behm et al., 2001; Oskouei et al., 2003; Sheild & Zhou, 2004). Failure to consider the implications of a curvilinear relationship when calculating voluntary activation may introduce potential error in the calculation. Despite its relatively wide spread use, a number of authors have identified issues with the reliability, sensitivity and validity of the interpolated twitch measurement method to provide an accurate estimation of voluntary activation (Allen et al., 1995; Allman & Rice, 2002; Behm et al., 2001; Behm, St-Pierre, & Perez, 1996; Bulow, Norregard, Mehlsen, & Danneskoid-Samsoe, 1995). These issues relate to the relationship between MVC and twitch size and to methodological concerns with interpolated twitch application during fatigue tasks.

The relationship between twitch size and MVC

A number of factors are thought to influence the relationship between MVC and twitch size and to, in part, account for a curvilinear relationship being observed between twitch size and MVC. These include; the viscoelastic properties of muscles at low MVC's, the ability of participants to perform an MVC which matches MEC, the contribution of synergists to force generation at high MVC's and the capacity of interpolated twitch to consistently stimulate the muscle.

Viscoelastic Factors

When interpolated twitch values are collected at low MVC's the predicted MVC from these measures demonstrates an underestimation of MVC by up to 33.3% from the true MVC (Behm et al., 1996; Bulow et al., 1993; Polkey et al., 1996). This error is usually ascribed to the viscoelastic properties of the muscle, where force loss occurs as the muscle contraction initially takes up the viscoelastic slack within the muscle. This theory is, upheld by differences seen in muscles that have a proportionally greater compliant segment, for example the plantar flexors (Behm et al., 1996). This may influence the estimation of voluntary activation at low MVC's, providing inaccurate measure of voluntary activation and potentially over-estimating voluntary activation. This finding may have particular relevance in people who have had stroke. People with stroke generate lower MVC's than people without pathology (Andrews & Bohannon, 2000, 2003) and it has been suggested that they are also likely to have changes to the viscoelastic composition of their muscles (Gracies, 2005a). Therefore, measures of voluntary activation maybe more susceptible to the influence of viscoelastic factors in participants with stroke. This

problem may be ameliorated in part by placing the muscle in a lengthened position or using a multiple stimuli (Bulow et al., 1993).

Capacity of participants to generate a consistent MVC

It has been established that normal participants are generally unable to perform MVC's that are equal to the MEC generated by electrical stimulation (Allen, McKenzie, & Gandevia, 1998; Behm, Whittle, Button, & Power, 2002; Gandevia, 2001; Yue, Ranganathan, Siemionow, Liu, & Sahgal, 2000). In most cases, the MVC equates to approximately 95-99% of MEC (Strojnik, 1995). The level of voluntary activation also varies dependent on the muscle being investigated and the participant being tested (Behm et al., 2002; Gandevia, Allen et al., 1995). The knee extensors are recognized as a muscle group that have between 10-23% deficit in voluntary activation in normal participants (Behm et al., 2002). Some authors have identified that the level of MVC generated can be improved with habituation sessions, where the participants spend one or two sessions 'practicing' generating 100% MVC (Allman & Rice, 2002) The use of habituation sessions therefore, has the potential to improve the reliability of estimations of voluntary activation. In addition, other investigators recommend the use of consistent verbal encouragement and visual feedback of force generated to improve the likelihood that MVC is as close to MEC as possible (Gandevia, Allen et al., 1995).

Synergistic muscle activity contributing to MVC

At high MVC in some muscle groups, such as the elbow flexors, synergistic activity influences force generation (Allen et al., 1998). The contribution of synergists is likely to result in an underestimation of voluntary activation failure by falsely increasing the torque of the MVC in relation to the twitch size for the target muscle. This is relevant if the CAR method of calculating voluntary activation is

utilized, because this method normalizes MEC force (twitch) to MVC (Kent-Braun & LeBlanc, 1996). Testing of muscles which do not have significant synergist input, such as the quadriceps, may address this problem. However evidence suggests that synergist activity is not likely to be fully responsible for the curvilinear relationship between MVC and twitch size (Allen et al., 1998).

Antidromic Effects

Some researchers have proposed that during electrical stimulation of muscle there is likely to be an antidromic occlusion effect which results in a net reduction in force output. Antidromic occlusion effects may involve a number of mechanisms which produce inhibition of motor unit output including; stimulation at a phasing which reduces the rate of motor unit discharge, hyperpolarisation, evoking inhibitory post-synaptic potentials in motor neurons, and the stimulation of short and long latency reflexes which decrease the spindle afferent discharge (Herbert & Gandevia, 1999). There is also potential for antidromic effects to differ between twitches at rest and twitches during MVC due to differences in resting thresholds of inhibitory and reflex inputs at different levels of contraction. This overall inhibitory anitdromic effect would result in a reduction in twitch size and hence an over estimation of voluntary activation. The occurrence of such an inhibitory effect is supported by a study using computer modelling of interpolated twitch application to the adductor pollicis motor neuron pool (Herbert & Gandevia, 1999) and by the consistent experimental finding of an electromyographic silence following interpolated twitch stimulation, which is thought to represent antidromic inhibition of motor unit activity following stimulation.

Capacity to provide consistent measures of peripheral capacity

A number of methodological issues associated with the application of the twitch interpolation appear to influence both the reliability and the size of the twitch. These factors include; frequency, intensity, number and timing of stimulation and the size and site of stimulating electrodes. Inconsistency in twitch size would limit the reliability of calculations of voluntary activation.

Twitch size can be affected by the frequency of the stimulating electrical impulse. Stimulation applied above 100Hz has been shown to generate larger and more consistent twitch sizes (Sheild & Zhou, 2004).

Researchers advocate different stimuli intensities, this difference is usually based on whether the twitch size represents the total peripheral capacity of the muscle or is a proportional representation of the peripheral capacity of the muscle. Some researchers utilize a supra-maximal stimulus, where the intensity of the stimulus is generally set at 115-125% of the stimulus required to elicit a maximal evocable contraction. The rationale for this level of stimulation is that supramaximal stimulation ensures the muscle is fully activated during the twitch. However, participants are frequently unable to tolerate such high levels of electrical stimulation (Behm et al., 2001). This may result in an over-estimation of voluntary contraction by a failure to fully stimulate the muscle due to discomfort. Other researchers recommend a sub maximal stimulus based on research which has suggested that sub-maximal stimulation provides similar estimates of voluntary activation as supra-maximal stimulation in unfatigued muscle (Sheild & Zhou, 2004). However, this finding has not been tested in fatigued muscle and there is a risk that successive stimulation, such as that used during trains of stimulation or in

repeated measures over time, stimulates different portions of the muscle due to movement of the muscle under the electrode during contraction (Sheild & Zhou, 2004). Sheild and Zhou (2004) also assert that sub maximal stimulation is inappropriate for use during fatiguing contraction because the threshold of motor axons increases during fatiguing contractions and therefore, stimulates progressively fewer motor units over time.

Another key methodological issue that has received significant attention is the number of stimuli applied in succession to the muscle at each test. Researchers have established that application of a doublet stimulus generates a larger and more reliable twitch size than a single stimulus (Suter & Herzog, 2001). While other authors state that even greater reliability and sensitivity can be achieved by using a train of stimuli (Behm et al., 2001; Kent-Braun & LeBlanc, 1996). Multiple stimuli are advocated where the stimulus intensity is set at a sub-maximal level. Multiple stimuli allow for summation of the twitch with successive stimuli, however, this does pose the risk of an increased antidromic effect (Sheild & Zhou, 2004). An additional benefit of multiple stimuli maybe the resolution of viscoelastic forces loss at low MVC's (Sheild & Zhou, 2004). However, it has been noted that at high force levels no difference is seen in twitch size between single, doublet and train stimulation (Allen et al., 1998; Stackhouse et al., 2001). There appears to be considerable ongoing conflict in the literature regarding this issue. Differences in measures of reliability between single; doublet and trains of stimulus are likely influenced by other stimulus parameters and methodology, making the comparison of findings difficult.

The timing of twitch application has been found to influence the size of the twitch applied during MVC and at rest. Two methods to identify the correct timing

of twitch related to level of contraction are utilized. The first method involves computer identification of contraction plateau or a set threshold level of contraction (i.e. 95% of MVC). Alternatively, visual identification of contraction plateau by the researcher is utilized. Neither method has been evaluated for reliability.

The timing of stimulus application for control or resting twitches is also relevant. Using a single twitch Suter and Herzog (2001) found that a twitch applied within 5ms of the end of contraction evoked higher and more consistent twitch sizes. They hypothesized that the application of trains of twitches ameliorated problems with timing of twitch application by the potentiation or sensitization of the activated motor units. Potentiation of twitch relates to the sensitivity of the muscle to preceding contraction history, where a muscle, which has just completed an MVC, is likely to produce a much larger twitch size than a muscle that was at rest. Potentiation may also be influenced by joint position, contraction duration and intensity (Kufel et al., 2002). The findings of Bulow et al (1993) and Kufel et al (2002) demonstrated that twitch size is potentiated or increased when applied immediately following a contraction of greater than 70-80% MVC and that the level of potentiation decreased rapidly within the first two minutes following contraction. This suggests that the application of stimulation to measure control twitch size should occur immediately following a contraction of at least 70% MVC.

Occlusion of force output maybe seen when electrical stimulation inadvertently stimulates the antagonist muscle. Stimulation of the antagonist muscle would result in a net reduction in torque generated by the agonist muscle and hence an underestimation of twitch size. This is a particular risk when using large electrodes relative to muscle size, when antagonist and agonist muscles lie anatomically close to one another and where agonist and antagonist muscles are

supplied by the same peripheral nerve, such as in forearm muscles supplied by the ulnar nerve and lower leg muscles supplied by the peroneal nerve (Sheild & Zhou, 2004).

2.6.3.3. Section Summary

Quantifying decline in voluntary activation calculated using twitch interpolation provides a measure of central neuromuscular fatigue. However, a number of factors are likely to influence the reliability and sensitivity of measures of voluntary activation using twitch interpolation. By failing to acknowledge and attempting to control these factors, large errors may be introduced in the calculation of voluntary activation. This is highlighted by a study of intra-participant test-retest reliability, which demonstrated that despite excellent test-retest reliability for both MVC and twitch size (ICC = 0.99 & 0.97 respectively), the reliability of voluntary activation was only good at 0.858 (Allen et al., 1995). In another study Suter et al (2001) found a within participant variation of 10-15% in measures of voluntary activation. These issues of reliability of twitch interpolation measurements demonstrate the importance of establishing the reliability of individual laboratory setups and processes. Multiple factors are likely to influence the reliability of voluntary activation and central neuromuscular fatigue measures. From a methodological perspective, research suggests that twitch interpolation should be carried out at a 100Hz, using a doublet or train of stimulation (particularly if taking measures at lower MVC or with sub maximal stimulus) and with a potentiated control twitch. Accurate calculation of voluntary activation ideally requires the establishment of the relationship between twitch size and MVC prior to the calculation of voluntary activation (Allen et al., 1998). These factors are also very important when evaluating research investigating central neuromuscular fatigue.

2.7. General Summary

Neuromuscular fatigue is an activity induced reduction in the capacity to produce force, and is the result of changes which may occur in both the peripheral and central structures of the neuromuscular system in response to a motor task. Evidence of alterations in both neural circuitry and muscular properties following stroke suggest that the neuromuscular fatigue profile of people following stroke is likely to be altered when compared to normal participants. While the relationship between the neural circuitry and muscular properties changes identified following stroke, and neuromuscular impairments is not well understood, there is evidence of changes at multiple levels of the neuromuscular system. It may therefore be asserted that differences in both the amount of central neuromuscular fatigue and peripheral neuromuscular developed during motor tasks are likely to occur.

There is scant research which specifically investigates neuromuscular fatigue following stroke. Current research in people with mild stroke provides some evidence that people with stroke fatigue differently from control participants during motor tasks; however there is a paucity of knowledge regarding the exact mechanism of these differences. There are a number of indications that following stroke there is a relative increase in the amount of central neuromuscular fatigue and a reduction in the amount of peripheral neuromuscular fatigue experienced.

Evidence from younger people without pathology suggests that during sustained isometric contractions of the quadriceps muscle neuromuscular fatigue is predominately peripheral in origin, with central neuromuscular fatigue representing a less than 30% decline in voluntary activation. The disparity of results seen in

studies investigating central neuromuscular fatigue in both older and younger adults has highlighted the importance of providing clear task parameters and an age matched control group when evaluating the development of central neuromuscular fatigue in a stroke population. Review of methodological issues related to the measurement of total neuromuscular fatigue, peripheral neuromuscular fatigue and central neuromuscular fatigue has also been considered.

3. Method

3.1. Introduction

The purpose of this study was to examine and compare the contribution of central neuromuscular fatigue and peripheral neuromuscular fatigue to neuromuscular fatigue during a sustained maximal voluntary isometric contraction of the quadriceps muscle in the hemiplegic leg of people with stroke, with that of age, height and weight matched controls. Performance on a range of measures of neuromuscular fatigue, neuromuscular function and physical function by participants with chronic stroke were compared to the performance of a group of control participants. This chapter describes the method utilised to answer the research question by outlining the study design, participants, equipment, procedure, data management and statistical analysis used in the study.

3.2. Study Setting and Design

This study was undertaken at the Physical Rehabilitation Research Centre of Auckland University of Technology, Auckland, New Zealand. A repeated measures block design was utilized.

3.3. Sample Size

To achieve the main study objectives, sample size calculations were undertaken using an online power calculator (ucla STAts). Power was set at 0.80 and significance at 0.05. The key outcome measures that were examined were; total neuromuscular fatigue, central neuromuscular fatigue and peripheral neuromuscular fatigue. As no previous studies of central neuromuscular fatigue in stroke participants involving statistical analysis have been published, power calculations were based on studies in normal and multiple sclerosis populations. Means and standard deviations from a study of central neuromuscular fatigue in normal participants undertaking a sustained isometric task of the quadriceps indicated that a sample size of eight per group was required (Babault et al., 2005). Another study investigating central neuromuscular fatigue in people with Multiple Sclerosis indicated a sample size of seven per group (Sheean et al., 1997). Data from studies investigating voluntary activation in people with stroke indicated sample sizes of seven (Newham & Hsiao, 2001) and four respectively (Riley & Bilodeau, 2002). Given the need to establish the reliability of the measurements in the stroke population, the heterogeneity of motor impairment in the stroke population and the risk of dropouts the sample size was elevated to fifteen per group.

3.4. Study Participants

3.4.1. Recruitment

Participants were recruited to the study through advertisement in local newspapers at local Stroke Foundation meetings (a nationwide not-for-profit support and advocacy group for people following stroke) and at Auckland University of Technology Physiotherapy Clinics (refer to Appendix A). The basic purpose of the

study, and participant inclusion criteria were outlined and participants were invited to volunteer for the study.

3.4.2. Control Participants

A group of fifteen neurologically unimpaired participants were studied. All participants satisfied the following inclusion criteria:

- Absence of a neurological condition
- Absence of peripheral neuropathy
- Absence of an orthopaedic pathology in the knee of the tested leg
- Absence of an uncontrolled medical problem which would prevent sustained, high intensity exercise.

3.4.3. Stroke Participants

A group of fifteen participants with a history of stroke were studied. All stroke participants satisfied the following inclusion criteria:

- A self-reported history of a single stroke at least six months previously, resulting in hemiplegia
- Able to walk ten metres indoors
- Absence of other neurological conditions
- Absence of peripheral neuropathy
- Absence of orthopaedic pathology in the knee of the tested leg
- Absence of an uncontrolled medical problem which would prevent sustained, high intensity exercise.
- Absence of significant hypertonia of the quadriceps muscle, as measured by a score of less than 4/5 on the Modified Ashworth Scale (Bohannon & Smith, 1987)
- Absence of significant cognitive, perceptual and/or language deficit, which would limit ability to participate in the study, as measured by a

score of greater than 22/30 on the Mini-Mental State Examination and greater than 43/54 on the Star Cancellation Test (Wade, 1992)

3.5. Ethical and Cultural Considerations

Ethical approval was obtained from the Auckland University of Technology Ethics Committee (see Appendix B). The key principles of the Treaty of Waitangi, including principles of partnership, participation and protection, and the related ethical responsibilities of researchers were understood and implemented. However, the research was non-ethnic specific in that it neither specifically aimed to include or exclude Maori participants. Recruitment of participants occurred in such a way that Maori people who met the inclusion criteria had an equal opportunity to participate in the study.

3.6. Study Procedure

3.6.1. Preliminary Preparation and Pilot Testing

This section describes the preliminary preparation and pilot testing which assisted in the development of the final study procedure. Initially the primary researcher underwent training in the use of the laboratory based equipment and computer software under the supervision of a researcher familiar with the experimental setup. Two small pilot studies were completed.

3.6.1.1. Pilot Study One

Method

Repeated measures of MVC, voluntary activation and predicted true maximal force over two separate testing sessions were carried out, with three control participants. Variations to the number of twitches delivered (single, doublet or trains

of twitch stimuli) were used during measures of voluntary activation to establish the sensitivity and reliability of this measurement technique.

Results

Analysis of these findings suggested that doublet twitches provided the most reliable results, with single twitches giving more variable within participant responses and trains of stimuli demonstrating clear summation of each stimulus, presenting difficulty in evaluating twitch size

Implications for Main Study Procedure

The instructions for orientation to testing equipment were altered based on participant feedback. The use of submaximal voluntary activation measures to predict true maximal force was discarded in order to limit the number of electrical stimuli delivered and the total number of contractions each participant underwent. This phase of the pilot testing also allowed clarification of twitch identification rules and modifications to the Superscope programme to enable easier identification of twitches by marking the delivery of twitch interpolation stimuli on the force file during the data collection process.

3.6.1.2. Pilot Study Two

Method

The full study procedure was carried out with ten participants with stroke, to establish the feasibility of the proposed testing procedure and the test-retest reliability of key measures. The fatigue task was set such that participants performed a sustained maximal contraction of the quadriceps until their level of force dropped below 50% MVC.

Results

Nine participants completed the testing procedure, however, three participants failed to complete the fatigue task, as they did not fatigue to 50% MVC within 90 seconds. Intraclass correlation coefficients (ICC 95% confidence interval) were 0.988 (0.946-0.998) for MVC measures and 0.870 (0.321-0.974) for voluntary activation measures. Reliability of fatigue measures were not calculated due to low subject numbers.

Implications for Main Study Procedure

A number of changes to the testing procedure were made based on this process; the order of individual testing sessions was altered to limit the amount of moving around the laboratory, cycle ergometry warm-up was discarded as this fatigued participants and the physical function testing appeared sufficient warm-up prior to neuromuscular function and fatigue testing. The fatigue task was modified to be time limited (90 seconds) rather than terminated based on decline in MVC, as some participants failed to exhibit a decline in torque to 50% MVC and the time to 50% MVC varied widely between participants.

3.6.2. Main Study Procedure

This section outlines the testing procedure used during the main study in light of findings from the pilot testing and research into methodological issues.

All potential participants who volunteered for the study and met the inclusion criteria were informed of the study purpose and process verbally and in writing (refer to Appendix C). Eligible participants, who expressed an interest in the study, were invited to attend two testing sessions held one day apart. At each testing session, the researcher followed a standardised procedure with each participant. At the first session participants were asked relevant personal details, screened again in regard to inclusion criteria, and provided written informed consent (refer to

Appendix D). In both testing sessions, prior to neuromuscular function and fatigue testing participants completed tests of physical function, with body mass, height and the 30s Chair Stand Test being completed in the first testing session and Comfortable Paced Walking Speed and Fast Paced Walking Speed tests being completed in the second.

Participants were then prepared for neuromuscular function and neuromuscular fatigue testing; this process was identical in both testing sessions (see below). Refer to Figure 3.1 for an outline of the main study procedure. Neuromuscular function and fatigue testing was repeated in both testing sessions to enable the reliability of these measures to be evaluated. Testing was carried out on the hemiplegic leg of participants with stroke, while the leg of control participants was randomly selected using a computer generated randomisation plan (www.randomization.com).

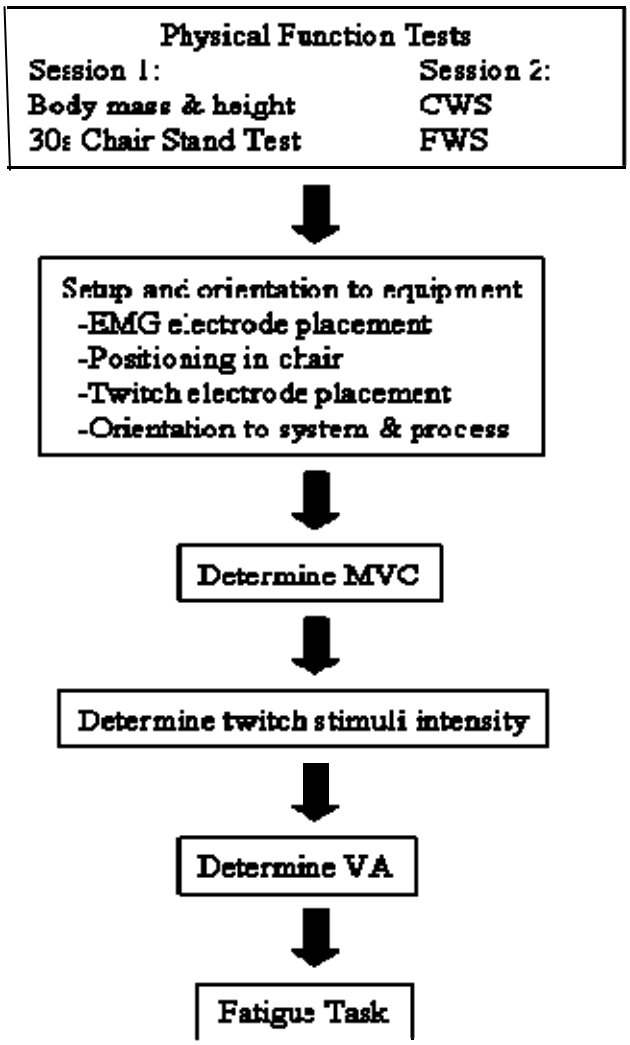


Figure 3.1: Outline of Main Study Procedure

3.6.2.1. Physical Function Measures

Anthropometric Measures

Age, height and weight of participants were recorded. Weight was measured using digital platform scales (Seca Scales Model 708) and concurrent measurement of height was taken using the attached telescopic height system. Body mass index was calculated from height and weight measures using the equation;

$$\text{Body Mass Index} = \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$$

Thirty second Chair Stand Test

The 30s Chair Stand Test evaluates a person's ability to stand and sit as quickly as possible in 30 seconds, and is regarded as an indirect measure of lower limb strength and functional mobility status (Jones, Rikli, & Beam, 1999). The equipment required for this test was a stopwatch, and a chair with no arm rests and a seat height of 43cm. The investigator gave verbal instructions and demonstration as per the instructions outlined by Jones and colleagues (1999). The total number of correct sit-to-stand manoeuvres performed in 30 seconds was recorded for data analysis. This measure has excellent test-retest reliability in both older participants and people with chronic stroke (Jones et al., 1999; Mo, Signal, & Taylor, 2005).

Comfortable Paced Walking Speed

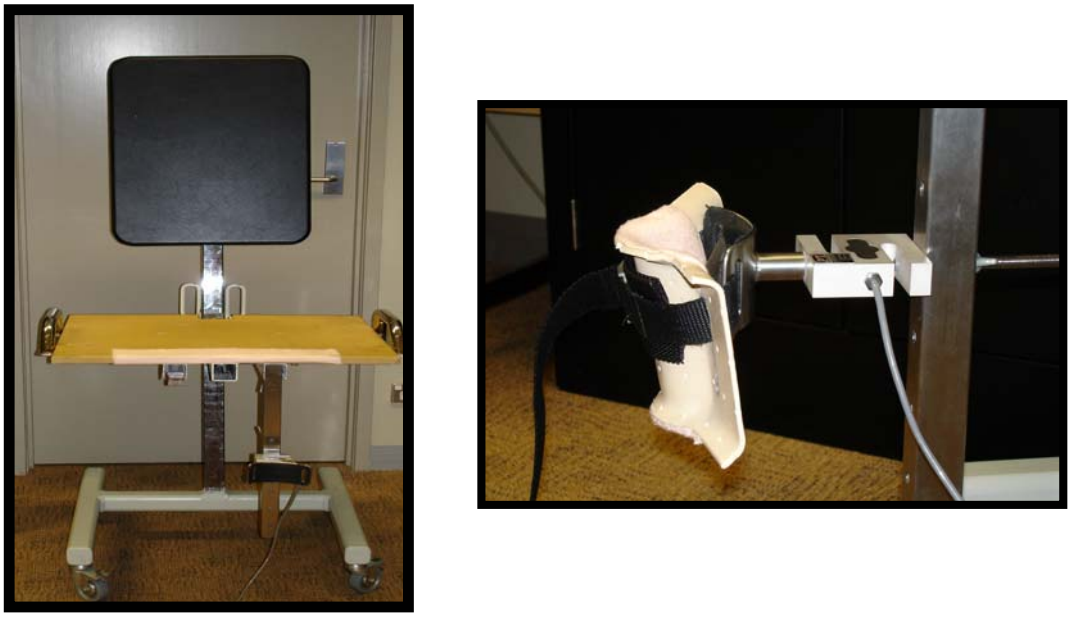
Comfortable Paced Walking Speed is a measure of the participants walking velocity at a self-paced comfortable speed. The equipment required included a marked walkway and a stopwatch. Participants were asked to walk at their comfortable pace along a ten metre walkway. The investigator recorded the length of time it took the participant to walk the middle six metres and walking velocity (metres/second) was calculated. The average of three trials was collected for data analysis (Hill, Denisenko, Miller, Clements, & Batchelor, 2005)**.**

Fast Paced Walking Speed

The Fastest Walking Speed test is a measure of the participants walking velocity at a self-paced fast speed. Data collection was as described for Comfortable Paced Walking Speed except that the participant was asked to walk at their fastest possible speed. The test-retest reliability of walking speed measures has been shown to be high in both older participants and people with stroke (Hill et al., 2005)

3.6.2.2. Neuromuscular Function Measures

For all neuromuscular function and neuromuscular fatigue testing participants were seated in a purpose built chair which allowed position to be standardised with the knee flexed 90 degrees, the hip flexed to 80 degrees and the thigh and trunk fully supported (Bohannon & Walsh, 1992; Colombo et al., 2000)(refer to Figure 3.1). The participants' upper body was secured across the pelvis and trunk to minimize movement during testing (Place, 2005). The chair had no padding in order to reduce the impact of damping on force measures. The lower part of the tested leg was fixed to a metal attachment in series with the strain gauge at the level of the ankle, just proximal to the lateral malleolus, via a non-extensible strap and moulded thermoplastic cuff. This prevented movement of the lower leg during contractions.



(a) (b)

Figure 3.2: (a) Purpose built chair, (b) Strain gauge with metal attachment, thermoplastic cuff and non-extensible strap

Torque data was collected using an ST model, 250kg-maximum strain gauge (Precision Transducers Ltd, Auckland, New Zealand), which has a manufacturer reported linearity error of 0.017%. The strain gauge was used to measure both MVC force and twitch interpolation force of the quadriceps muscle during the testing procedure. The strain gauge was calibrated prior to each testing session to produce an output of 1V/98N and an output balance of 0V without load. Force signals were collected from the strain gauge via a custom made amplifier by an Apple G4 personal computer at a sampling rate of 2000Hz. A real time force trace was displayed on a computer monitor using a customised computer software programme (Superscope II 3.0 GW Instruments, Washington, USA). This provided visual feedback to the participant of force being generated during the testing procedure.

EMG recordings were collected from the hamstring muscles of the tested leg through out testing of neuromuscular function and fatigue. The purpose of EMG measurement was to rule out activation of the hamstring muscles during twitch interpolation (Sheild & Zhou, 2004), and to rule out significant co-activation of the hamstring during quadriceps activity (Newham & Hsiao, 2001).

Skin preparation for the application of EMG electrodes involved shaving hair from the participants with significant body hair, then abrading the skin with fine sandpaper, cleaning the area with alcohol and wiping dry to remove any residue. Skin impedance was evaluated using an Ohmmeter (Dick Smith Electronics, Auckland, New Zealand) and accepted when less than 5000Ω. Ag/AgCl electrodes (3M, Auckland, New Zealand) were applied in parallel with the assumed direction of the muscle fibres at an inter-electrode distance of 2.5cm over the lower two thirds of the hamstrings muscle. During testing a 10mm thick high density foam pad (10cm x 8cm) with a central cut-out was placed under the thigh to prevent contact between

the EMG recording electrodes and the surface of the chair. An earth electrode was applied to the anterior tibia over the area of the tibial plateau.

The EMG signal of the hamstrings muscle was sampled at a rate of 1000Hz via a Grass P5 Series amplifier (Grass Instruments Company, USA) by an Apple G4 personal computer and stored with a customised computer software programme (Superscope II 3.0 GW Instruments, Washington, USA). All EMG data was visually screened for alterations from baseline during the testing procedures.

Once participants were prepared for EMG data collection and positioned in the chair they were orientated to the equipment setup and the visual display. They then completed four or five sub maximal warm-up contractions of the quadriceps muscle (Allman & Rice, 2002).

Maximal Voluntary Contraction

MVC was established by completing three, 3-5 second contractions with at least three minutes rest between each contraction (Bohannon & Walsh, 1992; Horemans, Beelen, Nollet, Jones, & Lankhorst, 2004; Tripp & Harris, 1991). Participants were provided with continuous, loud verbal encouragement (McNair, Depledge, Brettkelly, & Stanley, 1996) and visual feedback of performance (Kim, H. J. & Kramer, 1997). The highest value of the three trials was recorded for data analysis (Hoagland et al., 1997; Horemans et al., 2004; McNair et al., 1996)

Voluntary Activation

Voluntary activation was established using a percutaneous electrical stimulation (twitch interpolation) applied to the muscle during a MVC. Self-adhesive 7cm x 12cm Dura-stick electrodes (Chattanooga Group Inc., Tennessee, USA) were applied to the anterior thigh over the quadriceps muscle; the negative electrode was placed 5-10cm proximal to the superior border of the patella and the positive electrode placed just distal to the femoral crease and slightly medially

orientated. A constant current stimulator (DS7AH, Digimeter Ltd, Welwyn Garden City, England) was used to deliver the twitch interpolation stimuli to the quadriceps muscle via the electrodes. Twitch interpolation stimuli were 10 millisecond doublet pulses, with a square wave form, a pulse width of 100μs, at a voltage of 300V and a current ranging from 155 to 455 mA. The variation in current was utilised to gain an unpotentiated twitch amplitude of at least 25% MVC (Bulow et al., 1993; Oskouei et al., 2003; Strojnik, 1995).

Based on the MVC measurement, a 25%MVC target was set on the visual display and the twitch interpolation stimulus intensity was gradually increased while the participant was at rest, by 20-25 mA increments, until the target of 25% MVC was reached with the twitch interpolation force. This stimulation intensity was recorded and used for all twitches delivered within the testing session. The resultant potentiated control twitch on average equated to 33% MVC ±10%.

Voluntary activation was established by providing a visual target of 100% MVC force on the visual display and asking the participant to perform a voluntary contraction which reached or exceeded the target. Participants were provided with continuous, loud verbal encouragement and visual feedback of performance. The timing of the twitch interpolation stimuli delivery was controlled by the researcher to ensure it was generated at the maximum level of force (Suter & Herzog, 2001) and the delivery of a control twitch within 1-2 seconds of force relaxation (Bulow et al., 1995; Kufel et al., 2002). Voluntary activation measures were repeated three times, with three minutes rest between each contraction.

Twitch interpolation data was analysed offline, by viewing the range of filtered data where a known stimulus was delivered, using a customised computer software programme (Labview, National Instruments Limited, Texas, USA). The force data was filtered using a Butterworth filter (Low frequency cut off = 10Hz,

High frequency cut off = 500Hz). Twitches were visually identified by a steep rise in the force trace with a clear peak. Cursors were manually adjusted until the baseline and peak were identified. The programme automatically identified the amplitude of the twitch based on the cursor positions.

During voluntary activation measures the twitch data recorded during muscle contraction was discarded if; the baseline level of force was not within 15% of the 100% MVC value at the time of twitch delivery, the participant was unable to sustain a continuous level of force prior to or following twitch delivery, the twitch did not have a clear peak (i.e. there were two peaks) (Bulow et al., 1993; Oskouei et al., 2003; Strojnik, 1995). In addition, the twitch data recorded at rest was discarded if the participant failed to relax fully prior to twitch interpolation. Voluntary activation was calculated using the equation;

$$\text{Voluntary activation (\%)} = [1-(\text{STmva} / \text{avCTmva})] \times 100$$

where the superimposed twitch (STmva) is the force increment recorded during the maximum contraction and the control twitch (CTmva) is the average of the three potentiated control twitches as described above (refer to Figure 3.2). The average of the three measurement calculations was recorded for data analysis.

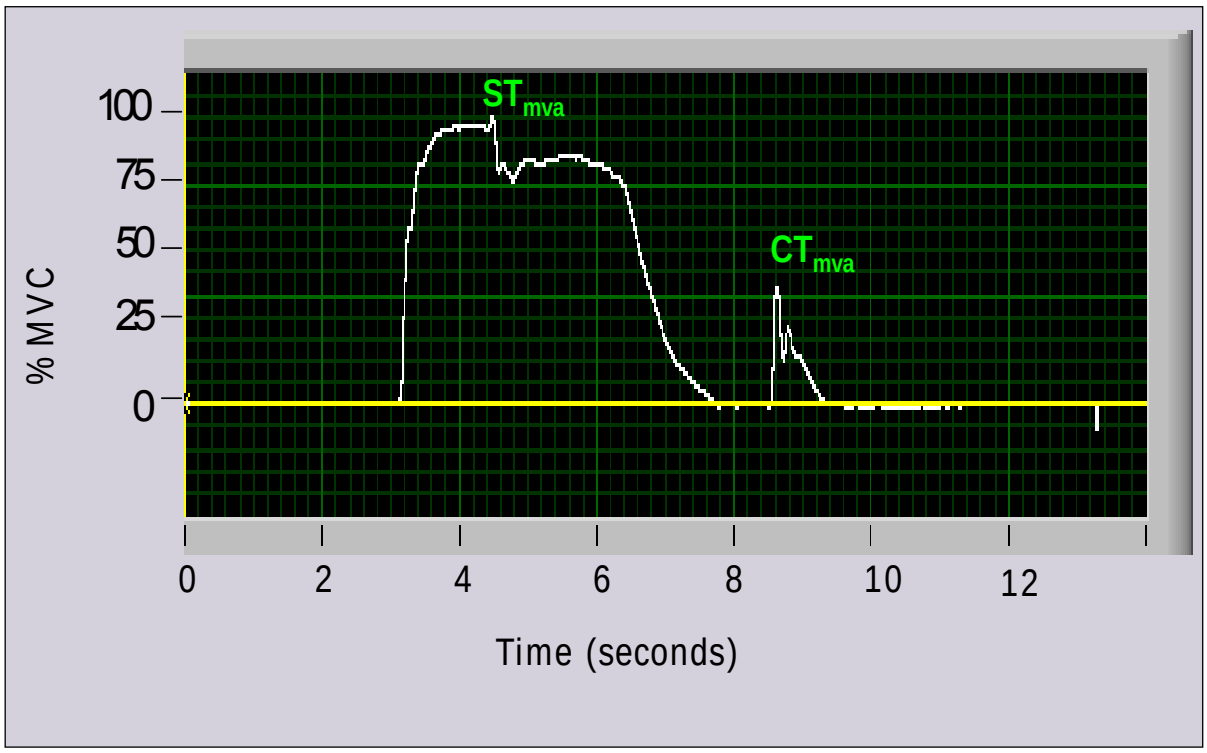


Figure 3.3: A typical force trace of voluntary activation measurement

Note: STmva = Superimposed Twitch delivered at maximal force, CTmva = Control Twitch delivered at rest

3.6.2.3. Neuromuscular Fatigue Measures

The fatigue task involved a 90-second continuous maximal isometric contraction of the quadriceps. A visual target of 100% MVC force was displayed on the visual display, participants were instructed to,

> "push fast and hard to ensure that you touch the target with the force line, then maintain a steady, continuous force for ninety seconds. You need to be pushing as hard as you possibly can. The aim of this last test is to fatigue you, even if the force line drops away you must keep on pushing as hard as you possibly can. Keep pushing until I say stop"

Participants were provided with continuous, loud verbal encouragement and visual feedback of performance throughout the task. The delivery of the first twitch was controlled by the researcher to ensure the twitch was delivered at the maximum level of force, then twitch stimuli were delivered every six seconds by a customised computer software programme (Superscope II 3.0 GW Instruments, Washington, USA). In addition, a control twitch was delivered within 1-4 seconds of completion of the fatigue task. All twitch interpolation data was analysed offline.

Total Neuromuscular Fatigue

Total neuromuscular fatigue across the task was determined by subtracting the percentage of MVC just prior to the last twitch delivery (at or about 90 seconds) from the percentage of MVC just prior to the first twitch delivery (at or about 0 seconds). Total neuromuscular fatigue was calculated using the equation;

Total neuromuscular fatigue (%) = Initial % MVC – Final % MVC

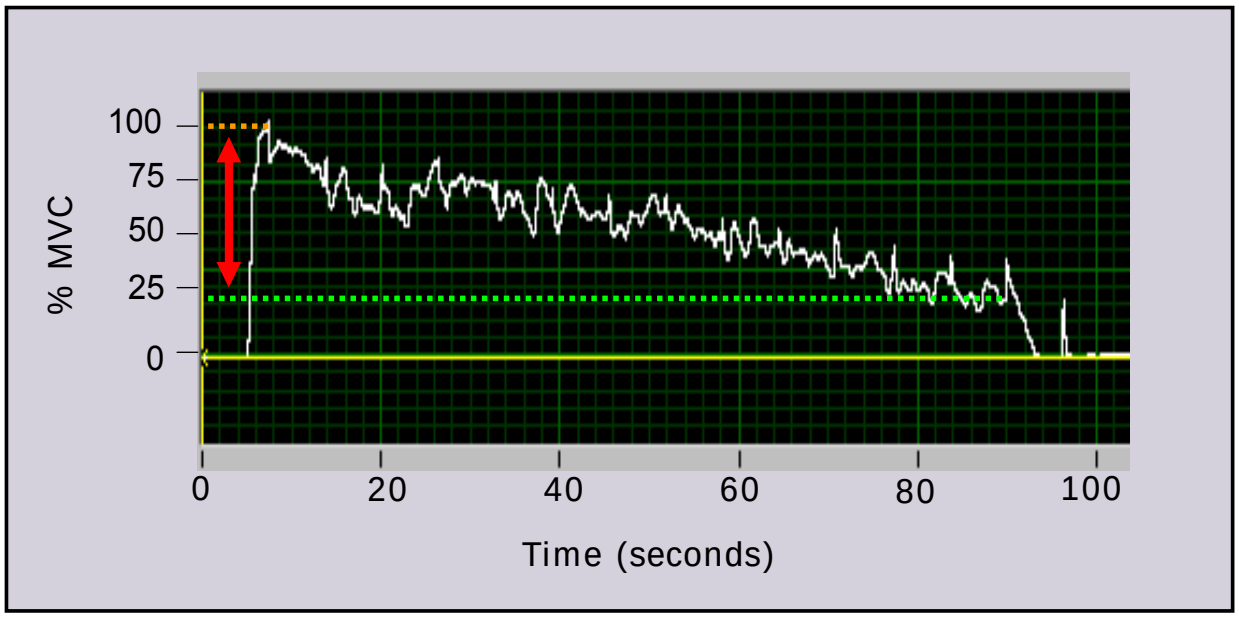


Figure 3.4: A typical force trace of the fatigue task indicating total neuromuscular fatigue

Note: Orange dotted line = Initial % MVC, Green dotted line = Final % MVC, Red arrow = Total neuromuscular fatigue

Central Neuromuscular Fatigue

Central neuromuscular fatigue was calculated as the difference between the voluntary activation measured at the beginning of the fatigue task and the voluntary activation measured at the end of the fatigue task. Therefore, central neuromuscular fatigue was calculated using the equation;

Central neuromuscular fatigue (%) = Beginning VA - End VA

where;

Beginning VA (%) = [1-(ST1 / CTmva)] x 100

End VA (%) = [1-(ST2 / CTfat)] x 100

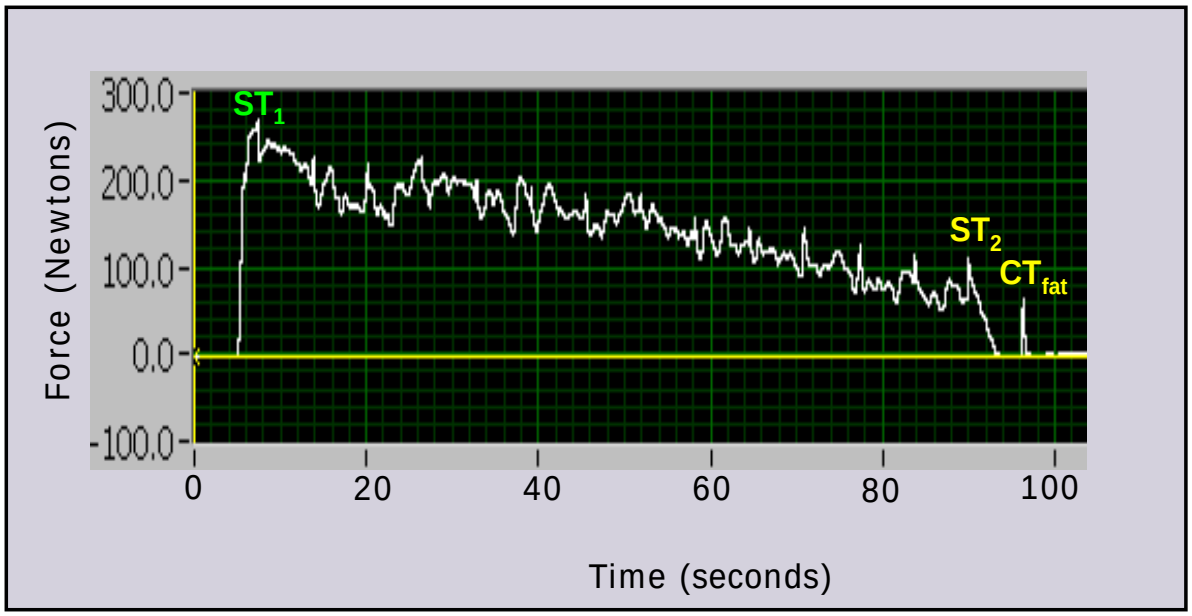


Figure 3.5: A typical force trace of the fatigue task indicating central neuromuscular fatigue

Note: ST_1 = First superimposed twitch, ST_2 = last superimposed twitch, CTfat = Control Twitch at end of fatigue task

Peripheral neuromuscular fatigue

Peripheral neuromuscular fatigue was calculated as the percentage change in the amplitude of the control twitch measured at the end of the fatigue task, normalised to the control twitch amplitude taken during MVA measurement in the same testing session Therefore, peripheral neuromuscular fatigue was calculated using the equation,

$$\text{Peripheral neuromuscular fatigue (\%)} = [1-(CTfat / CTmva)] \times 100$$

3.7. Data management

All written raw data were stored in a locked cabinet in the principal researchers office. Computer based data was stored in a password protected file on the laboratory computer and a backup copy was saved to CD-ROM and stored along with the written raw data. Confidentiality was maintained through the allocation of a study code to each participant, which appeared on all information related to that participant. Only the principal researcher had access to the corresponding code number and name of participant.

Once data was collected and analysed it was visually checked and entered into an SPSS software package (SPSS 12.0.1 for Windows, SPSS Inc., Chicago, USA) by the principal researcher. Screening of data involved a visual check of the range of scores and consideration of the mean and standard deviation for each dependent variable. In addition, a random check of twenty percent of the results (six participants) was carried out, by checking all values entered into SPSS against the raw data.

3.8. Data Analysis

Data analysis was performed using SPSS statistical software package (SPSS 12.0.1 for Windows, SPSS Inc., Chicago, USA). Inspection of raw data and testing for the normality of the distribution of the dependent variables using Kolmogorov-Smirnov test revealed that the distribution of three variables (voluntary activation, peripheral neuromuscular fatigue and 30s Chair Stand Test) was non-normal. Therefore, non-parametric tests were selected for statistical analysis to maintain consistency throughout data analysis.

Analysis involved four phases, first the descriptive analysis of group characteristics, then statistical analysis of test-retest reliability of measures of neuromuscular function and neuromuscular fatigue. Statistical analysis then focused on the other study objectives; to evaluate whether the performance of people with stroke differed from control participants during a sustained maximal voluntary isometric contraction of the quadriceps muscle in measures of neuromuscular fatigue, and to consider whether there were associations between the variables of interest. For all statistical analyses a significance level of $p<.05$ was set.

Descriptive analysis of group characteristics and physical function provided information on the mean, standard deviation, minimum and maximum of continuous data including age, weight, height, body mass index, 30s Chair Stand Test, Comfortable Paced Walking Speed and Fast Paced Walking Speed. Descriptive analysis of the stroke group characteristics also included summaries of each participant's results on stroke related variables including; side of hemiplegia, time since stroke, Mini-Mental State examination, Star Cancellation Test, Modified Ashworth Scale and Manual Muscle Test.

Test-retest reliability of measures of neuromuscular function and neuromuscular fatigue were evaluated using; intraclass correlation coefficients (ICC) two-way random, absolute agreement, ICC 95% confidence intervals and typical error of measurement and typical percentage errors. As the data for some variables was not normally distributed natural log-transformations were utilised prior to intra-class correlation testing. Transformation did not alter the outcome of the reliability testing; therefore the original data was used for all tests. The ICC provides an assessment of the reproducibility of the rank order of the participants on a given measure, while the ICC 95% confidence interval indicates the likely range of the ICC in the true population (Hopkins, 2004). The typical error of measurement

provides an indication of the within participant variation of the measure, and the typical percentage error references that variation to the value of the group mean to allow comparison of error between measures (Hopkins, 2000). Typical percentage error provides an indication of the precision of the measure and is not influenced by the heterogeneity of the sample, which may be a key factor when evaluating the reliability of a measure in the stroke population (Batterham & George, 2003).

Since data was not normally distributed, Mann-Whitney U tests were selected to compare the groups' performance on measure of voluntary activation, MVC, total neuromuscular fatigue, central neuromuscular fatigue and peripheral neuromuscular fatigue. The Mann-Whitney U test uses the ranks of the data rather than their raw value to compare two independent groups (Pallant, 2001), and is a considered a powerful non-parametric statistical test (Dickinson Gibbons & Chakaraborti, 2003).

In order to investigate associations' betweens variables of interest Spearman Rank correlation coefficients were calculated. The Spearman's Rank correlation coefficient calculates the strength of the relationship between two continuous variables and is the non-parametric alternative to the Pearson's product moment correlation (Pallant, 2001).

4. Results

4.1. Introduction

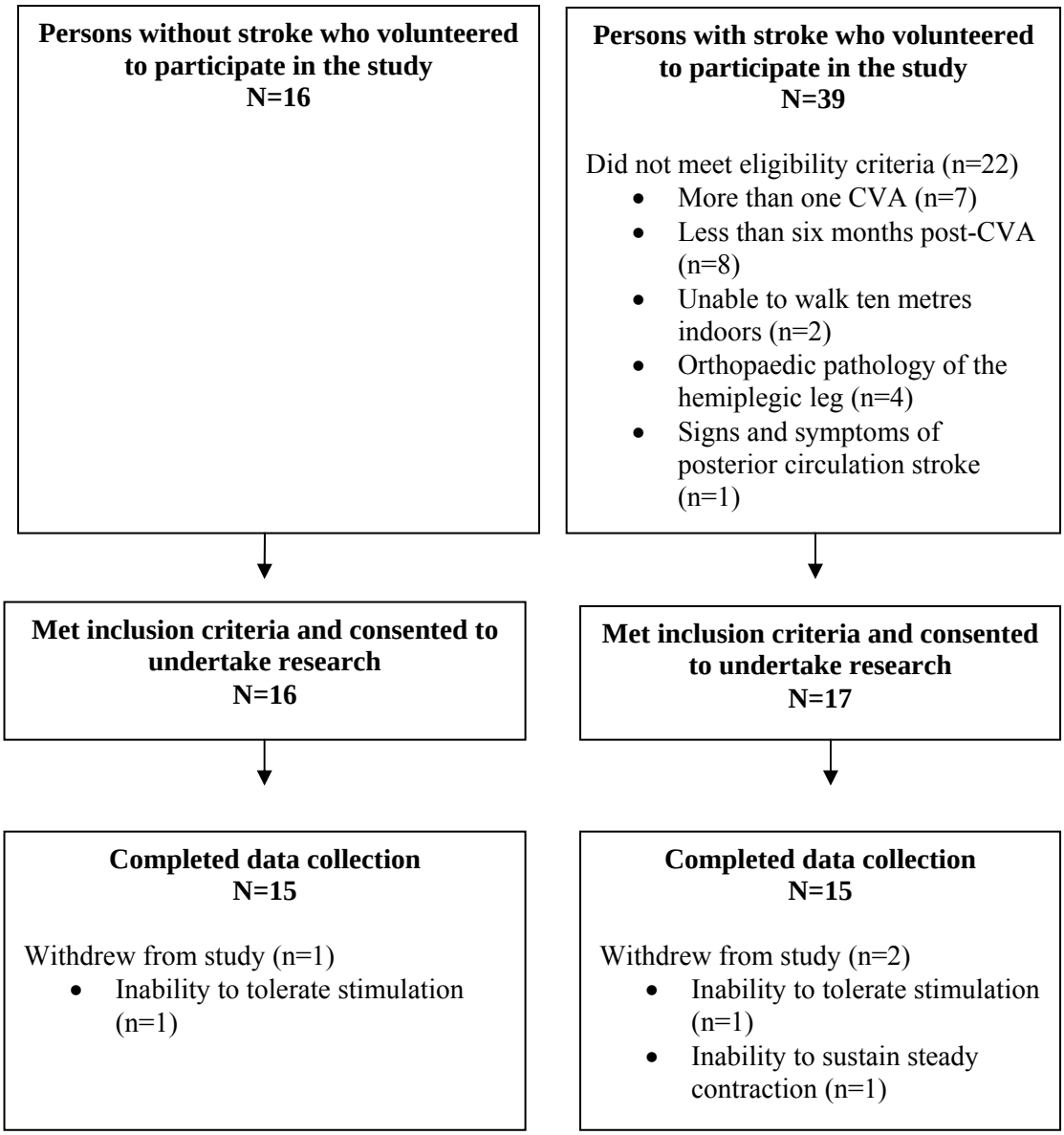
This chapter presents the results of this repeated measures experimental study. The purpose of the study was to examine and compare the contribution of central neuromuscular fatigue and peripheral neuromuscular fatigue to total neuromuscular fatigue during a sustained maximal voluntary isometric contraction of the quadriceps muscle in the hemiplegic leg of people with stroke, with a control group. In addition, the study considered the associations between measures of neuromuscular function and neuromuscular fatigue, and the test-retest reliability of measures of neuromuscular function and neuromuscular fatigue in these populations.

This chapter initially provides an overview of recruitment and retention, and data screening. Then a description of the sample characteristics of both the control and stroke populations is provided. Thirdly, analysis of the test-retest reliability of neuromuscular function and neuromuscular fatigue measures are presented. Finally, the results of descriptive and statistical analysis for the other study objectives are presented.

4.2. Recruitment and Retention

Sixteen control participants volunteered for the study. One participant withdrew at the first testing session due to an inability to tolerate electrical stimulation. Of the thirty nine people with stroke who volunteered for the study, seventeen met the inclusion criteria. Two stroke participants withdrew from the study at the first testing session; one was unable to tolerate electrical stimulation, while the other participant was unable to sustain a steady isometric contraction of the quadriceps. Data collection was completed from March to July 2005.

Figure 4.1: Diagram of recruitment and retention



4.3. Data Screening

Immediately following data collection, visual checking of raw data revealed partial errors in data collection of four participants which resulted in that data being removed from the data set. One stroke participant (S10) had an erratic force profile during the fatigue task during the first testing session; therefore fatigue data for this session was discarded. Force data for the second testing session for another stroke participant (S9) was corrupted due to a computer error. One control participant (C7) failed, during the second testing session, to reach an MVC level close to that recorded during the first testing session. The participant reported undertaking high intensity exercise on the previous day. Therefore all neuromuscular function and neuromuscular fatigue measures for this session were discarded. One control participant (C13) failed to attend the second session.

Cross checking of data entered into SPSS against raw data was carried out to ensure the accuracy of data entry. Data from twenty percent of the total sample (three stroke participants and three control participants) were randomly selected for cross checking. No inconsistencies were identified. Visual checking of the range of scores and consideration of the plausibility of the mean and standard deviation for each variable also revealed no inconsistencies. Outlier values were identified on a number of measures. However, no one participant was an outlier on more than one measure. When statistical testing was repeated with exclusion of the outlier values, no difference in the outcome of any of the statistical tests was noted. Therefore, outlier values were included in all statistical analyses.

4.4. Sample Characteristics

4.4.1. Age and Anthropometric Data

The anthropometric and age data for participants in the stroke and control groups is presented in Table 4.1. The mean age of the control sample was 61.33 years (range 37-82), with eight male and seven female participants. The mean age of the stroke sample was 61.80 years (range 41 – 79), with eight male and seven female participants.

Visual comparison of mean, minimum and maximum values suggests that the samples were similar in terms of age, weight, height and body mass index.

Table 4.1: Age and anthropometric data for Control and Stroke groups

	M		**SD**		**Minimum**		**Maximum**	
	Control	**Stroke**	**Control**	**Stroke**	**Control**	**Stroke**	**Control**	**Stroke**
Age(yrs)	61.3	61.8	11.5	10.9	37	41	82	79
Weight(kg)	76.6	73.4	13.8	14.6	57.7	57.1	102.6	108.9
Height (m)	1.71	1.67	.05	.09	1.60	1.53	1.78	1.86
BMI	26.1	26.1	4.2	4.4	20.4	20.5	33.2	36.0

Note. M= Mean, SD= Standard Deviation, BMI= Body Mass Index.

4.4.2. Stroke Group Characteristics

Table 4.2 presents pertinent information about the stroke group including; age, sex, side of hemiplegia, time since stroke and scores on the Mini-mental State Examination, Star Cancellation test, Modified Ashworth Scale and Manual Muscle Test.

Table 4.2: Stroke group characteristics

Participant	Age	Sex	Hemiplegia	Time	MMSE	SC	MAS	MMT
S1	68	M	Right	43	29	53	0	5
S2	51	F	Left	97	30	48	2	4
S3	51	M	Right	60	29	53	0	3
S4	60	M	Left	133	30	52	0	4
S5	76	M	Right	55	27	54	0	5
S6	66	F	Right	115	27	53	0	4
S7	75	M	Left	31	26	44	0	3
S8	55	M	Left	27	30	54	1	4
S9	50	F	Left	28	29	54	0	5
S10	79	M	Left	29	30	54	3	5
S11	57	F	Left	53	30	54	1	5
S12	41	F	Left	19	30	54	1	5
S13	65	M	Right	63	30	54	0	4
S14	69	F	Left	33	28	53	3	3
S15	34	F	Left	23	30	54	2	5
M	61.8					53.93		
SD	10.9					35.09		

Note. Time= Time in months since stroke, MMSE= Mini-mental State Examination, SC= Star cancellation, MAS= Modified Ashworth Scale, MMT= Manual Muscle Test.

Five participants in the stroke group had right hemiplegia and ten participants had left hemiplegia. The mean time since onset of stroke was 53.93 months (range 19-133). The scores on the Mini-Mental State Examination ranged from 26-30 and the Star Cancellation Test ranged from 44-54. It should be noted that of those participants who scored less than 52/54 on the Star Cancellation Test, none exhibited the unilateral deficit which is characteristic of unilateral visual neglect. The Modified Ashworth Scale scores ranged from zero to three, with two participants scoring three. The Manual Muscle Test scores ranged from three to five, with three participants scoring three.

4.4.3. Physical Function

The results of the baseline physical function of the control and stroke samples are shown in Table 4.3. The table shows the descriptive statistics of; 30s Chair Stand Test, Comfortable Paced Walking Speed and Fast Paced Walking Speed.

The mean number of Sit to Stand repetitions completed in 30 seconds by the control group was 16.47 (SD=4.58), while the mean number in the stroke group was 9.20 (SD=3.75). The stroke group on average completed less sit to stands in the allotted time than the control group.

The stroke group demonstrated slower walking scores than the control group on both comfortable paced and fast paced walking measures. The mean comfortable walking speed for the control group was 1.48m/s (SD=.14), while the mean of the stroke group was 0.92m/s (SD=.38). The mean fast paced walking speed of the control group was 2.07m/s (SD=.25), while the mean of the stroke group was

1.17m/s (SD=.54). The standard deviation of both measures was larger in the stroke group.

Table 4.3: Baseline physical function of the control group and stroke group

a) Control Group

	N	M	SD	Mdn	Minimum	Maximum
30s Chair Stand (reps)	15	16.47	4.58	15	11.00	28.00
Comfortable Walk (m/s)	14	1.48	.14	1.48	1.21	1.81
Fast Walk (m/s)	14	2.07	.25	2.04	1.72	2.68

b) Stroke Group

	N	Mean	SD	Mdn	Minimum	Maximum
30s Chair Stand (reps)	15	9.20	3.75	10	.00	15.00
Comfortable Walk (m/s)	15	.92	.38	.90	.11	1.45
Fast Walk (m/s)	15	1.17	.54	1.08	.12	2.05

Note. N= Number of participants, M= Mean, SD= Standard Deviation, Mdn= Median.

4.5. Test-retest Reliability

An initial objective of the study was to evaluate whether measures of neuromuscular function and neuromuscular fatigue demonstrated test-retest reliability. The study hypothesis states that in people with stroke and control participants, measures of MVC, voluntary activation, total neuromuscular fatigue,

central neuromuscular fatigue and peripheral neuromuscular fatigue will demonstrate test-retest reliability.

4.5.1. Neuromuscular Function Measures

The intraclass correlation coefficients (ICC), ICC 95% confidence interval, typical error of measurement and the typical percentage error of MVC and voluntary activation in the control and stroke samples are presented in Table 4.4.

Table 4.4: Test-retest reliability of Neuromuscular Function measures

	Control Participants				**Stroke Participants**			
	N	**ICC (95%CI)**	**TEM**	**TPE**	**N**	**ICC (95% CI)**	**TEM**	**TPE**
MVC	13	.96 (.88-.99)	44.48	.09	15	.90 (.73-.96)	34.11	.11
VA	13	.95 (.85-.99)	2.13	.02	15	.98 (.94-.99)	3.82	.05

Note. N= Number of participants, ICC (95%CI) = intraclass correlation coefficient (95% confidence interval), TEM= typical error measurement, TPE= typical percentage error, MVC= maximal voluntary contraction, VA= voluntary activation

The ICC measures were excellent (>.90) across both measures, for both groups. The 95% confidence intervals of the ICC's were correspondingly high. There were differences between the two groups in terms of ICC's on the same measures. Notably, the stroke group had a lower ICC (.90) for MVC than the control group (.96), whereas, the stroke group had a higher ICC (.98) for voluntary activation than the control group (.95).

The typical error of measurement and the typical percentage error for MVC were similar between the two groups. The typical error of measurement was 44.48N for the control group and 34.11N for the stroke group, this represented a typical percentage error of .09 and .11 respectively. The typical error of measurement and the typical percentage error for voluntary activation were also similar. The typical error of measurement for the control group was 2.13% and for the stroke group was 3.82%. These values corresponded to a typical percentage error of .02 and .05 respectively. Both MVC and voluntary activation measures appear to have low relative and absolute error levels in both control and stroke groups.

Therefore, measures of MVC and voluntary activation demonstrate test-retest reliability and low error in people with stroke and control participants.

4.5.2. Neuromuscular Fatigue Measures

The intraclass correlation coefficients (ICC), ICC 95% confidence interval, typical error of measurement and the typical percentage error of total neuromuscular fatigue, central neuromuscular fatigue and peripheral neuromuscular fatigue in the control and stroke samples are presented in Table 4.5.

Table 4.5: Test-retest reliability of Neuromuscular Fatigue measures

	Control Participants				Stroke Participants			
	N	**ICC(95%CI)**	**TEM**	**TPE**	**N**	**ICC(95%CI)**	**TEM**	**TPE**
TNMF(%)	13	.73 (.32-.91)	9.04	.17	13	.83 (.53-.95)	9.78	.24
CNMF(%)	13	.83 (.53-.95)	5.85	.26	13	.82 (.51-.94)	10.49	.40
PNMF(%)	13	.68 (.24-.89)	9.72	.21	13	.66 (.20-.88)	12.76	.61

Note. N= number of participants, ICC (95%CI) = intraclass correlation coefficient (95% confidence interval), TEM= typical error measurement, TPE= typical percentage error, TNMF= total neuromuscular fatigue, CNMF= central neuromuscular fatigue, PNMF= peripheral neuromuscular fatigue

The ICC measures were good (.82-.83) for central neuromuscular fatigue across both groups, while ICC's for total neuromuscular fatigue were good for the stroke group (ICC=.83) and adequate for the control group (ICC=.73). ICC's for peripheral neuromuscular fatigue were fair (.66-.68). The two groups had similar ICC's for measures of central neuromuscular fatigue (control= .83, stroke= .82) and peripheral neuromuscular fatigue (control= .68, stroke= .66). However, the control

group had a lower ICC (.73) than the stroke group (.83) for the total neuromuscular fatigue measure.

The typical error of measurement and the typical percentage error for total neuromuscular fatigue were similar between the two groups. The typical error of measurement was 9.04% for the control group and 9.78% for the stroke group, this represented a typical percentage error of .17 and .11 respectively. This represents moderate absolute and relative error in this measure.

The typical error of measurement and the typical percentage error for central neuromuscular fatigue measures were disparate across the groups, with the control group having lower values, and therefore less error than the stroke group. The typical error of measurement for the control group was 5.85% and for the stroke group was 10.49%. These values corresponded to a typical percentage error of .26 and .40, respectively. This may represent moderate absolute error in the control group measures and high absolute error in the stroke group measures.

The typical error of measurement and the typical percentage error for peripheral neuromuscular fatigue measures were also disparate across the groups, with the control group again having lower values, and therefore less error than the stroke group. The typical error for the control group was 9.72% and for the stroke group was 12.76%. These values corresponded to a typical percentage error of .21 and .61, respectively, again indicating moderate relative error in the control group measures and high relative error in the stroke group measures.

These findings suggest that in people with stroke and control participants measures of total neuromuscular fatigue and central neuromuscular fatigue demonstrate adequate test-retest reliability, while measures of peripheral

neuromuscular fatigue have only fair test-retest reliability. All measures appear to have moderate to high levels of relative error.

4.6. Group Comparisons

4.6.1. Neuromuscular Function

As the results of the voluntary activation in the stroke group were non-normally distributed, and for some comparisons the groups were of uneven sizes, Mann-Whitney U tests were used to determine whether there was a statistically significant difference between the two groups. The results of the neuromuscular function measures of the control and stroke samples taken during the second testing session are shown in Table 4.6. The table presents the median, interquartile range and the results of Mann-Whitney *U* tests.

Table 4.6: Group comparison of MVC and voluntary activation

	Control Group			**Stroke Group**			**U**	**p**
	N	**Mdn**	**IRQ**	**N**	**Mdn**	**IRQ**		
MVC	15	426.3	346.0	15	295.9	153.5	42.00	.011*
VA	15	92.6	11.26	15	83.2	21.35	31.00	.002**

Note. Mdn= Median, IRQ = Inter-quartile range, U= computed value of Mann Whitney Test, p= probability

*p<.05

** p<.01

The control group had a median MVC of 426.3N (IRQ=346.0N) and the stroke group had a median MVC of 311.4N (IRQ=153.5N). It should be noted that the spread of the control group data was larger than that of the stroke group as noted

by the interquartile range. There was a statistically significant difference (U=42.00, p=.011) between the MVC of the control group and the stroke group, with the stroke group having a lower MVC than the control group.

Voluntary activation measures differed between the two groups, with lower voluntary activation scores in the stroke group. The control group median voluntary activation was 92.6%, whereas the stroke group mean was 83.2%. The spread of the stroke group data was larger than that of the control group (IRQ= 21.35% and 11.26% respectively). The difference between the stroke group and control group in voluntary activation was statistically significant (U=31, p=.002).

4.6.2. Neuromuscular Fatigue

The objective of this study was to investigate whether the performance of people with stroke differed from control participants during a sustained maximal voluntary isometric contraction of the quadriceps muscle in measures of total neuromuscular fatigue, central neuromuscular fatigue and peripheral neuromuscular fatigue. Specific hypotheses were that:

a. Stroke participants would demonstrate greater total neuromuscular fatigue, when compared to control participants
b. Stroke participants would demonstrate greater central neuromuscular fatigue, when compared to control participants
c. Stroke participants would demonstrate less peripheral neuromuscular fatigue, when compared to control participants

Figure 4.2 provides a pictorial representation of the difference in fatigue profile between the stroke and control groups by presenting the median of total neuromuscular fatigue, central neuromuscular fatigue and peripheral neuromuscular fatigue measures for each group respectively.

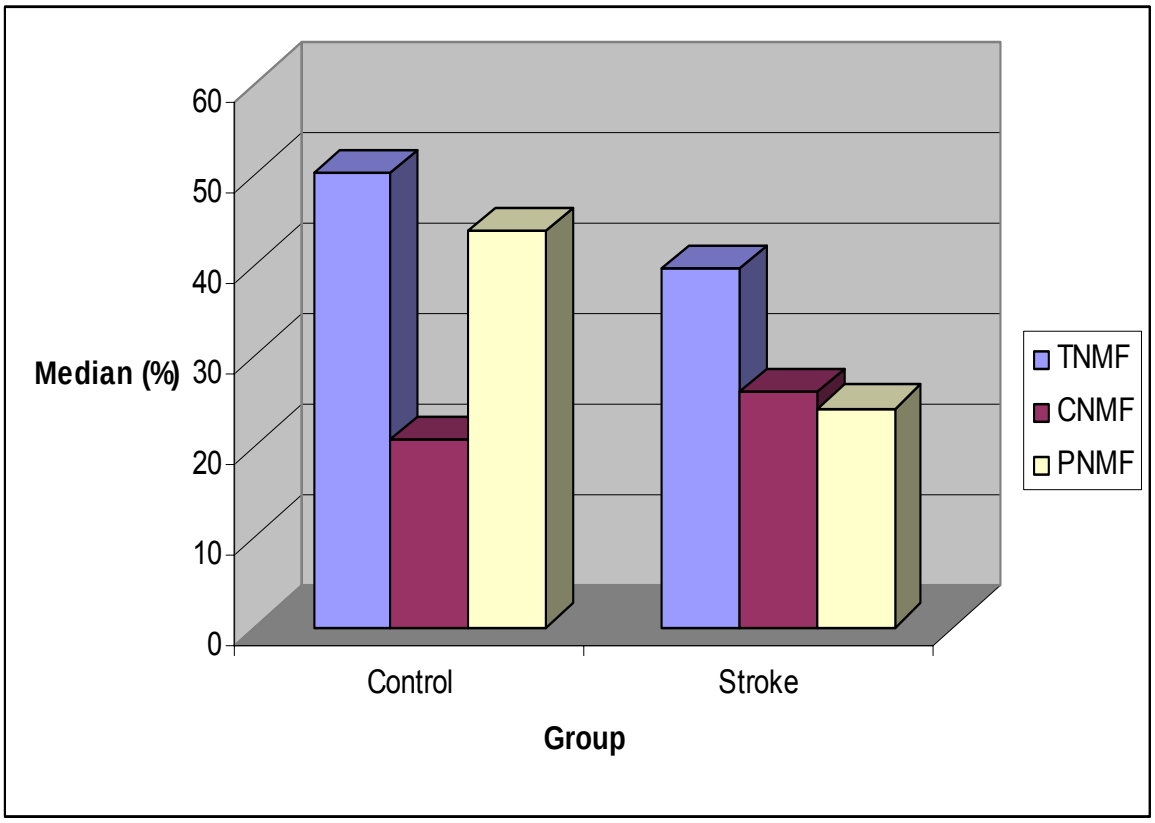


Figure 4.2: Fatigue profile of Control and Stroke Group

Note:. TNMF= total neuromuscular fatigue, CNMF= central neuromuscular fatigue, PNMF= peripheral neuromuscular fatigue

As the results of the peripheral neuromuscular fatigue in the control group were non-normally distributed Mann-Whitney U tests were used to determine whether there was a statistically significant difference between the two groups. The results of the neuromuscular fatigue measures taken during the 90 second fatigue task of the second testing session are presented in Table 4.7 for both the control and stroke groups. The table presents the median, interquartile range and the results of Mann-Whitney *U* testing of total neuromuscular fatigue, central neuromuscular fatigue and peripheral neuromuscular fatigue measures.

Table 4.7: Group comparison of neuromuscular fatigue measures

	Control Group			**Stroke Group**			**U**	**p**
	N	**Mdn**	**IRQ**	**N**	**Mdn**	**IRQ**		
TNMF	13	50.2	19.1	13	39.6	25.4	41.00	.026*
CNMF	13	20.7	17.8	13	25.9	34.8	80.00	.817
PNMF	13	43.8	15.5	13	24.1	19.4	14.00	.000**

Note. Mdn= Median, IRQ = Interquartile range, U= computed value of Mann Whitney Test, p= probability, TNMF=total neuromuscular fatigue, CNMF= central neuromuscular fatigue, PNMF= peripheral neuromuscular fatigue

* p<.05

** p<.01

The median total neuromuscular fatigue score of the control group was 50.1% and the median score of the stroke group was 39.6%. The spread of data in the samples was greater in the stroke group than the control group (IRQ=25.4% and 19.1% respectively). There was a statistically significantly difference (U=41.00, p=.026) between the total neuromuscular fatigue of the control group and the stroke

group, with the stroke group having a lower total neuromuscular fatigue than the control group. This finding does not support the stated hypothesis that, Stroke participants will demonstrate greater total neuromuscular fatigue, when compared to control participants

The stroke group had a greater level of central neuromuscular fatigue compared with the control group. The median of the control group was 20.74%, while the median of the stroke group was 25.88%. However, this difference was not statistically significant (U=80.00, p=.817). It should be noted that the spread of the data was much greater in the stroke group than the control group (IRQ= 34.8% and 17.8% respectively).The statistical analysis does not support the hypothesis that, stroke participants demonstrate greater central neuromuscular fatigue, when compared to control participants.

The median peripheral neuromuscular fatigue score of the control group was 43.84% and the median score of the stroke group was 24.12%. The spread of the data of the two samples was slightly greater in the stroke group (IRQ= 19.4%) than in the control group (IRQ= 15.5%). There was a statistically significant difference (U=14.00, p=.000) between the peripheral neuromuscular fatigue of the control group and the stroke group, with the stroke group having a lower peripheral neuromuscular fatigue score than the control group. Hence this finding supports the hypothesis that stroke participants demonstrate less peripheral neuromuscular fatigue, when compared to control participants.

4.7. Associations between Variables of Interest

An objective of the study was to investigate the associations between variables of interest. In particular, to investigate the relationships between neuromuscular function, physical function and neuromuscular fatigue in people with stroke. As the results of the 30s Chair Stand Test, voluntary activation and peripheral neuromuscular fatigue were not normally distributed Spearman's rank correlation coefficient were used to determine whether there was a statistically significant association between all variables of interest.

4.7.1. Association between Voluntary Activation, Strength and Physical Function

Table 4.8: Spearman rank correlations between Voluntary Activation and MVC in both control and stroke groups

Control Group N=13		**Stroke Group N=15**	
r_s	**p**	**r_s**	**p**
-.088	.775	.593	.020*

Note. N= Number of participants, r_s = Spearman rank correlation coefficient, p= probability

*p<.05

In the control group there was no statistically significant relationship between voluntary activation and MVC. In contrast, in the stroke group there was a large positive correlation between the two variables (r=.593, p=.020), indicating that higher levels of voluntary activation are associated with higher levels of strength.

Table 4.9 presents the results of Spearman rank correlations between MVC and measures of physical function in both control and stroke groups. In the control group there was no significant correlation between MVC and any of the measures of function. In the stroke group MVC had a strong positive correlation with both comfortable paced walking speed (r=.804, p<.001) and fast paced walking speed (r=.643, p=.010). Therefore, higher levels of quadriceps MVC was associated with both faster comfortable and fast-paced walking speeds. There was no statistically significant correlation between MVC and 30s Chair Stand Test in the stroke group.

Table 4.9: Spearman rank correlations between MVC and measures of physical function in both control and stroke groups.

	Control Group N=13		**Stroke Group N=15**	
	r_s	**p**	**r_s**	**p**
30s Chair Stand Test	-.077	.802	.422	.118
Comfortable Walk	-.547	.053	.804	.000**
Fast Walk	-.011	.972	.643	.010*

Note. N= Number of participants, r_s = Spearman rank correlation coefficient, p= probability

*p<.05

** p<.01

Table 4.10: Spearman rank correlations between Voluntary Activation and measures of Physical Function in both control and stroke groups

	Control Group N=13		**Stroke Group N=15**	
	r_s	**p**	**r_s**	**p**
30s Chair Stand Test (reps)	.157	.608	-.056	.844
Comfortable Walk (m/s)	-.418	.155	-.496	.060
Fast Walk (m/s)	-.074	.809	.272	.327

Note N= Number of participants, r_s = Spearman rank correlation coefficient, p= probability

There were no statistically significant correlations between voluntary activation and any of the measures of physical function in either of the groups.

4.7.2. Associations between Strength, Voluntary Activation and Measures of Fatigue

Table 4.11: Spearman rank correlations between MVC and measures of fatigue in both control and stroke groups

	Control Group N=13		Stroke Group N=15	
	r_s	**p**	**r_s**	**p**
TNMF	-.181	.553	.313	.297
CNMF	-.225	.459	.357	.231
PNMF	.544	.055	.280	.354

Note N= Number of participants, r_s = Spearman rank correlation coefficient, p= probability

There were no statistically significant correlations between MVC and any of the measures of neuromuscular fatigue in either of the groups

Table 4.12: Spearman rank correlations between Voluntary Activation and measures of Neuromuscular Fatigue in both control and stroke groups

	Control Group N=13		Stroke Group N=15	
	r_s	p	r_s	p
TNMF	**.863**	**.000****	**.665**	**.027***
CNMF	**.610**	**.027***	**.560**	**.046***
PNMF	**-.033**	**.915**	**.264**	**.384**

Note. N= Number of participants, r_s = Spearman rank correlation coefficient, p= probability, TNMF=total neuromuscular fatigue, CNMF= central neuromuscular fatigue, PNMF= peripheral neuromuscular fatigue

*p<.05

** p<.01

In the control group voluntary activation had a very large positive correlation with total neuromuscular fatigue (r_s =.863, p=.000) and a large positive correlation with central neuromuscular fatigue (r_s =.610, p=.027). In the stroke group voluntary activation had a large positive correlation with both total neuromuscular fatigue (r_s =.665, p=.027) and central neuromuscular fatigue (r_s =.560, p=.046). This indicates that higher levels of voluntary activation are associated with greater total neuromuscular fatigue and central neuromuscular fatigue in both the control and the stroke groups. There was no clear relationship between voluntary activation and peripheral neuromuscular fatigue in either the control or the stroke group.

Table 4.13: Spearman rank correlations between measures of neuromuscular fatigue and measures of physical function in the control and stroke groups

a) Control Group

	30s Chair Stand Test		Comfortable Walk		Fast Walk	
	r_s	p	r_s	p	r_s	p
TNMF	.314	.295	-.261	.388	.017	.957
CNMF	.543	.055	.261	.388	.259	.394
PNMF	.306	.309	-.011	.972	.545	.054

b) Stroke Group

	30s Chair Stand Test		Comfortable Walk		Fast Walk	
	r_s	p	r_s	p	r_s	p
TNMF	.055	.858	.346	.247	.363	.223
CNMF	.224	.462	.330	.271	.325	.279
PNMF	.655	.015*	.319	.289	.440	.132

Note. N= Number of participants, r_s = Spearman rank correlation coefficient, p= probability, TNMF=total neuromuscular fatigue, CNMF= central neuromuscular fatigue, PNMF= peripheral neuromuscular fatigue

*p<.05

There were no statistically significant correlations between any of the measures of neuromuscular fatigue and any of the measures of physical function in the control group. There was a very large and statistically significant association

between peripheral neuromuscular fatigue and 30s Chair Stand Test in the stroke group. There were no other statistically significant correlations between measures of neuromuscular fatigue and physical function in the stroke group.

4.8. Summary

This chapter has presented the results of this experimental study comparing a group of people with mild to moderate stroke with an matched control group during a neuromuscular fatigue task. Differences between the groups were not as expected by the study hypotheses. Stroke participants demonstrated statistically significant differences when compared to the control group in the amount of total neuromuscular fatigue and peripheral neuromuscular fatigue developed, and while they did demonstrate greater central neuromuscular fatigue, this finding was not statistically significant.

Associations were identified between voluntary activation and strength, strength and physical function in the stroke group, and voluntary activation and neuromuscular fatigue in both the stroke and control groups.

Results of reliability testing partially supported the study hypotheses, with measures of neuromuscular function demonstrating excellent test-retest reliability, while measures of neuromuscular fatigue demonstrated fair to good reliability and moderate to high levels of error.

5. Discussion

5.1. Introduction

The purpose of this study was to examine and compare the contribution of central neuromuscular fatigue and peripheral neuromuscular fatigue to total neuromuscular fatigue during a sustained maximal voluntary isometric contraction of the quadriceps muscle in the hemiplegic leg of people with stroke, with that of control participants. Specifically it was hypothesised that performance of people with stroke would differ from control participants by demonstrating greater total neuromuscular fatigue, greater central neuromuscular fatigue and less peripheral neuromuscular fatigue. The results indicate that the performance of people with stroke did differ from control participants during the fatigue task, however not in the manner anticipated.

Contrary to the hypothesis, stroke participants demonstrated less total neuromuscular fatigue when compared to control participants, and while they did demonstrate greater central neuromuscular fatigue, this finding was not statistically significant. The study findings supported the hypothesis that, stroke participants demonstrate less peripheral neuromuscular fatigue, when compared to control participants.

This chapter discusses the potential effects of the sample and method on the study findings, compares the results of the current study to those previously reported in normal and stroke populations and considers the potential explanations for the study findings based on the physiological changes which occur following stroke and the influence of the task parameters on the likelihood that fatigue would develop in

either the stroke or control populations. Finally, consideration is given to the future research directions.

5.2. Study Samples

The study sample reflected a population of people with mild to moderate chronic stroke. Matching with control participants appeared to be largely successful with the groups being similar in terms of age, sex, weight, height and body mass index. Study participants volunteered to take part, which is likely to have introduced a significant selection bias in both the control and stroke groups; in all likelihood the samples represent people who are relatively healthy and physically active. As expected, there were marked differences between the stroke group and the control group in terms of physical and neuromuscular function. The stroke participants were able to perform fewer sit to stand manoeuvres, had slower walking speeds, were weaker and had lower levels of voluntary activation than the control participants.

In comparison to other studies of neuromuscular fatigue following stroke (Lindstrom et al., 1998; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999), the samples of the current study represents a group of slightly older people (M=61.8 years, SD=10.9), with a greater range of ages represented (34-79 years). Unlike some previous studies, no attempt was made to control the age of participants in this study (Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999). This may have resulted in a sample which is more representative of the general stroke population, given that stroke is an age-related pathology. However it also introduces the influences of age-related neuromuscular changes on all measures, which was controlled for by an age-matched control group.

In the current study the average time since onset of stroke was longer than that seen in previous studies of neuromuscular fatigue (Lindstrom et al., 1998; Riley & Bilodeau, 2002; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999).The time since onset of stroke may be relevant when considering fatigue related changes following stroke, potentially the longer the time since onset of stroke, the greater the likelihood for secondary neural changes, muscle atrophy and muscle composition changes.

As previous studies have been conducted with stroke participants who had minimal physical disability, one aim of this study was to consider neuromuscular fatigue in participants with mild to moderate disability. Comparisons of walking speed suggest that the stroke participants in the current study had significantly greater physical disability, with slower comfortable paced (on by average 0.15-0.3m/s) and fast paced walking speeds (on by average 0.45-0.47m/s) (Sunnerhagen et al., 1999; Svantesson et al., 1999). It was not possible to make comparisons with other studies based on muscle strength as similar measurement techniques were not used, however, comparison based on hypertonia suggested greater levels of neuromuscular impairment in the participants of the current study than in past studies (Riley & Bilodeau, 2002; Svantesson et al., 1998; Svantesson et al., 1999). It is expected that any differences between the stroke and control groups in terms of neuromuscular fatigue would be more marked when stroke participants had greater neuromuscular impairments and physical disability.

An important consideration with respect to the stroke sample is the influence of heterogeneity of the sample on the internal validity of the study. Little or no effort was made to control for the severity of neuromuscular impairment or physical disability. Participants were only excluded from the study if they could not walk

10m indoors without physical assistance or if they had an impairment which was likely to influence their ability to participate in the testing procedure. This potentially resulted in a heterogeneous stroke sample. The heterogeneity of the stroke sample is illustrated by the variation seen in sit to stand ability (range = 0-15 repetitions), walking speed (comfortable walking speed range= 0.11-1.45 m/s) and voluntary activation measures (range = 28-95%). The inclusion of people with varied levels of neuromuscular impairment and physical disability may obscure the identification of group based similarities in fatigue profile. To avoid the problem of heterogeneity researchers could rigorously define the study sample based on lesion location or size, for example; to only include participants with middle cerebral artery infarcts or with those with cortical lesions. In addition in the study sample there was a predominance of participants with left hemiplegia, with ten participants having left hemiplegia and only five having right. This is similar to other studies of neuromuscular fatigue and other studies of people following stroke, likely reflecting the need to gain informed consent and to recruit participants who are able to follow complex verbal instructions. This imbalance potentially challenges the external validity of the study and limits extrapolation of the results. These issues are particularly relevant if the development of neuromuscular fatigue is lesion or hemisphere specific. However, studies of subjective fatigue have failed to identify specific area of the brain which is relevant to its development (Choi-Kwon et al., 2004; Ingles et al., 1999; van der Werf et al., 2001).

Other factors not controlled for in this experimental process may have influenced the internal validity of the study, for example; caffeine consumption (Kalmar & Cafarelli, 1999), medications which act on the central nervous system (Newham & Hsiao, 2001) and other orthopaedic conditions such as those affecting

the spine, hip or ankle. Levels of physical activity were also not considered as part of this study, this may be a potential confounder. Recent research has suggested that levels of physical activity may be relevant in the development of peripheral neuromuscular changes in people with stroke (Hachisuka et al., 1997) and have been identified as relevant to neuromuscular impairment and physical function in older adults (Duchateau & Enoka, 2002).

The characteristics of age, time since stroke and level of neuromuscular impairment and physical disability of the participants in this study is dissimilar to the participants of previous studies investigating neuromuscular fatigue in people following stroke. These differences are important in that they provide an indication of how neuromuscular fatigue might affect people who are older and more severely affected following stroke than those previously reported. A number of factors have been highlighted related to recruitment, inclusion and exclusion criteria and sample characteristics which challenge the internal and external validity of the current study.

5.3. Reliability of measures

An aim of the study was to evaluate whether measures of MVC, voluntary activation and neuromuscular fatigue demonstrate test-retest reliability in control and stroke populations. Results of reliability testing partially supported this hypothesis. Measures of MVC and voluntary activation had excellent test-retest reliability and low levels of absolute and relative error in both groups. However, measures of neuromuscular fatigue had more disparate results, with measures of central neuromuscular fatigue and total neuromuscular fatigue demonstrating good to adequate test-retest reliability, whereas measures of peripheral neuromuscular fatigue demonstrated only fair test-retest reliability in both groups. All measures of

neuromuscular fatigue had moderate to high levels of relative error, across both groups.

5.3.1. Maximal Voluntary Contraction

The test-retest reliability of isometric quadriceps MVC, in both control and stroke participants, was excellent (ICC >.90) and are similar to that reported in previous studies in control participants (Allen et al., 1995; Colombo et al., 2000; Todd, Gorman, & Gandevia, 2004), and stroke participants (Bohannon & Andrews, 1990; Bohannon & Walsh, 1992; Eng et al., 2002; Flansbjer, Holmback, Downham, & Lexell, 2005; Hsu et al., 2002; Tripp & Harris, 1991). Few studies have reported error in measures of MVC as an indication of the technological error and/or biological variation inherent within an individuals measurement (Hopkins, 2004). Values for the typical error of measurement and typical percent error in both control and stroke participants indicated low levels of absolute and relative error in measures of MVC. The relative error seen in the control population was similar to that reported by Todd, et al (2004) and Colombo et al, (2000) but slightly higher than that reported by Allen et al (1995), while the relative error in stroke participants was similar to that reported by Flansbjer et al (2005) when evaluating isokinetic strength of the quadriceps in people with stroke.

The high reliability and low error of MVC measures in both stroke and control participants may have been supported by the use of a standardised procedure, familiarisation period, visual feedback, loud verbal encouragement and sufficient rest time between measures.

5.3.2. Voluntary Activation

The test-retest reliability of voluntary activation was excellent (ICC = .95-.98) in both control and stroke groups. ICC measures in control participants were

similar to that reported in another study of the reliability of voluntary activation of the quadriceps in participants without pathology (Behm et al., 1996) and higher than those reported in studies of other muscle groups (Allen et al., 1995; Todd, Gorman et al., 2004). Differences between the reliability of voluntary activation measures in the current study and those reported in other muscle groups (Allen et al., 1995; Todd, Gorman et al., 2004) may reflect the contribution of synergist muscle activity to the other muscle groups tested or other methodological issues. No studies were identified which evaluated test-retest reliability of voluntary activation measures in people with stroke. One study by Horemans et al (2004) considered the reliability of voluntary activation of the quadriceps muscle in people with post-polio syndrome, determining only moderate test-retest reliability (ICC = .73) in this group. Methodological issues, particularly the timing of the control twitch delivery and the duration between test and retest (three weeks), may have affected reliability in Horemans et al (2004) study. The high test-retest reliability of the stroke group in the current study may also have been enhanced by the heterogeneity of the sample, given that ICC is determined based on the rank order of the participants, a more heterogeneous group is more likely to maintain their rank order from test to retest, despite changes in individuals scores (Hopkins, 2000).

Values for typical error of measurement and typical percent error in both control and stroke participants indicated low levels of absolute and relative error in measures of voluntary activation. Error in measures of voluntary activation has been evaluated using a number of different statistical methods in other studies (Allen et al., 1995; Horemans et al., 2004; Morton et al., 2005; Todd, Gorman et al., 2004). The level of relative error in the measure of voluntary activation in both the control and stroke groups in the current study appears to be similar to that found by Allen et

al (1995) and Morton et al (2005) and lower than that found by Horemans et al (2004) and Todd et al (2004).

Potential sources of error in the measurement of voluntary activation in the current study include viscoelastic effects on twitch size, the ability of the participant to generate a consistent MVC and the timing of twitch delivery. As discussed previously, twitch force may be lost due to the influence of viscoelastic properties of the muscle, which cause a reduction in twitch size due to taking up of the viscoelastic properties within the muscle (Behm et al., 1996). This effect is potentially greater in the stroke population due to their lower levels of MVC. However the similarity in levels of absolute error between the stroke and control groups suggests that this was not an issue. High levels of test-retest reliability and low levels of error in measures of MVC suggest that the ability of the participants to generate a consistent MVC was not an issue in either the control or stroke group. The timing of twitch delivery in the current study was controlled by the researcher and was therefore open to error. While efforts were made to provide consistent timing of twitch delivery, the size of the superimposed twitch is influenced by the exact level of MVC at the time of stimulus and the size of the control twitch is influenced by the length of time since termination of contraction (Suter & Herzog, 2001). Variations in the exact timing of twitch delivery may have introduced some technological error into measures of voluntary activation.

5.3.3. Total Neuromuscular Fatigue

As discussed in Section 2.6 the reliability of measures of fatigue are not routinely discussed in the literature, but are often justified by citing the reliability of the constituent parts of the measure, for example, discussing the reliability of MVC rather than the reliability of *decline* in MVC during the fatigue task. The current

study identified that the measure of total neuromuscular fatigue, as determined by decline in MVC across the task, had good test-retest reliability in the stroke sample (ICC=.83) and reasonable test-retest reliability in the control sample (ICC=0.73). Only one previous study was identified which reported poor test-retest reliability (ICC= 0.55) of decline in MVC of the quadriceps during an isometric task as a measure of fatigue (Schwid et al., 1999). The test-retest reliability of the total neuromuscular fatigue measure found in the current study is higher than that previously reported. The reliability of total neuromuscular fatigue measures have been reported in people with Multiple Sclerosis by both Schwid et al (1999) and Surakka et al (2004). The test-retest reliability in these studies ranged from 0.68-0.80, and was dependent on the exact method used to quantify total neuromuscular fatigue. These results are similar to the test-retest reliability found in the current study. Measures of total neuromuscular fatigue may be more reliable in groups with pathology, possibly due to the heterogeneity of the group. This highlights the importance of considering error rates when evaluating reliability. The absolute and relative error seen in both the control and stroke samples in the current study were similar between the groups. Similarities in the error rates between the stroke and control groups indicates that differences in the ICC between the groups is likely to relate primarily to the variability within the stroke group.

Stand alone measures of MVC taken during the same testing session as fatigue measures demonstrated excellent test-retest reliability and low error rates in both groups. Given that change in MVC was used to quantify total neuromuscular fatigue, it may be that the lower level of test-retest reliability of total neuromuscular fatigue in comparison to MVC measures reflects biological variation, rather than technological error. Although the testing procedure was identical from test to retest

the participant's approach to the task may have varied. This may be due to prior knowledge of the fatigue task on the second testing occasion, which is likely to be particularly relevant in an arduous task that involves a noxious stimulus. In addition, participants only had one days rest between testing sessions and hence there may have been some residual effect from the first testing session on the second testing session. Alternatively, there may be a learning effect from the first testing session to the second. Error levels in total neuromuscular fatigue measures may have been reduced by a more extensive familiarisation period, more than one days rest between testing sessions and further restriction of the sample as described in Section 5.2.

5.3.4. Central Neuromuscular Fatigue

Factors affecting the reliability of total neuromuscular fatigue measures are also likely to impact on the reliability of both peripheral neuromuscular fatigue and central neuromuscular fatigue measures, given that these measures both evaluate components of total neuromuscular fatigue. Central neuromuscular fatigue was determined by the level of decline in voluntary activation across the fatigue task. The test-retest reliability of central neuromuscular fatigue, as measured by ICC, was good in both groups. However, the level of absolute and relative error was moderate to high. Sources of error within the measure of central neuromuscular fatigue include those which affect the reliability of voluntary activation, as outlined above. Additional sources of error include; viscoelastic effects, the use of a submaximal stimulus intensity, movement of the electrodes during the task and the exact level of MVC when voluntary activation measures were calculated at the beginning and end of the task. As force levels decline during the fatigue task, the impact of viscoelastic properties on twitch size may increase, this may be more of an issue in the stroke group. The use of a submaximal stimulus intensity during a contraction where the

threshold of motor axons is likely to increase and electrode movement during the fatigue task may introduce error (Sheild & Zhou, 2004). The exact level of MVC at which the initial and final measures of voluntary activation measures were taken may have also varied from testing session to testing session due to variation in the timing of twitch delivery of the initial and final superimposed twitch. In particular, the influence of force fluctuations at the time of the final superimposed twitch may have affected the exact level of MVC at the time of the final superimposed twitch delivery. The exact level of MVC at the time of voluntary activation calculation has been shown to influence the size of the interpolated twitch (Oskouei et al., 2003).

There were differences between the groups with respect to both absolute and relative error, the stroke group had higher levels of error than the control group. It may be that the stroke group had greater levels of biological variation and more scope for technological error in the measure. This may be associated with enhanced viscoelastic effects in the stroke group and increased force fluctuations impacting the exact level of MVC during measurement calculation.

In summary, error levels in the central neuromuscular fatigue measure may relate to, a) the biological variation in the fatigue task itself, b) factors which influenced the reliability of measures of voluntary activation, and c) factors which specifically influenced the measurement of central neuromuscular fatigue such as viscoelastic effects, the use of a submaximal stimulus intensity, movement of the electrodes during the task and the exact level of MVC during the initial and final measures of voluntary activation. Some of these factors may have had a greater impact on the error of measures in the stroke group compared to the control group.

5.3.5. Peripheral Neuromuscular Fatigue

Peripheral neuromuscular fatigue was measured by calculating the percentage decline in the control twitch torque taken following the fatigue task, when normalised to the control twitch taken during the maximal voluntary activation measure. The test-retest reliability of the peripheral neuromuscular fatigue measures were similar in both the control and stroke samples (ICC .68 and .66 respectively). The absolute error of the measures was similar; however, when referenced to the mean to establish the typical percentage error, the stroke group was much higher than the control group. This difference in relative error relates to the differences in the mean of the two groups, where the stroke group had a much lower mean level of peripheral neuromuscular fatigue.

Like central neuromuscular fatigue, peripheral neuromuscular fatigue test-retest reliability is likely to be influenced by factors which affect total neuromuscular fatigue. The timing of control twitch delivery may also be a key issue in this measure. While every effort was made to standardise the timing of twitch delivery, this was by no means exact, and subjects relaxed at different rates at the end of the task. Past studies clearly show the effect of potentiation of the twitch from the preceding contraction degrades over time (Binder-Macleod, Dean, & Ding, 2002; Hamada, Sale, MacDougall, & Tarnoplosky, 2000; Suter & Herzog, 2001). Therefore, differences in the timing of the control twitch delivery are likely to impact on the twitch size. The influence of viscoelastic properties within the muscle may also be important in peripheral neuromuscular fatigue measures, as the twitch is delivered at rest.

5.4. Study Power

As no previous studies of central neuromuscular fatigue in stroke participants involving statistical analysis had been published, power calculations for this study were based upon studies in normal and multiple sclerosis populations. The need to establish the reliability of the measurement technique in the stroke population, the potential heterogeneity of neuromuscular impairment in the stroke population and the risk of dropouts was acknowledged, and the sample size elevated accordingly. However, the heterogeneity of results seen within the stroke population and the level of error in neuromuscular fatigue measures suggest that it is likely the study was underpowered for measurement of differences between the groups in terms of the study hypotheses. Negative results should therefore be interpreted in the context of the limited power of the study, given that the likelihood of a type II error is high. In light of this, interpretation of the results may benefit from consideration of the magnitude of the difference between the samples, as well as the statistical significance.

5.5. Neuromuscular Function

5.5.1. Maximal Voluntary Contraction

The current study clearly demonstrated a difference between the control and the stroke groups in terms of MVC. The stroke group were significantly weaker than the control group. This finding is in accord with other studies which have considered strength of the quadriceps muscle in people with stroke, compared to control participants (Davies et al., 1996; Harris et al., 2001; Newham & Hsiao, 2001). The stroke group had approximately 62% ± 20% of the strength of the control group. This level of deficit falls within the range previously reported in studies which have

compared the strength of people with stroke to control participants or population based data across various muscle groups (Ada et al., 2000; Andrews & Bohannon, 2000, 2003; Bohannon & Walsh, 1992; Davies et al., 1996; Lindstrom et al., 1998; Newham et al., 1995; Newham & Hsiao, 2001; Svantesson et al., 1998; Svantesson et al., 1999).

5.5.2. Voluntary Activation

In concurrence with past studies investigating voluntary activation following stroke (Harris et al., 2001; Newham & Hsiao, 2001; Newham et al., 1996; Riley & Bilodeau, 2002), the current study identified deficits in voluntary activation in the stroke sample. Previous studies have investigated the quadriceps muscle (Newham & Hsiao, 2001; Newham et al., 1996) and the elbow flexors (Riley & Bilodeau, 2002), and reported voluntary activation of 59 -66.4% (± 6-10.3%). The level of voluntary activation found in the stroke group of the current study was 83.2% (IRQ= 21.35%), which is higher than previously reported. This difference may relate to differences in the method of quantifying voluntary activation or the level of disability and neuromuscular impairment of the participants. No comparisons of the level of disability and neuromuscular impairment could be made as similar measures were not taken across studies. The fact that the stroke participants in the current study were longer since onset of stroke may also be relevant. While voluntary activation deficits have been identified in acute and sub-acute stroke participants, gains in voluntary activation over time are less well investigated. Although Newham & Hsiao (2001) reported no statistically significant change in voluntary activation over time in participants with stroke who were followed up from three weeks to six months post-stroke. Alternatively the heterogeneity of the stroke sample in the current study, may have distorted the results.

5.6. Neuromuscular Fatigue

Interpretation of the findings of the current study in relation to fatigue measures is limited by two factors. Firstly, the reliability of fatigue measures was not high, which limits the power of the study and thus the probability if obtaining significant results. Therefore the results of measures of fatigue should be interpreted with caution. Secondly, comparison to previous studies is limited to a small number of studies in normal participants which use similar fatigue protocols in the quadriceps muscle (Babault et al., 2005; Bigland-Ritchie et al., 1978; Rattey et al., 2005; Schwid et al., 1999) and to a small number of studies in stroke subjects which use disparate fatigue protocols.

To facilitate scrutiny of the research findings, comparison of the control group results to previous fatigue studies in normal participants is initially made. Then comparison of stroke group and control group findings is made, with reference to previous studies in the stroke population. Consideration is then given to physiological differences between the stroke and control participants which may explain the results and then to the potential influence of the fatigue task parameters on differences identified between the two groups.

5.6.1. Control Group

The median total neuromuscular fatigue of the control group in the current study was 50.2%. Previous studies of fatigue in normal participants during a sustained maximal isometric contraction of the quadriceps have reported a 19.2% - 77% decline in MVC during tasks of varying durations (range = 30 - 100 seconds) (Babault et al., 2005; Bigland-Ritchie et al., 1978; Rattey et al., 2005; Schwid et al., 1999). In the current study the task was sustained for 90 seconds, both the task time

and the level of total neuromuscular fatigue are within the ranges of previously reported results, suggesting that the results of the current study are consistent with previous studies in normal participants.

The median central neuromuscular fatigue in the control participants was 22.4%. This level of central neuromuscular fatigue is similar to that previously reported for the quadriceps during sustained isometric tasks (range=14-27.5%) in normal participants (Babault et al., 2005; Bigland-Ritchie et al., 1978; Place, 2005; Rattey et al., 2005). The difference between the exact level of central neuromuscular fatigue in the current study and those previously reported likely relates to the measurement method (Bigland-Ritchie et al., 1978; Rattey et al., 2005) and the task parameters (Babault et al., 2005; Bigland-Ritchie et al., 1978; Place, 2005).

The median peripheral neuromuscular fatigue of the control group in the current study was 43.8 %. This finding is higher than that reported by previous studies (range = 18.3 - 39%) which used decline in twitch amplitude to quantify peripheral neuromuscular fatigue (Babault et al., 2005; Rattey et al., 2005). The difference in results probably reflects differences in the length of time the task was sustained for, which ranged from 48 to 100 seconds, and differences in stimulation parameters.

Review of the control group findings in relation to past studies in normal participants with similar fatigue task protocols and measurement methods suggest that the results of the control group in the current study are consistent with past studies. In summary, during the course of a 90 second sustained isometric contraction of the quadriceps the control group developed a median level of 50% total neuromuscular fatigue, 20% central neuromuscular fatigue and 44% peripheral neuromuscular fatigue.

5.6.2. Stroke Group

The median level of total neuromuscular fatigue of the stroke group was 39.6%. This was statistically different from the control group, indicating that the stroke group developed significantly less total neuromuscular fatigue than the control group. This finding was in contrast to the stated study hypothesis, that stroke participants would develop more total neuromuscular fatigue than control participants.

Prior studies which have evaluated total neuromuscular fatigue in people with mild neuromuscular impairment following stroke have demonstrated no difference in the level of total neuromuscular fatigue of stroke participants when compared to control participants (Lindstrom et al., 1998; Riley & Bilodeau, 2002; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999). Therefore, the findings of the current study are also in contrast to those previously reported. The difference between the current study and previous studies in people with stroke may relate to, differences in the level of neuromuscular impairment and physical disability of the subjects, differences in the fatigue task or differences in the method used to quantify total neuromuscular fatigue.

The median central neuromuscular fatigue of the stroke group was 25.9%, suggesting that the stroke group had a higher level of central neuromuscular fatigue than the control group. However, this finding was not statistically significant. Only one other study has considered the development of central neuromuscular fatigue in the stroke population (Riley & Bilodeau, 2002). This study demonstrated increased central neuromuscular fatigue in the more affected limb compared to the less affected limb in two stroke participants during a sustained maximal isometric contraction of the elbow flexors, when central neuromuscular fatigue was calculated using the CAR method. Riley and Bilodeau (2002) reported central neuromuscular

fatigue of, “around 20%” (pp 965), this level of central neuromuscular fatigue is similar to the median of the control group of the current study and less than the median of the stroke group. However, direct comparison is hampered by the differences in the muscle being evaluated, the length of time the task was sustained for and the method used to quantify central neuromuscular fatigue. Nevertheless, review of the data presented by Riley and Bilodeau (2002) supports the finding of the current study that there is variation in the development of central neuromuscular fatigue within the stroke population.

The median level of peripheral neuromuscular fatigue of the stroke group was 24.1%. This was statistically different from the control group, indicating that the stroke group developed less peripheral neuromuscular fatigue than the control group. This finding was in agreement with the stated study hypothesis and is also in agreement with studies in people with mild neuromuscular impairment following stroke (Lindstrom et al., 1998; Riley & Bilodeau, 2002; Sunnerhagen et al., 1999; Svantesson et al., 1998; Svantesson et al., 1999).

The fatigue profile of a group of people with mild to moderate neuromuscular impairment and physical disability following stroke, was different from an age, weight and height matched control group. The stroke group demonstrated less total neuromuscular fatigue, greater or similar levels of central neuromuscular fatigue and less peripheral neuromuscular fatigue than control participants. These differences may relate to physiological differences between the stroke and control groups or alternatively to the influence of the task parameters on the level of fatigue that would develop in either group.

The fatigue profile of stroke participants in the current study was unlike those previously reported in stroke participants with mild levels of neuromuscular

impairment, particularly in relation to the amount of total neuromuscular fatigue developed. However the variation seen in the stroke group on measures of total neuromuscular fatigue, central neuromuscular fatigue and, to a lesser extent, peripheral neuromuscular fatigue, is in agreement with previous reports of variability in fatigue measures in people following stroke (Lindstrom et al., 1998; Sunnerhagen et al., 1999; Svantesson et al., 1998).

5.6.3. Potential physiological explanations for findings

The amount of total neuromuscular fatigue a person experiences during a given task is made up of both peripheral and central neuromuscular fatigue components. In the current study, people with stroke experienced less total neuromuscular fatigue than control participants. Total neuromuscular fatigue should be considered as the net result of the contribution of central neuromuscular fatigue and peripheral neuromuscular fatigue. In order to consider possible physiological explanations for the level of total neuromuscular fatigue it is essential to consider the relative contribution of both central and peripheral neuromuscular fatigue and the interaction between the two.

The central neuromuscular fatigue of the stroke participants was similar or slightly greater than that experienced by the control participants. The amount of central neuromuscular fatigue may have been elevated by; an increased sense of effort (Gandevia, 1998), deficits in the ability to recruit additional cortical areas as the task was being sustained (Korotkov et al., 2005; Liepert, 2003; Liu et al., 2003), reductions in the level of cortical excitability (Liepert, 2003; Taylor & Gandevia, 2001) and reductions in the ability to increase and modulate the firing rate of motor units in response to sustained activity (Frontera et al., 1997; Gandevia, 2001). Alternatively the level of central neuromuscular fatigue may have been reduced in

stroke participants by the impact of reduced afferent feedback at the spinal and cortical levels due to sensory deficits following stroke (Gandevia, 1998, 2001). The level of peripheral neuromuscular fatigue developed may also have in turn affected the amount of central neuromuscular fatigue. It is asserted that the role of afferent feedback at the spinal and supraspinal levels is to modify the descending drive to the muscle in response to peripheral neuromuscular fatigue. If the net level of peripheral neuromuscular fatigue is reduced in people with stroke this may in turn cause a reduction in the level of central neuromuscular fatigue experienced. From the above explanations it can be seen that changes in the CNS have the potential to increase and to decrease the amount of central neuromuscular fatigue experienced following stroke. It is not possible, based on the measures taken in the current study, to comment on which mechanisms are more likely to contribute to any alterations in the level of central neuromuscular fatigue following stroke. However it is clear that, during a sustained maximal isometric contraction of the quadriceps, the net result of any physiological changes in the CNS in stroke participants is a similar or slightly increased level of central neuromuscular fatigue. Identification of the exact mechanisms of differences between control and stroke participants would require studies involving; neuroimaging, transcranial magnetic stimulation and manipulation of afferent feedback.

The level of peripheral neuromuscular fatigue in the stroke group was markedly reduced compared to the control group. This could be explained by an increase in the proportion of type I muscle fibres in comparison to type II fibres in the stroke group (Datolla et al., 1993; Hachisuka et al., 1997). However, this change in muscle composition has not been rigorously established following stroke. It may be argued that reductions in muscle size and structure, and in the size and number of

muscle fibres and the possibility of an increase in the proportion of type II muscle fibres, should have resulted in an elevation in the amount of peripheral neuromuscular fatigue experienced following stroke. On the other hand, it is important to consider the influence of the level of voluntary activation of the muscle during the task in the stroke population. Reduced activation of the muscle during the fatigue task may have spared the muscle from being sufficiently taxed to cause peripheral neuromuscular fatigue. In addition there are likely to have been differences in the level of intramuscular pressure and resultant restriction of blood flow between the two populations, the stroke population may have been less influenced by compromised energy supply and the accumulation of metabolites than the control population (Paul & Wood, 2002). These possibilities highlight the importance of considering the impact of the task parameters, and the equality of the task across the two groups, when evaluating group differences.

5.6.4. Task parameters

The impact of the task parameters on the likelihood that fatigue would develop in either group requires careful consideration. The intensity of the fatigue task and the quantification of the amount of total neuromuscular fatigue experienced were both determined based on the level of MVC. This is standard practice when evaluating fatigue in both normal and pathological populations (Allman & Rice, 2002; Babault et al., 2005; Behm & St-Pierre, 1997; Bigland-Ritchie et al., 1978; Gandevia et al., 1998; Kent-Braun & Miller, 2000; Lindstrom et al., 1998; Nardone, Buffone, Florio, & Tezzon, 2005; Nordlund et al., 2004; Riley & Bilodeau, 2002; Schillings et al., 2003; Sharma et al., 1995; Sunnerhagen et al., 1999; Surakka et al., 2004; Svantesson et al., 1999; Taylor, Allen, Butler, & Gandevia, 2000; Todd,

Petersen et al., 2003; Urbach & Awiszuzs, 2002). However, in participants who have impaired muscle strength the intensity of the fatigue task is set based on the participants' level of neuromuscular impairment (McComas et al., 1995).

In people without pathology it has been identified that the task parameters are likely to influence both the source and degree of fatigue developed in the neuromuscular system (Gandevia, 2001). There is evidence to suggest during a sustained maximal task, central neuromuscular fatigue develops at low levels in proportion to fatigue attributable to peripheral factors (Bigland-Ritchie et al., 1995; Kent-Braun, 1999). During sub maximal sustained tasks central neuromuscular fatigue appears to play a proportionally greater role in the overall development of neuromuscular fatigue (Loscher & Nordlund, 2002). These findings were established in normal participants who have high levels of voluntary activation and similar capacity to generate force, making it difficult to apply the findings to the stroke population who have reduced levels of voluntary activation and impairment in their ability to generate force. However, it may be asserted that in the current study the stroke group were being tested on a task which was essentially submaximal.

The criticism that the use of fatigue tasks referenced to MVC influences the ability to identify differences between stroke and control populations and between stroke participants with varying levels of neuromuscular impairment can be levelled at other studies of neuromuscular fatigue following stroke (Lindstrom et al., 1998; Riley & Bilodeau, 2002; Sunnerhagen et al., 1999; Svantesson et al., 1999). When comparing participants with weakness and impaired voluntary activation to normal participants it may be more appropriate to set the fatigue task intensity based on a level of predicted MVC (i.e. based on age, weight and height) or a level of voluntary

activation (i.e. based on the peripheral capacity of the muscle). It is also important to consider that people with weakness must still generate and sustain the similar levels of force as normal participants to successfully perform functional tasks (i.e. sit-to-stand). Therefore evaluation of fatigue based on predicted MVC or level of voluntary activation is likely to give a more realistic view of the impact of neuromuscular fatigue on functional ability (McComas et al., 1995).

5.7. Associations between variables of interest

The study sought to investigate the relationship between variables of interest. The relationship between measures of physical function, neuromuscular function and neuromuscular fatigue was considered.

5.7.1. Strength, Voluntary Activation and Physical Function

There was a large, statistically significant relationship between strength and voluntary activation in the stroke group indicating that high levels of voluntary activation were associated with high levels of MVC. This was in contrast to the control group, where no relationship was identified. This finding supports the theory that muscle weakness following stroke is related to CNS changes which has long been purported (Bourbonnais & Vanden Noven, 1989; Landau & Sahrmann, 2002; Newham et al., 1996), but received limited actual investigation. The findings are consistent with one small study which reported a non-significant relationship between voluntary activation and strength following stroke. The current study provides clear evidence that the strength of people following stroke is strongly related to the level of voluntary activation of the muscle.

The maximal isometric strength of the quadriceps of the more affected side in stroke participants was strongly correlated with both comfortable paced and fast paced walking speed. This is in line with previous studies of strength following

stroke, which have identified a relationship between strength and transfer capacity, sit to stand ability, balance, walking, stair climbing, upper limb function and capacity for activities of daily living (Bohannon, 1986; Bohannon & Andrews, 1990; Cameron, Bohannon, Garret, Owen, & Cameron, 2003; Hamrin et al., 1982; Hsu et al., 2003; Kim, C. & Eng, 2003; Lomaglio & Eng, 2005; Nakamura et al., 1988; Pohl et al., 2002). A significant body of research has evaluated the correlation between strength measures in the more affected lower limb and gait parameters following stroke, identifying varying correlations with both temporal and spatial parameters of gait (Bohannon, 1986; Bohannon & Andrews, 1990; Hsu et al., 2003; Kim, C. & Eng, 2003; Nakamura et al., 1988; Pohl et al., 2002). The findings of the current study are in agreement with previous studies which have specifically considered the relationship between isometric knee extensor strength and gait speed (Bohannon & Andrews, 1990; Pohl et al., 2002).

One unexpected finding of the current study was the failure to identify a relationship between isometric quadriceps strength and sit to stand ability. This finding was in contrast to previous studies which have looked at quadriceps muscle strength and sit-to-stand ability after stroke (Cameron et al., 2003; Lomaglio & Eng, 2005). This may relate to the fact that the current study considered the number of sit-to-stand repetitions a person could complete in 30 seconds rather than a single manoeuvre.

The study considered the relationship between the level of voluntary activation and physical function following stroke. No relationship between voluntary activation and sit-to-stand ability, comfortable walking speed and fast walking speed was identified, nor was any relationship identified in the control group. Therefore, despite a strong relationship between voluntary activation and muscle strength, and a

strong relationship between muscle strength and physical function following stroke there does not appear to be a relationship between the level of voluntary activation and physical function. This may reflect the need to reach an absolute level of force generation to achieve a given level of function (Cress & Meyer, 2003). This finding may also reflect the importance of other factors in determining functional ability following stroke, such as, peripheral muscle changes, co-ordination, hypertonicity, postural control and cardiovascular endurance (Cameron et al., 2003; Hachisuka et al., 1997; Hamrin et al., 1982; Hsu et al., 2003).

5.7.2. Strength, Voluntary Activation and Neuromuscular Fatigue

There was no relationship between the level of isometric strength of the quadriceps and any of the measures of fatigue in either group. This suggests that strength and neuromuscular fatigue are independent phenomenon in both control and stroke participants, or, that other variables influence the relationship. This finding also brings into question whether differences in the absolute level of force at which the fatigue task was being performed had any bearing on the development of fatigue in either of the groups, as discussed in Section 5.6.4.

There was a large positive correlation between the level of voluntary activation and the amount of total neuromuscular fatigue and central neuromuscular fatigue developed in both the control and stroke groups, indicating that higher levels of voluntary activation were associated with greater levels of total and central neuromuscular fatigue. This relationship appeared stronger in the control group than the stroke group. This suggests that higher levels of voluntary activation are related to higher levels of total neuromuscular fatigue and central neuromuscular fatigue when a task is sustained maximally. Given the difference in the magnitude of the relationships between control and stroke groups, it may be suggested that other

factors are also likely to be influencing the amount of total and central neuromuscular fatigue in the stroke group. The lack of relationship between voluntary activation and the development of peripheral neuromuscular fatigue brings into question the concept that reduced levels of voluntary activation in the stroke group during the fatigue task may have spared the muscle from being sufficiently taxed to cause peripheral neuromuscular fatigue as discussed in Section 5.6.3.

5.7.3. Neuromuscular Fatigue and Physical Function

No associations between neuromuscular fatigue and physical function were identified in either the stroke or control groups, other than a relationship between the level of peripheral neuromuscular fatigue and sit-to-stand ability in the stroke group. This may suggest that neuromuscular fatigue has little bearing on function in either population or alternatively it may suggest that the measures of physical function selected are unlikely to tax the neuromuscular system sufficiently to result in neuromuscular fatigue and therefore are unlikely to reflect the effect of neuromuscular fatigue on function. It may have been more appropriate to consider measures of function which sustain activity at high intensities over longer periods of time, such as the six-minute walk test (Hill et al., 2005).

5.8. Conclusion

This study has compared a group of people with mild to moderate physical disability following stroke, with a matched control group, during a sustained maximal isometric contraction of the quadriceps muscle. The stroke participants demonstrated a different fatigue profile than control participants, with less total neuromuscular fatigue, similar or slightly greater levels of central neuromuscular fatigue and less peripheral neuromuscular fatigue. The fatigue profile of the stroke

participants in the current study was not as anticipated by the study hypothesises, nor was it like the fatigue profile of previously reported studies in stroke participants with mild levels of neuromuscular impairment. Consideration has been given to both the sample characteristics and potential physiological characteristics of the stroke group which may explain the study results. However, the influence of the task parameters on the likelihood that fatigue would develop in either group has also been highlighted as a key issue.

Consideration of the association between neuromuscular function, neuromuscular fatigue and physical function has confirmed the relationship between voluntary activation and strength, and strength and physical function in people following stroke. While it appears that strength and neuromuscular fatigue are independent phenomenon, there is a strong relationship between voluntary activation and neuromuscular fatigue in both people without pathology and people with stroke.

Throughout the discussion suggestions have been made regarding future research, these suggestions are summarised and additional concepts proposed in the following section.

5.9. Further Research

Future research investigating neuromuscular fatigue following stroke may consider the following issues:

1. Future studies of neuromuscular fatigue should consider greater restriction of the stroke sample, through identification of participants based on lesion location or size or alternatively through more rigorously defined levels of neuromuscular impairment and physical function. This may assist to reduce the impact of heterogeneity of the stroke sample on analysis of the study findings.

2. Future studies should consider the unaffected side of stroke participants, in addition to the use an age, height and weight matched control group to act as a control. This may assist the researcher to further elucidate the fatigue process following stroke.
3. The effect of caffeine consumption, medications which act on the nervous system or muscle and the level of physical activity of the participants should be considered as potential co-variables when evaluating neuromuscular fatigue.
4. It is essential to consider the reliability of measures used to quantify fatigue. The current study revealed that commonly used measures of fatigue have moderate to high levels of error. This requires careful consideration when evaluating past and future research findings and when selecting sample sizes in future studies.
5. When comparing participants with and without pathology, particularly when the level of voluntary activation or strength of participants varies between groups, it may be useful to set the fatigue task based upon a level of voluntary activation or predicted MVC based on age, weight and height. This would allow groups to be evaluated on comparable tasks and the true functional significance of deficits in neuromuscular fatigue to be considered.
6. Future consideration of the relationship between neuromuscular fatigue and function should also aim to utilise physical measures which evaluate tasks that are sustained for a period of time, and therefore likely to be influenced by fatigue.
7. Further studies may also consider the relationship between neuromuscular fatigue and subjective fatigue in people following stroke.

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Appendix A

Advertisement

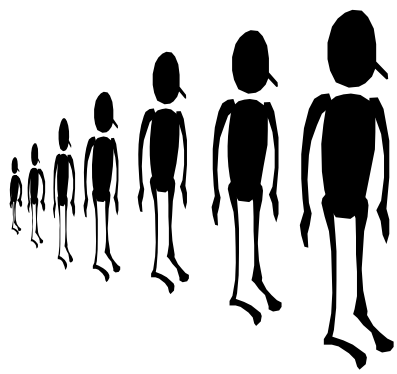
Volunteers required for strength and fatigue in stroke study

This study aims to look at aspects of muscle weakness and fatigue in people who have had a stroke.

If you...

- are interested in participating in this research and,
- have had a stroke more than six months ago, which affects one side of your body.

Participants will be required to attend two sessions at the Physical Rehabilitation Research Centre, AUT. The total time will be no longer than 4 hours.



Please contact Nada Signal for more information

917 9999
ext 7062

Appendix B

Ethical Approval

MEMORANDUM

Academic Services

To: Denise Taylor

From: **Madeline Banda**

Date: 2 March 2005

Subject: 05/02 **Voluntary activation and central neuromuscular fatigue of the quadriceps muscle in chronic stroke participants**

Dear Denise

Thank you for providing written evidence as requested. I am pleased to advise that it satisfies the points raised by the Auckland University of Technology Ethics Committee (AUTEC) at their meeting on 17 January 2005. Your ethics application is now approved for a period of three years until 2 March 2008.

I advise that as part of the ethics approval process, you are required to submit to AUTEC the following:

- A brief annual progress report indicating compliance with the ethical approval given using form EA2 which is available online at *http://www.aut.ac.nz/research_showcase/pdf/appendix_g.doc* , including a request for extension of the approval if the project will not be completed by the above expiry date;

- A brief report on the status of the project using form EA3 which is available online at *http://www.aut.ac.nz/research_showcase/pdf/appendix_h.doc* . This report is to be submitted either when the approval expires on 2 March 2008 or on completion of the project, whichever comes sooner;

You are reminded that, as applicant, you are responsible for ensuring that any research undertaken under this approval is carried out within the parameters approved for your application. Any change to the research outside the parameters of

this approval must be submitted to AUTEC for approval before that change is implemented.

Please note that AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to make the arrangements necessary to obtain this.

To enable us to provide you with efficient service, we ask that you use the application number and study title in all written and verbal correspondence with us. Should you have any further enquiries regarding this matter, you are welcome to contact Charles Grinter, Ethics Coordinator, by email at charles.grinter@aut.ac.nz or by telephone on 917 9999 at extension 8860.

On behalf of the Committee and myself, I wish you success with your research and look forward to reading about it in your reports.

Yours sincerely

Madeline Banda

Executive Secretary

Auckland University of Technology Ethics Committee

Cc: Nada Signal nada.signal@aut.ac.nz

Appendix C

Participant Information Sheet

AUT
AUCKLAND UNIVERSITY OF TECHNOLOGY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

Participant Information Sheet

Date Information Sheet Produced
20 December 2004

Project Title
Voluntary activation and central neuromuscular fatigue of the quadriceps muscle in chronic stroke participants.

Invitation
You are invited to take part in a study investigating aspects of muscle weakness and fatigue in people who have had a stroke.

What is the purpose of the study?
The purpose of the study is to determine the amount muscle strength and fatigue in the thigh muscle during different types of muscle contractions in people who have had a stroke. In particular, the research will consider how the brain contributes to muscle strength and fatigue. This research study is being undertaken as part of a Masters of Health Science degree by Nada Signal.

How are people chosen to be asked to be part of the study?
Potential participants, who have had a stroke more than six months ago, will contact the researchers and volunteer to participate in the study. In addition people with no known neurological disease will also volunteer to participate in the study.

What happens in the study?
The study involves two testing sessions, held one day apart.
During the first session the participant will be asked some questions about their condition and their ability to complete everyday tasks. Then testing will involve clinical measures of leg strength and activities that require good leg strength, such as walking and standing up from a chair. The last part of this session involves becoming familiar with the laboratory testing equipment and practising the test protocol in preparation for the second testing session. This session will take approximately two hours in total.
Two days later the participant will return to AUT, this second session involves laboratory testing of leg muscle strength and fatigue. This session will take approximately two hours.
The measurements of leg muscle strength, and the contribution of the muscle and brain to that strength, involve sitting in an apparatus that measures the amount of force your leg muscle can generate. The testing also involves the application of an electrical stimulus to the thigh muscle; this process does not cause harm, but can be uncomfortable.

What are the discomforts and risks?
The strength testing requires that the participants briefly work as hard as they can. In addition, the measurement involves stimulation of the thigh muscle using a brief electrical stimulus. This is not painful, but it can be uncomfortable.

How will these discomforts and risks be alleviated?
The researchers will ensure that the participants rest as long as necessary between testing to prevent fatigue.
The use of electrical stimulation will be brief and the intensity controlled to limit discomfort. Participants can indicate if they are feeling discomfort and the intensity of the stimulation will be adjusted accordingly

What are the benefits ?
There are no immediate benefits to participants. The general benefits will be to inform physiotherapists and health researchers about how the brain contributes to strength and fatigue in people who have had a stroke. This will help to analyse research into strength deficits in stroke subjects and plan future research in this area. In the future, this may assist in the development of better treatment programmes to address strength deficits following stroke.

What compensation is available for injury or negligence?
In the unlikely event of a physical injury as a result of your participation in this study, you will be covered by the accident compensation legislation with its limitations. If you have any questions about ACC please feel free to ask the researcher for more information before you agree to take part in this study.

How will my privacy be protected?
Confidentiality will be maintained throughout this study in the following ways:
No material, which could personally identify you, will be used in any reports on this study
All study data will be stored in locked files.

How do I join the study?
If you wish to join the study please contact the researcher.
Nada Signal (09) 917 9999 ext. 7062 nada.signal@aut.ac.nz

What are the costs of participating in the project? (including time)
Participating in this project will take about four hours of your time. Transport costs to and from the AUT campus (petrol or taxi fare) will be covered by the study.

Opportunity to consider invitation
You will have at least two weeks to decide whether you wish to take part in this study. If you need further information to help you make up your mind please feel free to contact the researcher listed.
You have a right to choose not to participate. If you do agree to take part you are free to withdraw from the study at any time, without having to give a reason.

Opportunity to receive feedback on results of research
The results of this study will be published in a rehabilitation journal and presented at a physiotherapy conference. It is usual for there to be a substantial delay between the end of the data collection and publication or presentation. The outcomes of this

study will be available to you by discussion with the researcher if you wish, along with a summary of your results.

Participant Concerns
Any concerns regarding the nature of this project should be notified in the first instance to:
Nada Signal
Lecturer Physiotherapy
School of Physiotherapy
Auckland University of Technology
Tel: 09 917 9999 ext. 7062
Email: nada.signal@aut.ac.nz

Concerns regarding the conduct of the research should be notified to the Executive Secretary, AUTEC, Madeline Banda, madeline.banda@aut.ac.nz , 917 9999 ext 8044.

Approved by the Auckland University of Technology Ethics Committee on 17/01/2005 **AUTEC Reference number** 05/02

Appendix D

Participant Consent Form

AUT
AUCKLAND UNIVERSITY OF TECHNOLOGY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

Consent to Participation in Research

Title of Project: Voluntary activation and central neuromuscular fatigue of the quadriceps muscle in chronic stroke participants.

Researchers: Nada Signal

- I have read and understood the information provided about this research project (Information Sheet dated 20 December 2004).
- I have had an opportunity to ask questions and to have them answered.
- I understand that I may withdraw myself or any information that I have provided for this project at any time prior to completion of data collection, without being disadvantaged in any way.
- I understand that my participation in this study is confidential and no material that could identify me will be used in any reports on this study.
- If I withdraw, I understand that all data collected from me will be destroyed.
- I agree to take part in this research.
- I wish to receive a copy of the report from the research. Yes / No
- I wish my GP to be notified of my participation in this study.
  Yes / No

If Yes, GP contact details: …….

…….

Participant signature: .....……..

Participant name: …….

Participant Contact Details:
……..
……..
……..
……..
Date:
Approved by the Auckland University of Technology Ethics Committee on xxx **AUTEC Reference number** 05/02

Note: The Participant should retain a copy of this form.

Appendix E

Data Collection Sheets

Subject Number

RAW DATA: SESSION ONE

Calibration	Internal	External	Proceed?
Name			
Study Phase			
Subject Number			
Sex			
Postal Address (if requiring copy of results)			
Telephone (for reminder phone call between appointments)			
Date of Stroke			
Date of Birth			
Hemiplegia		Left	Right
Exclusion questions: Do you have a history of significant lower limb trauma or OA? Other than this stroke, have you had another stroke or neurological illness or muscle wasting disease? Do you have an uncontrolled heart problem or uncontrolled hypertension (high blood pressure) or any other medical problems? Do you take medications such as sleeping tablets, anti-spasticity or anti-anxiety medications?		Y/N Y/N Y/N Proceed? Details	

Star Cancellation Test	/54	Proceed?
Mini-mental state examination	/30	Proceed?

Quadriceps Manual Muscle Test (MRC)	/5	Proceed?
Ashworth Scale	/5	Proceed?

Weight (kg)		*BMI=*	*Pred MVC=*
Height (cm)			*Twitch Size=*

30 second chair stand	# reps
Sub max Warm up	

MVC and MVA Results:		**Left leg**		**Right leg**
Twitch parameters	Pulse width=	Voltage =	mA=	
Max EMG	File name:	Comments:		
Max MVC	File name:	Comments:		
Control Twitch	Comments: Level Set:			
MVA 1	File name:	Comments:		
MVA 2	File name:	Comments:		
MVA 3	File name:	Comments:		
Fatigue Task	File name:	Comments:		

RAW DATA: SESSION TWO

Calibration	Internal	External	Proceed?
Adverse Effects?			
Comments			

10 m timed walk comfortable pace	1) 2) 3)	s s s	*av* = *m/s*=
10 m timed walk fast pace	1) 2) 3)	s s s	*av* = *m/s*=

Submax Warm up	

MVC and MVA Results:	**Left leg**		**Right leg**	
Twitch parameters	Pulse width=	Voltage =	mA=	
Max EMG	File name:	Comments:		
Max MVC	File name:	Comments:		
Control Twitch	Comments: Level Set:			
MVA 1	File name:	Comments:		
MVA 2	File name:	Comments:		
MVA 3	File name:	Comments:		
Fatigue Task	File name:	Comments:		

DATA MANAGEMENT

Travel reimbursed	
Thank you letter and results posted	
Data entered into Excel	

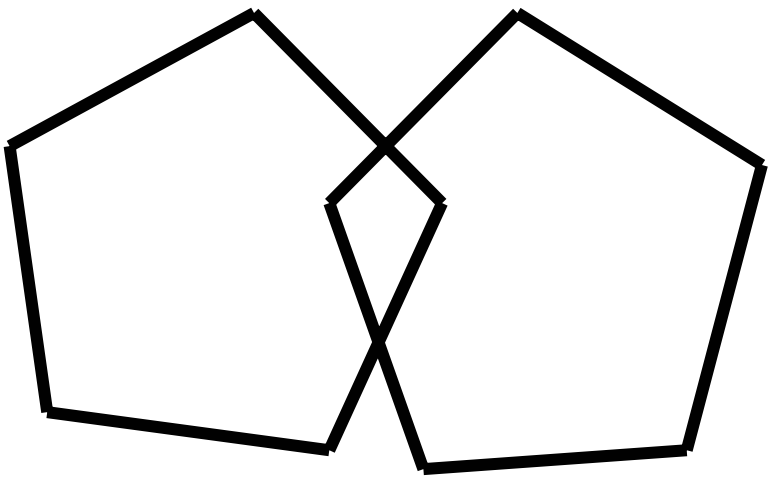
Appendix F

Mini-Mental State Examination

MMSE

Orientation		
1.	Ask the patient: "What is the year, season, date, day, month?"	/5
2.	Ask: "Where are you?" -- State, country, town, place, floor	/5
Memory registration		
3.	Tell the patient that you want him/her to remember something for you, then name three unrelated objects (speak clearly and slowly). Ask the patient to repeat the three objects (score 3 points if correct first time, 2 if correct second time, 1 if correct third time). Ask patient to keep the three things in mind.	/3
Attention and concentration		
4.	Ask the patient to take seven from 100, then seven from the result, and so on for five subtractions. Score 1 point for each correct answer.	
	OR	
	Ask the patient to spell "world" backwards, and score 1 point for each correct letter.	/5
Memory recall		
5.	Ask the patient to recall the three objects from test 3.	/3
Language		
6.	Show the patient two familiar objects (e.g., a pen, a watch) and ask him/her to name them.	/2
7.	Ask the patient to repeat a sentence after you: "No ifs, ands or buts".	/1
8.	Ask the patient to follow a three-stage command: "Please take this paper in your left hand, fold it in half and put the paper on the floor".	/3
9.	Ask the patient to read and follow a written instruction, e.g., "Close your eyes".	/1
10.	Ask the patient to write a simple sentence. The sentence should contain a subject and a verb and should make sense.	/1
11.	Ask the patient to copy a picture of intersecting pentagons.	/1
Total score		/30

Close your eyes



Appendix G

Verbal Instructions

INSTRUCTIONS

Calibration

To be completed everyday of lab based testing, or if equipment running for longer than 5 hours

1. Click: InstruNet, Network, View Page
2. Click on Ch1 Vin+(force channel)
3. Click on Settings, Mapping.
4. Alter parameters to:

Internal 1: 5
External 1: 5
Internal 2: -5
External 2: -5

5. Turn seat onto front, hold horizontal to ground
6. Collect feedback with no weight- record mean voltage
7. Add 10kg weight (98Newtons) hanging in series
8. Collect feedback with weight insitu – record mean voltage
9. Click: InstruNet, Network, View Page
10. Click on Ch1 Vin+(force channel)
11. Click on Settings, Mapping.
12. Alter parameters to:

Internal 1: voltage with no weight
External 1: 0
Internal 2: voltage at 98N
External 2: 98

13. Press Update
14. Return to collecting feedback and check baseline
15. Save programme to save calibration settings

Introduction

The purpose of the study is to determine the amount muscle strength and fatigue in the thigh muscle during different types of muscle contractions in people who have had a stroke. In particular, the research will consider how the brain contributes to muscle strength and fatigue. This research study is being undertaken as part of a Masters of Health Science degree by Nada Signal.

The study involves two testing sessions, held one day apart. Today we will ask you some questions about your stroke, do a few tests that look at changes following stroke and look at your ability to complete everyday tasks. After these tests we will take some time to orientate you to the equipment that we will use to measure muscle strength, and spend some time practicing the measurement tests. After that, we will start our formal test. The measurements of leg muscle strength and the contribution of the muscle and brain to that strength involve measuring the amount of force your leg muscle can generate in a special designed apparatus. The testing also involves the application of an electrical stimulus to the thigh muscle. This process can be very uncomfortable, but does not cause harm or pain.

The first session will take approximately two hours.

On_____we ask that you return to AUT to undergo your second test session. This session will be much quicker. It will take approximately one and half hours.

Consent Process

Do you feel comfortable that you understand the information provided about this research project?
Do you have any other questions?
You should be aware that your participation in the study is confidential and no material that could identify you will be used in any reports on this study
You should also know that if at anytime you may withdraw from the study, no questions asked. Any data collected from you, will be destroyed.
Are you happy to take part in the study?
Do you wish to receive a copy of the report from the research?
Do you wish to have your GP notified of your participation?
Please sign this consent form.

Personal Details

I would like to ask you some personal information for study records and to ensure that you meet the criteria of the study.
Do you have a history of significant lower limb trauma or OA?
Other than this stroke, have you had another stroke or neurological illness or muscle wasting disease?
Do you take medications such as sleeping tablets, anti-spasticity or anti-anxiety medications?
Do you have an uncontrolled heart problem or uncontrolled hypertension (high blood pressure)?

Mini-mental State Examination

This next set of questions is to ensure you are able to follow the instructions during the testing procedure, as some of the instructions are quite complicated.

Star Cancellation

The next test checks that you don't have any problems that may effect how you see the computer screen during the testing.

This page contains stars of different sizes. Look at the page carefully – this is a small star. Every time you see a small star, cross it out like this." (Illustrate by crossing out the two small stars immediately above the centralising arrow on the stimulus sheet.) "I would like you to go through this page and cross out all the small stars without missing any of them."		
Manual Muscle Test (MRC) (Don't say)	0	No contraction
	1	Palpable contraction
	2	Movement without gravity

	3 Movement against gravity 4 Movement against resistance lower than the resistance overcome by the healthy side. 5 Movement against resistance equal to the resistance overcome by the healthy side
.	
Ashworth Scale (Don't say)	Move the affected limb through its passive range of motion Grade Description 0 No increase in muscle tone. 1 Slight increase in muscle tone, manifested by a catch and release, or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension. 2 Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of movement (ROM). 3 More marked increase in muscle tone through most of ROM, but affected part(s) easily moved. 4 Considerable increase in muscle tone, passive movement difficult. 5 Affected part(s) rigid in flexion or extension.

BMI

In order to be able to compare your strength to other people, it is important to weigh you as strength varies depending on a person's weight.

Weight (kg)	Please step onto the scales while I record your weight.
Height (cm)	Please stand tall with your back against the wall while I measure your height.

Sit-To-Stand

The next test looks at your ability to stand from chair. Generally, the stronger your muscle is, the easier you stand up.

30-second sit-to-stand	With your arms folded across your chest you will rise to a full stand and return to be fully seated. Let's show you a correct performance. Can you do a correct stand up please? You are aiming to stand up as many times as possible in 30 seconds. Please begin when I say GO and stop when I say STOP. READY, SET, GO

Testing

Into chair	Lets get you sitting in the chair and secured. Please step up onto the step and sit in the chair with your back against the backrest.
Secure straps	Is the chair or cuff uncomfortable If it feels uncomfortable or painful at any time please tell me and we will alter the fit. Now we will apply the straps so you aren't moving around too much during testing. Ensure Knee against edge of chair Knee flexed to 90^0 Lap and chest belts fixed securely Ankle strapped to strain gauge above lateral malleolus
Procedure explanation	We are ready to go. The force will be measured from down here when you push against the cuff. Push now and watch the screen.
Calibrate	Press ***Calib***
Submax Warm Up	Lets begin by having you practice some contractions Push to this line, hold, relax Now to this line, hold, relax Now to this line, hold, relax Discard data by pressing ***Clear***
MVC ***File Name: c#A***	Press ***Calib*** Press ***Collect Max*** Repeat this three times (with the requisite rest periods, pressing ***Collect Max*** for each MVC). Do not press clear in between each test. After three tests, press ***Max f*** Now we will test the maximum amount of force you can generate. The aim is to push against the cuff like you are kicking a ball. You should push as FAST and HARD as you can. You should keep pushing until I say STOP Ready to start? Begin when I say GO! Are you READY, SET, GO! HARDER, HARDER, HARDER, GO, GO, GO, PUSH, PUSH, PUSH! STOP Whilst the subjects is resting: Arrange the cursors on the force trace so that the force data to be saved is between them. Once pressing ***Save EMG***, Alter the file name and ***Format*** to engineering text. The next prompt will be to save the force data and then the twitch trigger data. Press ***Save***
REST	I will ask you to rest for three minutes or until you feel

	completely recovered and then we will repeat the test again
REPEAT MVC AND REST	Twice
Electrode placement	Now I will clean your thigh skin of oils and apply the electrodes that give the electrical stimulus. Can you please pull up your shorts to expose the top of your thigh? Gain consent Clean skin with abrasive rub (Shave if very hairy) Secure electrodes • Negative electrode is distal • Distal electrode is just proximal to the patella (10cm proximal is arbitrary value in literature) • Proximal electrode should be as high in the femoral crease as possible, with a slight medial shift • Connect to stimulator
Explanation of the twitch	We will establish the stimulation level needed to do the testing. We are aiming for atleast 30% of your maximum contraction. Remember, It is a strange sensation to have your muscles work without you telling them to and it is more comfortable if you are able to relax. We will start with a very low stimulus and build up until the twitch can make your muscle work at about the same level as last time. Turn on Digisitm Check parameters (doublet 100Hz, 100μs, 300V, start at 10mA) Press ***Calib*** Use the ***Set limits*** function to set 30% of MVC to set the target at.
Twitch ***File Name: c#B***	Are you ready? Just try and relax. Was that OK? Any pain? Are you happy to have me turn it up slightly? Increases current to at least 30% + MVC Whilst the subjects is resting: Arrange the cursors on the force trace so that the force data to be saved is between them. Once pressing ***Save EMG***, Alter the file name and ***Format*** to engineering text. The next prompt will be to save the force data and then the twitch trigger data. Press ***Save***
MVA AND CONTROL TWITCH ***File Name: c#f*** ***File Name: c#g*** ***File Name: c#h***	Now we will test the maximum amount of force you can generate and apply the twitch at the same time. The aim is to push against the cuff like you are kicking a ball. You should push as FAST and HARD as you can. You should keep pushing until I say STOP, do not relax once I have applied the twitch.

	I will apply a twitch during your muscle contraction and immediately following it. Press ***Calib*** Press ***Feedback collection*** Ready to start? Begin when I say GO! Are you READY, SET, GO! HARDER, HARDER, HARDER, GO, GO, GO, PUSH, PUSH, PUSH! STOP Twitch the subject during the MVA once, and twitch again within 2 seconds of MVC completion. To stop the force trace, go to the ***Task – Stop – Collfeed*** drop-down menu. Whilst the subjects is resting: Arrange the cursors on the force trace so that the force data to be saved is between them. Once pressing ***Save EMG***, Alter the file name and ***Format*** to engineering text. The next prompt will be to save the force data and then the twitch trigger data. Press ***Save***.
REST	I will ask you to rest for three minutes or until you feel completely recovered and then we will repeat the test again
MVA and REST	Twice
Fatigue protocol ***File Name: c#i***	For the last part of the test you will do a contraction which is 100% of your maximum and hold it for as long as possible. You should aim to hold it for **90 seconds**, During the contraction I will apply some twitches. , “push fast and hard to ensure that you touch the target with the force line, then maintain a steady, continuous force for ninety seconds. You need to be pushing as hard as you possibly can. The aim of this last test is to fatigue you, even if the force line drops away you must keep on pushing as hard as you possibly can. Keep pushing until I say stop” Open Fatigue doublet programme. Use the ***Set limits*** function to 100% MVC to set the target. Start Stopwatch Press ***Calib*** Press ***Feedback collection*** Ready to start? Begin when I say GO! Are you READY, SET, GO! HARDER, HARDER, HARDER, GO, GO, GO, PUSH, PUSH, PUSH! KEEP GOING….

	STOP . Start Twitch programme. To stop the force trace, press the mouse cursor, ensure the control twitch has been delivered Whilst the subjects is resting: Arrange the cursors on the force trace so that the force data to be saved is between them. Once pressing ***Save EMG***, Alter the file name and ***Format*** to engineering text. The next prompt will be to save the force data and then the twitch trigger data. Press ***Save***.
Thanks.	Thank you so much for your time. That is the end of the testing. We have collected very good data and your results will be very helpful.

Functional Tests

The next set of tests look at your ability to stand and walk.

Please stand with your toes on the line. You will walk from here to here (demonstrate) at a pace that is comfortable to you. (You may use your walking aid.) Please begin when I say 'GO' READY, SET, GO
We will repeat the same test but this time you will walk as fast as you can. You will walk from here to here (demonstrate) as quickly as possible. (You may use your walking aid.) Please begin when I say 'GO' READY, SET, GO