UNIVERSITY OF SOUTHAMPTON

FACULTY OF ENGINEERING AND THE ENVIRONMENT
Institute of Sound and Vibration Research

Neuromechanical measurement of motor impairments in relation to upper limb activity limitations after stroke

by

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Thesis for the degree of Doctor of Philosophy
December 2011

UNIVERSITY OF SOUTHAMPTON

ABSTRACT

FACULTY OF ENGINEERING AND THE ENVIRONMENT
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Doctor of Philosophy

NEUROMECHANICAL MEASUREMENT OF MOTOR IMPAIRMENTS IN RELATION TO UPPER LIMB ACTIVITY LIMITATIONS AFTER STROKE

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Loss of upper-limb function is a problem following stroke. Recent research has led to the emergence of new treatments but progress is hampered by lack of reliable objective measures of impairment, and understanding of the underlying impairment mechanisms associated with loss and recovery of functional activity. The aim of this research was to identify, using neuromechanical measurement methods, inter-relationships between motor impairments, and correlates of motor impairments with functional activity limitation in the upper limb of acute and chronic stroke survivors.

An instrumented rig has been developed to measure impairments: muscle weakness, active range of movement, motor control accuracy in rhythmic and discrete tracking tasks, spasticity, coactivation, contracture and non-neural stiffness. In pilot studies, signal processing and data analysis techniques have been used to generate novel, clinically and physiologically relevant indices to quantify impairments. In a Main Study, 13 older impaired participants in the acute phase post-stroke, 13 in the chronic phase 14 age-matched unimpaired participants underwent rig assessments and performed a test of upper limb activity. A sub-group of impaired participants were tested on two days for test-retest reliability evaluation.

Statistical tests have confirmed the validity of the impairments to distinguish between acute and chronic patients and unimpaired individuals, except coactivation during discrete movements and non-neural stiffness. Repeatability coefficients for the active test indices have been presented as benchmark values for use in future trials. The muscle activation indices showed lower repeatability which highlights the challenge of using these to measure change over time. The impairments that contributed to lower motor control accuracy were reduced extensor weakness, delayed extensor onset timing, coactivation and smaller extension AROM and PROM; coactivation was more strongly associated with motor control accuracy than with spasticity or stiffness.

The most important contributors to functional activity in the acute group was extensor weakness, and in the chronic group was motor control accuracy and coactivation (rhythmic task). Contracture was important contributor in both groups, and was associated with weakness and loss of active range of movement rather than spasticity. The findings support the notion that rehabilitation strategies should focus on increasing muscle strength and prevention of contracture. However, assessment of more complex impairments like motor control accuracy and coactivation may be crucial to better target therapy, especially in the later phases post-stroke.

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Declaration of Authorship

I, Ruth Turk, declare that the thesis entitled: "*Neuromechanical measurement of motor impairments and how they relate to upper limb activity limitations of the older adult in sub-acute and chronic stages post-stroke"* and the work presented in the thesis are both my own, and have been generated by me as a result of my original research. I confirm that:

- This work was done wholly while in candidature for a research degree at this university;
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this university or any other institution, this has been clearly stated;
- Where I have consulted the published work of others, this is always clearly attributed;
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
- I have acknowledged all main sources of help;
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;
- Parts of this work have been published as:

Turk R, Burridge JH, Simpson DM, Pomeroy VM, Derivation of clinically driven indices for motor control and muscle activation during rhythmic and discrete wrist movement post-stroke, in preparation, submission to *Physiological Measurement* Nov. 2011

Poster presentation: Turk R, Simpson DM, Burridge JH (2010) Wrist motor control and coactivation during step-tracking in post-stroke hemiplegia and unimpaired adults, *18th International Conference of the Society of Electromyography and Kinesiology, 16-19 June, Aalborg, Denmark*

Poster presentation: Ruth Turk, David M. Simpson, Jane H. Burridge (*2010)* Quantifying motor impairments at the wrist post-stroke: does finger position matter? *Society for Research in Rehabilitation Winter Meeting 2nd February, Salford UK*

Poster presentation: Ruth Turk, David M. Simpson, Jane H. Burridge (2009) A pilot study to investigate the association between muscle activation patterns, wrist tracking performance and upper limb function in post-stroke hemiplegia, *Society for Research in Rehabilitation Summer Meeting 1st – 2nd July, Bath, UK*. **Awarded the Verna Wright Prize by the Society for Research in Rehabilitation for the best poster presentation during the year 2009 (over two meetings)**
Abstract published: *Clinical Rehabilitation* March 2010 vol. 24 no. 3 276-287*;* DOI: 10.1177/0269215509352055

Signed: ……

Date: ……

Acknowledgements:

Firstly I would like to thank my main supervisors, Dr David Simpson and Prof Jane Burridge, for their wisdom, guidance encouragement and support throughout the PhD. Thanks also goes to Prof Val Pomeroy who provided very useful advice, guidance and encouragement at critical times in the process.

During the PhD I have had assistance from many colleagues and collaborators. Firstly I would like to thank the patients and unimpaired participants for taking time to participate and show interest in this study. Working outside of health sciences in an engineering department has been a revelation, enjoyable but challenging. Thanks go to ISVR engineers and technicians. The build of the wrist rig was undertaken by: Dave Edwards, a Mechanical Engineer Technician, and Rob Stansbridge, Andy Westerman and Allan Waddilove, Electronics Engineer Technicians. The new Matlab® software programme was developed by Dr Oliver Baumann, a signal processing Engineer. Another thank you goes to Dr David Simpson for over-seeing the task of developing the wrist rig and software, for writing much of the signal processing and analysis programs, and for infinite patience in helping me to understand and write some myself.

Funding received from the Dunhill Trust via the British Geriatrics Society enabled me to undertake this PhD and still have a life, and was greatly appreciated.
PhD life can be lonely, and I am indebted to friends and colleagues at the Faculty of Health Sciences for their encouragement and support through discussion of methodology and findings and proof reading. Special thanks go to Cheryl Metcalf, Sara Demain, Maggie Donovan-Hall, Martin Warner and Ann-Marie Hughes.

Last, but by no means least, I would like to acknowledge the role of friends and family, without whose love, support and encouragement, I would never have got through this. To my Mother-in-law Trish Bell, and some wonderful friends who have graciously helped out with childcare, encouraged me and kept me strong, in particular Carolyn Young, Fiona Kleiven and Alexia Bylett. To my Brother Adam, and his family, for their love and pride in me. To my Mother, for her immense love, belief and pride in me, for helping me with contacts in the Farnham U3A and being a participant herself, and for proof reading the final thesis. Lastly to my Daughter, Bethany, age 4, who has never known Mummy without doing a PhD, and who has provided a lovely distraction; and to my Husband Chris, for always believing in me and being there through all the ups and downs, and who has been an immense support, especially in the last months of writing up.

Glossary of abbreviations

ARAT – Action Research Arm Test

AROM – active range of movement

BL – baseline

CC – cross correlation

CI – coactivation index

(s)EMG – (surface) electromyography

GBL – global baseline

ICC – Intraclass correlation coefficient

LBL – local baseline

LED – light emitting diode

MAE – mean absolute error

MVC – maximal voluntary contraction

MCP – metacarpophalangeal

MTI – mean torque index

PROM – passive range of movement

RMS(E) – root mean square(error)

SI – stretch index

SR – stretch reflex

TAI – torque-angle index

TI – tracking index

UMN – Upper motor neurone

(m)WMFT – (modified) Wolf Motor Function Test

Glossary of Terms

Active ROM	Range of movement capable without assistance
Anterior	Toward the front of the body
Coactivation	The simultaneous activity of agonist and antagonist muscles crossing the same joint that activate in phase and increase the stiffness of the joint
Coactivation index	Correlation of flexor and extensor EMG based on time-points when extensor EMG was increasing
Distal	Away from the centre of the body
Extension	Increasing inner angle of the joint
Flexion	Decreasing inner angle of the joint
Isometric Force	Force measured during muscle contraction with no movement taking place
Lateral	Away from the midline of the body
Posterior	Toward the back of the body
Mean torque index	Non-neural torque measured during passive stretch
Medial	Toward the centre, or midline of the body
Sample	A group of people, especially regarded as a class or subset within a larger group (OED, 1989)
Path length	Extent of corrective sub-movements at target end-point
Passive ROM	Range of movement capable with assistance
Proximal	Toward the centre of the body
Spasticity	'…*motor disorder characterized by a velocity dependent increase in the tonic stretch reflex (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motor neurone syndrome.'* (Lance 1980)
Stretch reflex / index	Neural response of flexor EMG to passive stretch
Torque	Rotational force around an axis
Tracking indices	Error between target and wrist movements
Weakness	Defined in this thesis as the ability to generate isometric force

1. Introduction

This thesis presents interdisciplinary research carried out at the Institute of Sound and Vibration Research and Faculty of Health Sciences, University of Southampton and forms the requirement for Doctor of Philosophy.

This chapter presents a justification for the research, introduces the specific aims and objectives of the research, outlines the original contributions made and summarises the programme of studies.

1.1. Justification for this research

1.1.1. The impact of stroke

Stroke is defined as a clinical syndrome, of presumed vascular origin, typified by rapidly developing signs of focal or global disturbance of cerebral functions, lasting more than 24 hours or leading to death (World Health Organisation 1978). Stroke is one of the top three causes of death in England (National Audit Office 2005) and is the most common cause of complex disability in older adults (Adamson et al. 2004). Approximately 110,000 strokes occur in England each year (National Audit Office 2005). Stroke care costs the NHS about £2.8 billion a year in direct care costs, and the total annual direct cost of stroke is about £4 billion or approximately 5.5% of the total UK expenditure on health care (Saka et al. 2009). Although the incidence of stroke in the UK over the past 20 years has fallen by approximately 40%, which has been associated with increased use of preventive treatments and major reductions in premorbid risk factors (Rothwell et al. 2004), there is a predicted increase in the percentage of people in England who are over 65 (from 16% in 2003 to 23% in 2031). It is therefore expected that stroke-related disability will have increased impact on healthcare resources with the largest cost being rehabilitation and community care (National Audit Office 2005).

1.1.2. Loss of upper limb function after stroke

Loss of arm/hand function is a common problem following stroke. It affects 85% of survivors (Nakayama et al. 1994) and has an impact on quality of life (Nichols-Larsen et al. 2005). Current therapy has limited effectiveness – less than half of those affected have regained upper limb function on discharge from hospital (Nakayama et al. 1994) and a longitudinal study of 102 patients with flaccid paralysis found that only 38% had regained ‘some dexterity’ at 6 months (Kwakkel et al. 2003). The inability to move effectively with associated limited functional activity is caused by a combination of impairments. The primary motor impairments following stroke are: weakness, fatigue and loss of dexterity (negative features), and

abnormal involuntary activity (positive features) such as spasticity, increased tendon reflexes, clonus and co-activation during movement (Barnes 2001). Later onset impairments, due to non-neural mechanical changes, are shortening and increased stiffness of muscles and soft tissue around joints, resulting in reduced range of movement and abnormal postures.

1.1.3. The need for better outcome measurement

1.1.3.1. Classification of Impairments, Activity and Participation

The WHO International Classification of Functioning, Disability and Health (ICF) (World Health Organisation 2001) is a classification framework which provides a unified and standard language to enable the impact of health and disability to be understood and measured in terms that are useful for the patient, carer, clinician and researcher (McPherson et al. 2005). The domains are classified into three areas: impairments (problems in body function or structure such as a significant deviation or loss), activity limitations (difficulties in execution of a task or action) and participation restrictions (problems an individual may experience in their life roles).The ICF framework is now commonly used both by clinical therapists in neurological rehabilitation and by rehabilitation researchers to classify and understand individual patient disability and evaluate interventions (an example is given in Figure 1-1 for spasticity). The terms impairment, activity limitation and participation restriction and the framework in which they are used are the basis for this research and are used throughout this report.

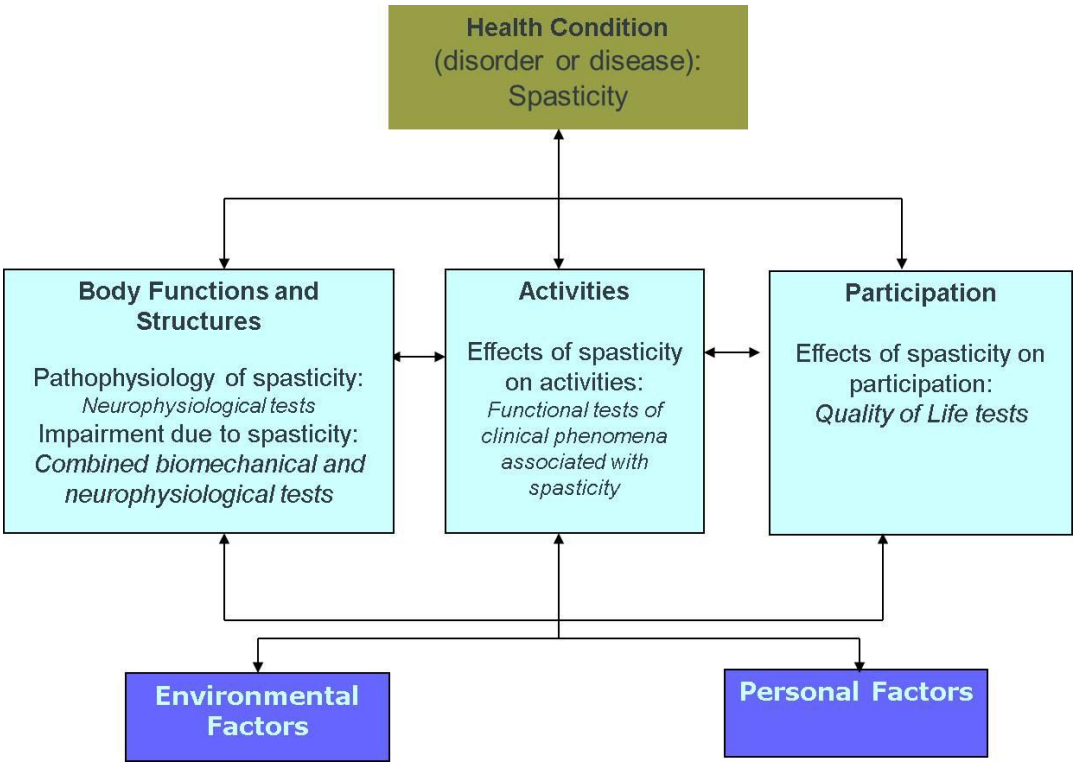


Figure 1-1: An example of the ICF framework and how it can be used to classify the problem of spasticity, adapted from WHO International Classification of Functioning, Disability and Health (ICF) (World Health Organisation 2001)

1.1.3.2. The need for impairment measures

The aim of physical rehabilitation after stroke is to achieve maximum recovery of function by reducing impairment, increasing activity and enabling people to participate as fully as possible in society (Kwakkel et al. 1999). The basis for the rehabilitation process is the assessment and prioritisation of patient's individual problems and goals in all these domains in order to target therapy. There is some two-way connection (see Figure 1-1) between the three domains, for example, therapists realise that targeting treatment at the impairment level will contribute to increasing functional activity. In my experience as a physiotherapist, patients often present with a complex mix of interrelated motor impairments, and, although skilled observation, handling and clinical judgement is used, it is still difficult to prioritise which impairments are important to target. Therapy is therefore often based on subjective assessment and a process of trial and error. Better objective quantitative measurement and understanding of the underlying impairment mechanisms would, one might expect, lead to better targeted therapy and improved outcomes for patients.

Similarly, in the field of upper limb rehabilitation research, although considerable advances in identifying the potential for recovery with intensive practice has led to the emergence of new treatments, progress in the development of rehabilitation therapies has been hampered by lack of reliable objective measures of impairment (Pomeroy and Tallis 2000). Commonly used standardised tests of upper limb activity are useful to determine functional change, but do not inform the underlying mechanisms of functional limitations. More recently, researchers have identified the importance of the understanding of the underlying mechanisms associated with loss and recovery of function (Kwakkel et al. 2008). Better identification and measurement of impairments is key to a greater understanding of a) movement dysfunction of the upper limb post-stroke and how it compares to normal movement, and of b) the underlying reasons for improvement or deterioration in function. This is expected to provide the foundation for better clinical diagnosis of specific individual impairments leading to better targeted treatments, as well as better measurement of "natural" recovery and the effectiveness of rehabilitation therapies.

1.2. Aims and Objectives

The primary aim of this research was to advance understanding of the physiological and biomechanical mechanisms associated with normal and impaired function and recovery and the relationship between motor impairments and loss of activity in the upper limb of older adults, early and late post-stroke. The findings of the research were then used to make recommendations on measurement of impairments related to upper limb activity.

The objectives were:

1. Development of a system of measuring and characterising motor impairments using the instrumented wrist rig; including the development of appropriate signal processing and data analysis techniques.
2. a) Characterisation and derivation of indices for key elements of motor impairments at the wrist early and late after stroke;
   b) Evaluation of the validity impairment indices i.e. their ability to distinguish impaired from unimpaired and repeatability.
3. Evaluate relationships between motor impairments and with functional activity early and late after stroke (using a standardised assessment of upper limb activity).

Further detailed objectives can be found at the end of Chapter 2 following the Literature Review.

1.3. Development of the wrist rig at Southampton

This interdisciplinary PhD research work was conducted within the Rehabilitation and Health Technologies (RHT) Research Group at the Faculty of Health Sciences (FHS), and the Signal Processing and Control Group at the Institute of Sound and Vibration Research (ISVR). The RHT group research is into the development, validation and evaluation of rehabilitation and health technologies. More specifically, this research is focussed in the ARM (Activity Rehabilitation and Measurement of the upper limb) research programme

To achieve the first objective required the development of a system of measuring and characterising motor impairments in the upper limb. I have used an instrumented wrist rig (a picture of a previous version of the wrist rig can be seen in Chapter 2 Literature Review Section 2.10 and the version used in this study in Chapter 4 Methodology Figure 4.2 and Chapter 6 Main Study Figure 6-2). In previous work, the wrist rig, modified from an original design, the Strathclyde wrist rig (Pandyan et al. 1997), was developed at the FHS in collaboration with the ISVR to objectively measure motor impairments in neurological conditions such as stroke, using a combined biomechanical and neurophysiological (neuromechanical) approach (Burridge et al. 2008; Notley et al. 2007; Turk et al. 2008a; Turk et al. 2008b). The wrist rig was instrumented to measure torque about the wrist joint and wrist angle in a horizontal plane combined with surface Electromyography (sEMG) of wrist flexors and extensors. In a small preliminary validation study, we used the wrist rig to develop neuromechanical measures of motor control, muscle activation patterns, weakness, spasticity, and non-neural stiffness (Turk et al. 2008b). This was in preparation for the rig being used as tool to measure impairment changes in a clinical study, testing the feasibility of implanted microstimulators to improve upper limb functional activity post-stroke (Turk et al. 2008a). The impairment measures were evaluated for reliability, sensitivity to distinguish

between people with and without stroke induced hemiplegia (Turk et al. 2008b), and relationship with upper limb activity (Burridge et al. 2008). Following this work, I identified ways in which the rig could be improved in terms of usability and ability to generate data that was more relevant to functional activity. Further details of the results of these studies and the research questions raised which led to the formation of this PhD research are outlined in Chapter 2 Section 2.10.

1.4. List of main original contributions

The following is a summary of original contributions from this research which extend the knowledge in the field:

1. Evaluation of the underlying impairment mechanisms associated with upper limb activity loss post-stroke through quantifying a wide range of negative, positive and secondary motor impairments using one neuromechanical measurement tool
2. Evaluation of upper limb motor impairments and functional activity in an older stroke population compared to an older unimpaired population
3. Evaluation of how a wide range of negative, positive and secondary upper limb motor impairments and functional activity relationships differ in the acute and chronic stages post-stroke
4. Evaluation of motor control during both rhythmic and discrete active tracking tasks. In particular, a novel step tracking task has been developed for the purpose of evaluating discrete movements
5. Evaluation of muscle activation patterns as a method of measuring spasticity in activity. In particular, a novel method of measuring abnormal coactivation has been developed.

1.5. Summary of thesis chapters and overview of studies

Chapter one has outlined the research problem, rationale for the research, and summarised the aim and objectives, as well as the original contributions. The programme of studies used to fulfil these aims and objectives is illustrated in the flowchart below (Figure 1-2).

Chapter 2 gives a review to date of the relevant background literature. The neurophysiology of normal motor control is considered, followed by a section on motor impairments of the upper limb post-stroke and, specifically, methods of measurement are reviewed and critiqued. The wrist rig, used in previous work as a measurement method, is detailed. Lastly, a discussion on standardised upper limb activity measures is followed by a summary of that literature which is found to date on the relationship between motor impairments and upper

limb functional activity. This is then followed by the research questions and hypotheses, and more detailed aims and objectives are presented.

Chapter 3 details a development phase during which the wrist rig hardware was re-designed and re-built including modified arm positioning. A new signal acquisition system, new human computer interface software and novel tracking tests were designed and implemented.

Chapter 4 describes the methodology. The study design, participant samples, confounding factors, clinical assessments, wrist rig testing protocol, modified Wolf motor function test protocol, impairment measure indices, and statistical analyses are discussed and justified.

Chapter 5 reports the pilot studies that were undertaken to optimise the design of the rig and to test the methodology of data collection and analysis used in the Main Study. A series of four studies are described through which the final protocol was defined. Firstly, new methods of measuring coactivation were developed and evaluated. Secondly, usability of active tracking tests and four hand positions with younger unimpaired participants was assessed. Thirdly all wrist rig tests and two hand positions were assessed with older unimpaired participants and participants with chronic post-stroke hemiplegia of all ages. From these data indices of function/impairment were developed and evaluated. Lastly, the stretch test was reassessed with younger and older unimpaired and chronic stroke participants. The study findings are discussed in the light of current evidence and lastly, a summary of the final wrist rig testing protocol and impairment indices to be used for the Main Study, is given.

Chapter 6 reports the Main Study where the wrist rig tests and an upper limb activity measure were conducted with three groups of older participants: those in the acute phase post-stroke, those in the chronic phase post-stroke and a control group of age-matched unimpaired participants. Results are reported and discussed.

Chapter 7 pulls the discussion sections from Chapters five and six together. The clinical implications of the findings are addressed as well as limitations of the study and plans for future research

Chapter 8 contains the final conclusions and recommendations on important functionally-related upper limb impairment measures which are relevant to clinical practice and rehabilitation research.

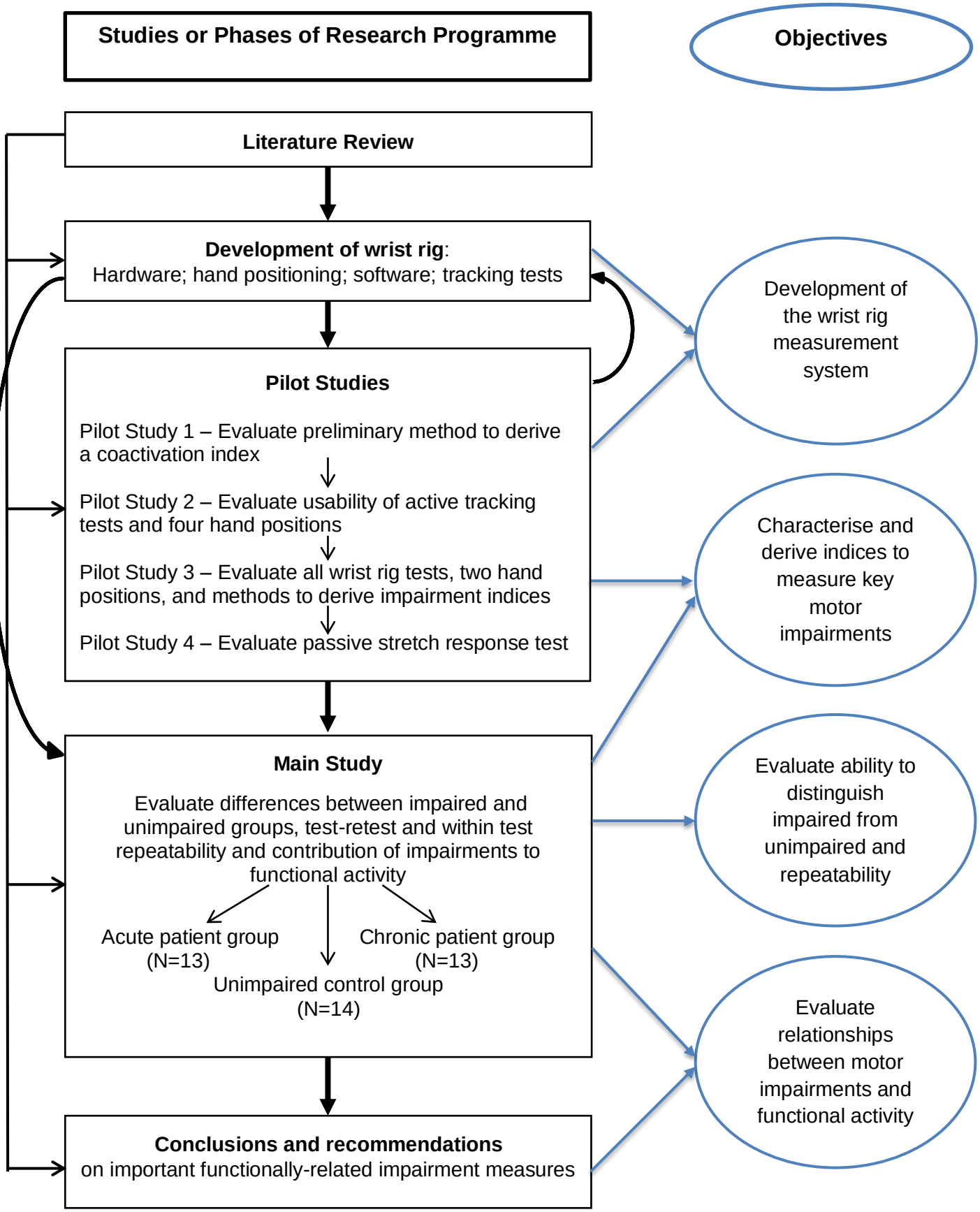


Figure 1-2 Flowchart of the interrelated studies and objectives of this research showing the iterative development of the wrist rig and impairment measurement methods in the pilot phase that feed into the Main Study data collection method, analysis and conclusions

2. Literature Review

2.1. Introduction

This literature review informs the selection of appropriate tests and methods of analysis for the main study with the following objectives:

- Increase understanding of the neurophysiology of motor control
- Identify key motor impairments of the upper limb after stroke
- Identify and critically appraise the biomechanical and neurophysiological methods used to measure motor impairments of the upper limb after stroke
- Identify and critically appraise the standardised measures of upper limb functional activity to select the most appropriate measure for the study
- Identify what is known so far about important relationships between motor impairments and functional activity.

The motor impairments include negative, positive and the secondary features of the upper motor neurone syndrome. The review of research on which impairments relate to functional activity suggests that the negative features are more important than spasticity measured during passive movements, but a debate exists in the importance of positive features having an effect during movement, particularly coactivation. A more detailed review has therefore been made on methods of measurement and analysis of coactivation.

2.2. Control of voluntary movement

2.2.1. Neurophysiology of motor control

Movement arises through the interaction of sensory / perceptual and motor systems, with cognition affecting both systems at many different levels. The focus of this literature review is on motor systems, however sensory systems will be included as they play a strong role in control of movement especially peripheral receptors such as muscle spindles and their afferent pathways, which will be discussed in reference to their primary role in spasticity.

Movement control is thought to be achieved through the cooperative effort of brain structures organised both hierarchically and in parallel (Shumway-Cook and Woollacott 2001). This means that a signal may be processed within ascending levels of the central nervous system (CNS) and the same signal may be processed simultaneously among many brain structures (Shumway-Cook & Woollacott 2001). Voluntary motor command has been divided into higher, middle and lower levels that can be seen in Figure 2-1 (Gracies 2005a). The higher level can be subdivided into two units, and the first generates the kinematic parameters of the

movement required through spatial and temporal representation and the second provides the motivation to move. The middle level corresponds to the planning and preparation of movement, i.e. the programming in time and space of the muscle contractions needed to achieve the higher level's movement representation. The anterior part of the supplementary cortex which has connections with the prefrontal cortex and basal ganglia, and the cerebellum are thought to be involved in this pre-programming. The execution of movement itself happens centrally at the lower level of command by the primary motor area, centrum semiovale, internal capsule and corticospinal tract, and peripherally by the lower motor neurone, neuromuscular junction and muscle (Gracies 2005a).

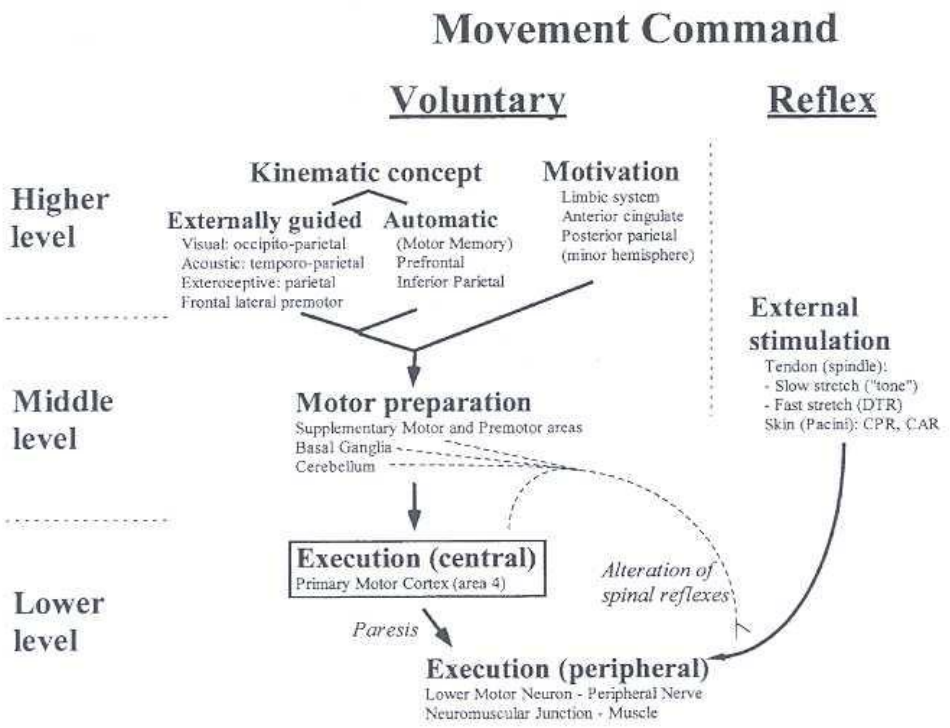


Figure 2-1 Movement generation (Gracies 2005a): the classically opposed types of movement command, voluntary and reflex, are schematised, and the components of each level of voluntary command are indicated with the location of the underlying pathways. The higher level is the generation of kinematic parameters of the movement required and the motivation to move, the middle level corresponds to the planning and preparation of movement, and the lower level is the execution of movement. CAR - cutaneous abdominal responses; CPR - cutaneous plantar responses; DTR - deep tendon reflexes

2.2.2. The neurophysiology of discrete and rhythmic upper limb movements

Normal upper limb activity involves reaching, grasping and manipulating objects as the basis for important functional activities such as feeding or dressing (Shumway-Cook & Woollacott

2001). These upper limb movements can be described as discrete i.e. they involve a distinct start and end point, and sometimes, in complex movements, with intermediary via points. On the other hand, some movements in the body can be described as rhythmic, most commonly in the lower limb during locomotion, but also the mouth while chewing, and the upper limb when scratching (Schaal et al. 2004). Animal neurophysiological studies have shown that rhythmic movements are associated with central pattern generators and there is some indirect evidence for these in human locomotion studies (Shumway-Cook & Woollacott 2001). Neurophysiological and computational research on human arm motor control has focused almost exclusively on discrete movements, essentially assuming similar neural circuitry for rhythmic tasks. In contrast, many behavioural studies have focused on rhythmic models, subsuming discrete movement as a special case. Recent research using functional magnetic resonance imaging (MRI), whilst performing rhythmic and discrete single-joint wrist flexion-extension movements, similar to those proposed for this study, found that in addition to areas activated in rhythmic movement, discrete movement involves several higher cortical planning areas (Schaal et al. 2004). This suggests that discrete and rhythmic movements use different neuronal circuits for control, and therefore should be considered separately in terms of neurophysiological and clinical research (Schaal et al. 2004). The study proposed in this research will involve investigating motor control accuracy of both rhythmic (sinusoidal tracking) and discrete (random step tracking) wrist movements of unimpaired subjects and those impaired by stroke.

2.3. Motor impairments of the upper limb post-stroke

Motor impairments of the upper limb post-stroke will be defined and grouped using a concept used regularly in the literature, the upper motor neuron (UMN) syndrome.

2.3.1. Features of the Upper Motor Neurone Syndrome

The UMN syndrome occurs following any lesion affecting some or all of the descending motor pathways of the brain and spinal cord and is a complex group of impairments that often has a considerable impact on a person's activity and participation (Barnes 2001). Hughlings Jackson, a neurologist in the 19th century, categorized the features of upper motor neuron lesions into two broad groups – positive features and negative features (Walshe 1961). The negative features of the UMN syndrome are characterised by a reduction in motor activity and include: muscle weakness, loss of dexterity and fatigueability (Barnes 2001). The positive features of the UMN syndrome are characterised by excessive and inappropriate motor activity and include: spasticity (exaggerated tonic stretch reflexes), dyssynergic patterns of coactivation during movement, associated reactions and other dyssynergic and stereotypical spastic dystonias, clonus, extensor and/or flexor spasms, increased tendon

reflexes with radiation and positive Babinski sign (Barnes 2001). In addition to the primary positive and negative features which are a direct result of the lesion, there are also secondary features that develop over time as a result of the primary impairments. These include stiffness, loss of active range of movement and contracture due to biomechanical changes of soft tissue including muscles, tendons, ligaments and joints (Barnes 2001; Thilmann et al. 1991b). There are also alterations in the histology of muscle tissue such as increased atrophy of type II muscle fibres, a predominance of type II fibres (though this may depend on the initial fibre type), structural changes mainly in type I fibres, and the presence of target fibres (Dietz et al. 1986; Gracies 2005a).

This review will focus on the features that can be measured in the wrist rig: muscle weakness, loss of motor control accuracy/ dexterity, spasticity, coactivation and stiffness. The next sections describe each impairment, their definition and underlying pathophysiology, and lastly how they have been measured in the literature using neuromechanical methods.

2.4. Weakness

Weakness of one side of the body, or hemiparesis, is the most immediate effect of a central lesion. Weakness is defined as an inability to generate normal levels of force or tension in a muscle for the purposes of posture and movement (Shumway-Cook & Woollacott 2001). After a stroke, the problem of reduced muscle force production may be compounded by a decreased rate of force production and relaxation (Canning et al. 1999)

2.4.1. Pathophysiology of weakness after stroke

Normal muscle force is generated when either the absolute number of active motor units is increased or the firing rates of already-active motor units are increased, and usually both processes occur simultaneously. Normal recruitment of motor units occurs according to their size and force-producing characteristics, so that small low-force motor units are the first to be recruited, and as force requirements increase, larger and higher force producing motor units are recruited (Henneman size principle), resulting in a smooth increase in muscle strength (Henneman et al. 1965). After a stroke there are changes at the motoneurone and muscle levels which can decrease the ability to produce force. These are loss of motor units, changes in the properties of motor units, disrupted recruitment order of motor units and decreased motor unit firing rates (Bourbonnais and Vanden 1989). A lesion in the higher centres of the CNS, discussed in section one, disrupts the access of volitional command and excitatory drive to the lower motor neurone. Only lesions involving the pathways of the lower level of motor command cause paresis, though lesions affecting higher levels may affect motivation and conception of movement, planning and monitoring (Gracies 2005a). The loss

of excitatory drive results in an inability to recruit and / or modulate the motor neurones leading to a loss of movement (Shumway-Cook & Woollacott 2001). This has been shown as impersistent motor unit recruitment with gaps in the interference pattern (Bourbonnais & Vanden 1989; Fitts et al. 1989), with low-threshold motor units (MUs) firing within the lower end of their normal range, high-threshold MUs firing below their normal range or are not recruited (Frontera et al. 1997), and a reduced integrated electromyogram (Frontera et al. 1997; Sahrmann and Norton 1977).

2.4.2. Measurement of Weakness

After stroke weakness is typically measured as the torque or force produced by a maximum voluntary contraction (MVC), and methods include handheld (Bohannon 2004) and isokinetic dynamometers (Kim and Eng 2003) and grip strength (Boissy et al. 1999; Wetter et al. 2005). These measures have been shown to be prognostic indicators (Bohannon and Smith 1987; Sunderland et al. 1989). There is another method of quantifying weakness by calculating the amplitude of electromyography (EMG) signals i.e. measuring the amount of EMG activation during a maximal voluntary contraction (Chae et al. 2002b). However this can be problematic because surface EMG (sEMG) signal amplitudes are not directly comparable so normalisation must be undertaken using maximum voluntary contraction or other methods. The method chosen for this study is measurement of torque during a MVC.

2.5. Loss of Motor Control Accuracy

2.5.1. Definition

Although loss of dexterity is within the list of negative features of the UMN syndrome, it is usually considered to be related only to the skilled use of the hands (manual dexterity). However loss of skilled control of movements in single joints or in the upper limb as a whole after stroke is of interest. Some researchers investigated motor control in the upper limb (elbow joint) and used the term dexterity but with a much broader definition (Ada et al. 1996; Canning et al. 2000; Canning et al. 2004). The task that they used in their studies that tested precise muscular coordination involved tracking a visual target by horizontal flexion-extension movements of the elbow joint and the definition they used was adroitness and competency in use of the limbs by coordinating muscle activity to adequately solve a task to meet environmental demands. This is the definition that will be used in this research programme and the term for this will be motor control accuracy.

2.5.2. Measurement of Motor Control Accuracy

The use of tracking tasks is a useful and established approach to the measurement of motor control accuracy. Various forms of tracking tasks have been used in the laboratory to provide

insight into sensory-motor behaviour such as patterns of muscle activation in unimpaired people (Fagg et al. 2002; Hoffman and Strick 1999), perceptual-motor performance of older adults (Jagacinski et al. 1995) and muscle activation patterns and motor control accuracy in people with post-stroke hemiplegia at the ankle (Burridge and McLellan 2000; Wirth et al. 2008); elbow (Ada et al. 1996; Canning et al. 2000; Canning et al. 2004; Patten et al. 2003), wrist (Burridge et al. 2008; Notley SV et al. 2007; Turk et al. 2008b; Yarosh et al. 2004) and finger joints (Carey et al. 1998; Carey et al. 2002; Halaney and Carey 1989). Through using a biomechanical approach coupled with sEMG, both accuracy of tracking and muscle activation patterns can be measured and related.

Tracking is mostly visual commonly using a target on a computer screen (Canning et al. 2000; Turk et al. 2008b) which tests not just motor control but also visuo-perceptual abilities (Jagacinski et al. 1995). An advantage to having a tracking target close to the line of sight of the moving joint is that it may reduce some of the visuo-perceptual demand of the task.

Upper limb tracking research has used sinusoidal waveforms (Patten et al. 2003; Turk et al. 2008b) or repeated random patterns (Canning et al. 2000) which can be described as rhythmic movements. Others have used step tracking (Hoffman & Strick 1999; Yarosh et al. 2004), moving to different points of displacement with variable rest periods in between, which are discrete movements. It is possible that step tracking may relate to more to normal functional use of the arm where functional movements are generally discrete. Although there are some functional rhythmic upper limb movements (e.g. brushing teeth or brushing hair), rhythmic sinusoidal tracking may be more associated to functional use of the lower limb in walking.

Accuracy of tracking is calculated using the signal from the target itself and the angle signal due to movement of the joint. Researchers use different methods to calculate the difference between the two signals including root mean square (RMS) error (Patten et al. 2003), cross-correlational and spectral analysis to assess coherence between the signals (Canning et al. 2000), and cross-correlation (Notley et al. 2007; Turk et al. 2008b). The RMS and cross correlation methods were investigated and it was found that cross correlation method most related to functional ability and therefore is arguably more clinically relevant.

2.5.3. Impairments that contribute to loss of motor control accuracy

Loss of control in movement performance may be due to any number of positive, negative or secondary features. A relationship has been shown between wrist tracking ability and wrist extensor strength (Burridge et al. 2008) however others suggest that weakness (Ada et al. 1996; Canning et al. 2000; Wirth et al. 2008) is not associated with loss of tracking

performance in the elbow and ankle. Spasticity was not considered to be associated with loss of motor control accuracy in two studies as the patients had low spasticity scores on the modified Ashworth score (MAS) yet still demonstrated poor tracking performance (Canning et al. 2000; Wirth et al. 2008). Another study showed a relationship between tracking motor control and the MAS but not the stretch reflex (Burridge et al. 2008). Neither slowness of muscle activation (Canning et al. 2000) nor excessive coactivation (Burridge et al. 2008; Canning et al. 2000) seem to be related to dexterity, yet Canning et al found that decreased coupling of muscle activation with respect to the target and excessive biceps activation distinguished those with low dexterity from those with high dexterity (Canning et al. 2000). It seems therefore that rather than slowness of activation, a lack of consistency of timing of muscle activation is more responsible. It has been hypothesized that a lack of precise modulation of the firing rate of motor units as well as their impaired synchronization, which has been reported in stroke patients (Farmer et al. 1993; Gemperline et al. 1995) might be the underlying factors (Canning et al. 2000). It is further suggested that this lack of precise modulation may be due to reduced corticospinal tract conductivity (Canning et al. 2000; Wirth et al. 2008).

2.6. Spasticity

2.6.1. Definitions

Spasticity is a well-known but complex phenomenon that remains difficult to define and terminology used to describe it can be confusing. It is easily recognisable by clinicians working in neurology as an increase in muscle tone (tension in a muscle experienced as resistance to passive movement), often with associated spasms and/or clonus (Stevenson and Marsden 2006). Spasticity is commonly used by clinicians and researchers alike as a generic term which encompasses a variety of the positive (e.g. exaggerated stretch reflexes, associated reactions, clonus and spasms) and secondary (e.g. stiffness) features of the UMN syndrome. However, the most commonly used and accepted definition in the literature is much more precise: '…*motor disorder characterized by a velocity dependent increase in the tonic stretch reflex (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motor neurone syndrome.'* (Lance 1980). More recently a European working group (EU-SPASM) of researchers have attempted to update this definition, suggesting that it did not reflect accurately recent research findings and current clinical interpretations (Pandyan et al. 2005). From their literature reviews of approaches to measurement of spasticity, they suggest that spasticity cannot be considered a pure motor disorder, as afferent activity is also involved. It does not exclusively result from hyper excitability of the stretch reflex, activity in other pathways (afferent, supraspinal, and changes in the α motor neurone) are also important. The velocity-dependent changes in resistance to passive movement are not solely due to neural changes but are

contributed to by the viscoelastic properties of soft tissues (Pandyan et al. 2005). Furthermore Lance's definition relates purely to passive movement of a limb and makes no reference to spasticity during active movement (Burridge et al. 2005). The EU-SPASM group therefore redefined spasticity as *'disordered sensory-motor control, resulting from an upper motor neurone lesion, presenting as intermittent or sustained involuntary activation of muscle'* (Burridge et al. 2005; Pandyan et al. 2005).

A specific aspect of spasticity (altered stretch reflexes), muscle activation patterns associated with spasticity (coactivation) and secondary biomechanical changes that are associated with or influence increased muscle tone in the upper limb post-stroke, and that will be measured as part of this research, will be further defined in the following sections.

2.6.2. Stretch Reflexes

In response to muscle stretch, sensory axons (group Ia and II afferents) arising from muscle spindles are activated and relay information to the spinal cord and brain about length changes (amplitude and speed of stretch) of the muscle (Figure 2-2). The Ia afferents wrap around the equatorial (middle) region of the muscle spindle, are sensitive to rate of change of muscle stretch and have a low threshold to stretch. The Type II afferents wrap around the juxta-equatorial (end) region of the spindle, are sensitive to changes in the length of the muscle and have a higher threshold to stretch (Shumway-Cook & Woollacott 2001; Vander et al. 2000). These afferents make monosynaptic (Type Ia) and disynaptic (Type II) connections with the α motor neurones leading to contraction of the same muscle (Figure 2-2). This is clinically seen as a tendon reflex caused by a very brief stretch of muscle (tendon tap) and is known as a phasic stretch reflex. The Ia afferents also excite the Ia inhibitory interneurone which connects to the α motor neurones of the antagonist muscles, thus causing simultaneous relaxation of the antagonist muscle (reciprocal inhibition) (Stevenson & Marsden 2006).

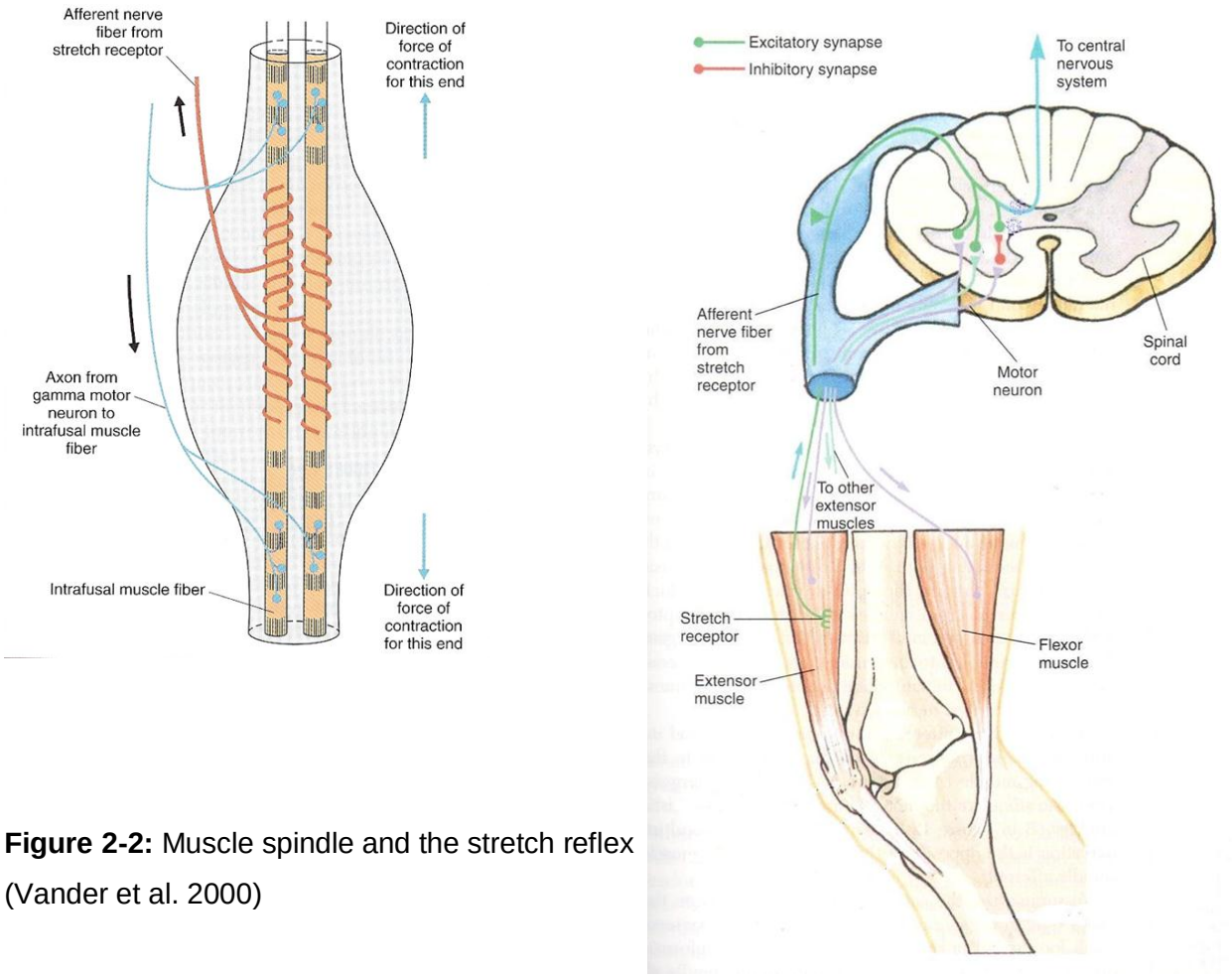


Figure 2-2: Muscle spindle and the stretch reflex (Vander et al. 2000)

In the UMN syndrome the clinical signs of hyperexcitability of phasic stretch reflexes include exaggerated tendon jerks, as per Lance's definition above (Lance 1980), irradiation of tendon reflexes and clonus (Sheean 2002). Another stretch reflex is detected in response to muscle stretch at the rate used clinically to measure for muscle tone, and that is the tonic stretch reflex. In patients with spasticity, long duration responses (tonic stretch reflexes) can be seen using EMG even at low stretch velocities (35˚/s in the elbow), which increase linearly with increasing velocity (Sheean 2001; Thilmann et al. 1991a). When stretching the muscles of unimpaired subjects at rest, however, a stretch reflex is not seen on EMG until a very fast stretch velocity (greater than 240˚/s in the elbow) is applied and the short burst of activity then may be analogous to a phasic tendon jerk reflex (Thilmann et al. 1991a). Long duration tonic reflexes are not present, even in elderly unimpaired subjects (Yeo et al. 1998), which suggests that spasticity is not an exaggeration of a normal reflex (Sheean 2002).

Another aspect of the tonic stretch reflex seen in the UMN syndrome is that although it is considered to be dynamic (responds to passive movement) often when the muscle is stretched and then maintained in a stretched position, the stretch reflex continues at least for a time and therefore there may be a static component (Sheean 2002). A further aspect is

that the excitability of the tonic stretch reflex depends on the length of the muscle at which it is stretched (Sheean 2002)

2.6.3. Pathophysiology of spasticity

2.6.3.1. Spinal reflex pathways

Given that hyperexcitability of the stretch reflex has a central contribution to spasticity, research on the pathophysiology of spasticity over the last 30-40 years has investigated which spinal reflex circuits may be involved in the development of spasticity. Excitation of the monosynaptic 1a afferents has a major role in the stretch reflex, but other spinal reflex pathways may increase or decrease the effect of this monosynaptic excitation: excitation of type II afferents; presynaptic inhibition of Ia afferent terminals; autogenetic inhibition; recurrent inhibition; and reciprocal inhibition from muscle spindle Ia afferents from antagonist muscles (Nielsen et al. 2007).

Increased excitatory postsynaptic potentials (EPSPs) of muscle spindle afferent information caused by presynaptic inhibition of Ia afferents has been demonstrated in patients with spasticity due to multiple sclerosis (Nielsen et al. 1995) and spinal cord injury (Faist et al. 1994) but not for hemiplegic stroke patients (Faist et al. 1994).

Autogenic inhibition is caused by activation of Golgi tendon organs via Ib afferents and is mediated by inhibitory interneurones connected to α motor neurones of the same muscle. A lack of autogenic inhibition has been shown in patients with hemiplegia (Delwaide and Oliver 1988), and as it has been argued that reciprocal inhibition at the wrist is mediated by Ib inhibitory pathways (Wargon et al. 2006) then the observation of reduced reciprocal inhibition at the hemiplegic wrist (Nakashima et al. 1989) provides further evidence that alteration of Ib inhibition may play an important role in the pathophysiology of spasticity. Two other inhibitory pathways that are thought to contribute to spasticity are disynaptic reciprocal 1a inhibition (this is discussed further in the pathophysiology of coactivation section) and recurrent inhibition. This is mediated by Renshaw cells which are located in the ventral horn of the spinal cord and receive excitatory connections from the motor axons and project back to motor neurones as well as Ia inhibitory neurones (Nielsen et al. 2007). Recurrent inhibition has been demonstrated to be normal at rest but impaired during voluntary movement in patients with hemiplegia (Katz and Pierrot-Deseilligny 1999). This implies that it does not contribute to spasticity when tested passively, but may play a role in often unexplained disordered motor control seen during activity.

2.6.3.2. Supraspinal descending pathways

The changes in reflex transmission in spinal pathways depend on the supraspinal drive via descending pyramidal (corticospinal) or parapyramidal pathways, which are altered due to the stroke lesion. Both the positive and negative features of the UMN syndrome are largely due to dysfunction of parapyramidal tracts and, less so, due to a lesion of the pyramidal tract (Sheean 2002). The modulatory parapyramidal pathways, particularly the dorsal reticulospinal tract, are important in inhibiting spinal reflex activity and in controlling the threshold and rate of α motor neurone activation (Brown 1994).

2.6.3.3. Plateau Potentials

If it were only a case of loss of inhibitory control on spinal reflexes then these would become hyperactive very quickly. More recent studies, however, have suggested other contributing factors to the onset of spasticity which fit better with the common clinical picture: one of slow development of spasticity. These include the possibility of new pathways or connections (collateral sprouting) or changes in receptor sensitivity (denervation hypersensitivity) that arise at cellular level in the spinal cord (Gracies 2005b; Sheean 2002), though the latter have been investigated only in animal models not patients with spasticity (Nielsen et al. 2007). Another concept is that of the discharge properties of motoneurones undergoing intrinsic changes that develop over time. These result in prolonged depolarized states called plateau potentials. The mechanism for this is thought to involve active membrane properties including voltage-dependent, persistent inward calcium and sodium currents that amplify and prolong the response of motor neurones to synaptic excitation (Gracies 2005b; Nielsen et al. 2007). Plateau potentials have been demonstrated in the chronic state following spinal lesions in animal studies (Bennett et al. 2001; Hultborn et al. 2004) and may contribute to the presence of spasms in chronic spinal cord injured patients (Gorassini et al. 2004), but to what extent they are involved in the development of spasticity following stroke remains unclear.

2.6.1. Measurement of spasticity

2.6.1.1. Clinical measures of spasticity

The most commonly used clinical scales for the measurement of spasticity have been the Ashworth and Modified Ashworth Scales (Van Wijck et al. 2001). However, recently their validity has been increasingly questioned, as they do not address the velocity-dependent neural aspect of the phenomenon as described by Lance (Lance 1980), and they have poor inter-rater reliability (Fleuren et al. 2010; Pandyan et al. 2003b). The Tardieu Scale, which was adapted from Tardieu's original research (Tardieu et al.) by Held and Pierrot-Deseilligny (Held and Pierrot-Deseilligny 1969) and translated by Gracies et al. (Gracies et al. 2000), demonstrates several advantages in the measurement of spasticity as it uses both a fast and slow speed of movement and incorporates an interval level measure (range of movement) as

well as a subjective rating scale. A recent study has demonstrated its validity in that it had statistically significant greater agreement with laboratory measures of spasticity (stretch-induced EMG) and contracture (passive range of movement) than the Ashworth scale (Patrick and Ada 2006).

2.6.1.2. Neurophysiological Measurement of the Stretch Reflex Response

Neurophysiological measurement methods of spasticity use sEMG to measure responses to movement (active and passive), mechanical tap of a tendon and electrical stimulation. Methods include the tendon reflex, Hoffmann reflex (H-reflex), and stretch reflex (SR) (Voerman et al. 2005). The tendon jerk is a commonly used method to illustrate a spinal reflex. Tapping a tendon and measuring the resultant muscle activation (latency and amplitude) using sEMG was thought to be evidence of the monosynaptic reflex but oligosynaptic pathways could also be involved (Rothwell 1994). The H-reflex is obtained by electrically stimulating Ia afferents by submaximal electrical stimulation of a mixed peripheral nerve. This activates the α motor neurones from the same muscle and the subsequent muscle activation is measured using sEMG.

The stretch reflex (SR) evoked by passive movement can be elicited by short muscle contraction, or displacement of a limb by rotation of a joint either by sinusoidal (Rothwell 1994; Turk et al. 2008b) or constant velocity movements (Kamper and Rymer 2000). Three peaks (M1, M2, M3) in the response correspond to the short latency reflex due to Ia afferents (M1), second due to group II afferents (M2) and the third peak the long-latency tonic reflex (M3) (Voerman et al. 2005). The SR can be quantified in terms of latency (in time (Cody et al. 1987) or joint angle (Levin and Hui-Chan 1993) of a threshold, amplitude (Cody et al. 1987) and duration (Levin & Hui-Chan 1993).

Factors that affect changes in SR are velocity of stretch (as velocity increases the amplitude of the EMG recording increases); limb position (this determines the length of the muscle which affects the SR); background muscle activity (evoking the SR when a muscle is contracted increases the size of the SR) (Voerman et al. 2005); and frequency of SR evocation (habituation and fatigue of M2 and M3 responses (Rothwell et al. 1986), and reduced joint torque (Schmit et al. 2000) occur after repeated joint movements. It is therefore important that velocity and displacement and limb position are controlled and standardised, that background activity is taken into account for normalisation, and that there are 10 second rest periods between repeated stretches to minimize habituation and fatigue (Voerman et al. 2005).

Often neurophysiological measures of SR are presented with biomechanical parameters which describe the relation between the occurrence of the reflex and the angle and / or velocity of displacement. In a study of spasticity measurement at the wrist the SR was quantified using a wrist rig instrumented with a potentiometer, tachometer and sEMG. The measurement method involved 10 passive 50˚ constant velocity displacements of the wrist joint at 500˚/s using a torque motor. This speed allowed comparison with unimpaired stretch reflex data. The SR latency and amplitude (area of flexor EMG) were quantified, as well as SR threshold speed (the minimum velocity able to evoke the SR). Others have used sinusoidal displacements at varying velocities and range of displacement. One research group found that speeds of at least 3 Hz with 10º sinusoidal displacement needed to be used to prevent voluntary tracking activity (Ada et al. 2006; Neilson 1972; O'Dwyer et al. 1996). In a preliminary study with the wrist rig (Turk et al. 2008b), our method involved manual passive sinusoidal displacements of +/- 30˚ around the subject's midpoint of their active range of movement and at 1.5Hz frequency. The SR was quantified by calculating the RMS value of the flexor EMG envelope above the baseline EMG for the first quadrant of the sinusoidal movement curve (from zero degrees to maximum extension) (Turk et al. 2008b). This method was found to be reliable between testing sessions however, because it used repeated movements without rest, and as such the resulting SRs were likely to be subject to habituation and fatigue.

Biomechanical methods focus on resistance to passive stretch (Wood et al. 2005). Resistance to stretch depends on tension generated by SR activity (neural component), voluntary activity which the individual might not be able to suppress, and the secondary biomechanical stiffness within the soft tissues (non-neural component) (Gracies 2005a). Burridge et al concluded that one of the purposes of an appropriate measurement tool is the ability to characterize and distinguish between these different components (Burridge et al. 2005).

2.7. Coactivation

2.7.1. Muscle activation patterns in normal movement

Normal movement is brought about by the synergic activation of muscles around joints which occurs through co-activation, reciprocal inhibition and reciprocal activation. Reciprocal inhibition and activation both involve alternating activity of the agonist and antagonist. For reciprocal inhibition, as the agonist contracts, the antagonist is simultaneously inhibited (Sherrington 1906), whereas reciprocal activation occurs through passive relaxation of the antagonist rather than inhibition (Damiano 1993). The pattern of alternating muscle interaction depends on the movement task. Step tracking, which involves rapid movement of a limb to a

target, is brought about by a characteristic tri-phasic muscle activation. Here a burst of agonist activity (AG1) which initiates the movement is followed sequentially by a burst of antagonist activity (ANT1) which breaks the movement, and another burst of agonist activity (AG2) which moderates the antagonist braking forces and redirects the movement to the target (Cooke and Brown 1990; Wierzbicka et al. 1986). In many instances additional bursts of activity alternate between agonists and antagonists until the limb is stabilised at the target (Hoffman and Strick 1990). Muscle interaction during rhythmic cyclic or sinusoidal movements has been less well researched, but a study of reversal movements shows ANT1 acting to decelerate and reverse movement direction and accelerate limb in reverse direction (Almeida et al. 2006).

2.7.2. Definition of Coactivation

Coactivation is defined as the simultaneous activity of agonist and antagonist muscles crossing the same joint (Sheean 2001; Shumway-Cook & Woollacott 2001) that activate in phase and increase the stiffness of the joint (Damiano 1993). Extensive coactivation is a normal feature in motor system development during the first four years of life (O'Sullivan et al. 1998).Controlled coactivation is used thereafter to stabilise joints and modulates in response to changing task requirements such as perturbing effects of external loads (De Serres and Milner 1991; Milner 2002), movement velocity (Suzuki et al. 2001) and accuracy requirements (Gribble et al. 2003), and reduces during motor learning (Gribble et al. 2003; Osu et al. 2002). Coactivation becomes abnormal at the point where the mechanical stiffness it creates impairs movement (Damiano 1993). This can occur as a result of neurological pathology and coactivation is seen in adult CNS lesions, though more commonly in cerebral palsy (O'Sullivan et al. 1998), and is associated with spasticity (Gracies 2005b; Gracies 2004; Sheean 2001). The extent to which coactivation is present and impairs function after stroke is debated with some authors finding it is (Burridge & McLellan 2000; Chae et al. 2002b; Hammond et al. 1988a; Hu et al. 2006; Kamper and Rymer 2001; Leonard et al. 2006; Neckel et al. 2006) and others not (Canning et al. 2000; Davies et al. 1996; Fellows et al. 1994; Gowland et al. 1992; Wagner et al. 2007). This debate is not surprising because coactivation is often seen as part of normal movement patterns (Damiano 1993) and this varies across movement tasks, and thus the point at which coactivation becomes abnormal may be difficult to define.

2.7.3. Pathophysiology of coactivation

When needed to control and stabilise a joint in normal movement, coactivation results from controlling reciprocal inhibition (Sheean 2002). It is suggested that a possible pathophysiological cause of coactivation is impairment of 1a reciprocal inhibition (Sheean 2001; Sheean 2002). In unimpaired motor control, the 1a afferents of an agonist muscle

inhibit, via 1a interneurones, the alpha moto-neurones of its antagonist. The interneurones have some control from higher centres, at a segmental level (including Renshaw cells) and at a supraspinal level (including corticospinal fibres) (Sheean 2001). If the 1a reciprocal inhibition is impaired (reduced) following a stroke then it follows that there will be greater activation of an antagonist muscle when it should be inhibited. 1a reciprocal inhibition can be studied by applying threshold conditioning electrical stimuli to a nerve supplying an antagonist and observing the effect on the H reflex obtained from the agonist. Two main inhibitory phases are seen, distinguished by timing: early, short duration disynaptic inhibition and later, long lasting presynaptic inhibition. Using this method, altered reciprocal inhibition has been observed in the lower limb (Okuma and Lee 1996) and upper limb (Artieda et al. 1991; Nakashima et al. 1989; Panizza et al. 1995) of patients with hemiplegia from stroke. In upper limb studies, reduced reciprocal inhibition was found in the forearm flexors and extensors in both the disynaptic and presynaptic phases. Although abnormal inhibition has been implicated in abnormal coactivation of the UMN syndrome (Crone et al. 1994) none of the studies have measured coactivation in order to test the correlation. However, a correlation has been shown in the post-stroke upper limb between impaired reciprocal inhibition and the presence of increased tone (specifically disynaptic inhibition) (Nakashima et al. 1989) and the severity of increased tone (Panizza et al. 1995).

2.7.4. Measurement of Coactivation

An extensive review of studies which measured coactivation in both unimpaired and impaired subjects with neurological lesions was conducted. The aim was to better understand the definition of coactivation used by researchers, and the methods of measurement and analysis used. Electronic databases were searched, including: Medline, CINAHL, AMED and EMBASE. The search strategy used the following keywords in various combinations: Stroke / CVA; hemiparesis / hemiplegia; measure$; coactivation / co-activation / cocontraction / co-contraction; muscle activation. Other sources were: reference lists from papers identified, conference proceedings, books and book chapters.

The summary table below (Table 2-1) reports the results of the studies found that measured coactivation with patients with stroke; both upper limb and lower limb studies are included.

The following conclusions have been reached:

- Study sizes were small with sample populations with varied levels of impairments.
- Studies testing coactivation during contraction without movement (isometric) mostly find coactivation to be present, whereas of the nine studies of coactivation during movement, five did not find coactivation to be significantly present.

- A number of studies which did not find significant presence of coactivation in the paretic limb did report that the presence of coactivation varied in the group, suggesting that coactivation may be a problem for some individuals but not for others and may therefore still be worth measuring.
- Results from one study suggested that patients with abnormal coactivation patterns also had more severe impairments and disabilities (Lamontagne et al. 2000), whereas another found abnormal coactivation minimally present in both low and high functioning groups (Canning et al. 2000).
- The methods of analysis used in stroke studies are varied; six main methods have been identified:
    1. Mean EMG activity of flexors during extension movement of the affected limb, compared with the unimpaired limb or unimpaired controls (Davies et al. 1996; Gowland et al. 1992; Kamper & Rymer 2001). There is a need to normalise the EMG data using this method (using % maximal voluntary contraction (MVC) or % of maximum activity).
    2. Ratio of flexor EMG during 0˚ - maximum flexion (when acting as agonist) to flexor EMG during 0˚ – maximum extension (when acting as antagonist) (modulation index) (Burridge et al. 2001; Turk et al. 2008b).

Neither of these two methods evaluates the co-activation relationship of the antagonist with the agonist, as defined in the literature.

3. Ratio of normalised agonist to normalised antagonist EMG (Chae et al. 2002b)
4. Ratio of antagonist activity to total (agonist + antagonist) activity (Hammond et al. 1988a; Yan et al. 2005)

These two methods included both muscles in their analysis but these were measured during isometric contraction not movement

5. The area of overlap between the agonist and antagonist muscles during activity (Hu et al. 2007; Lamontagne et al. 2000).

Although changes were observed over time using this method, validity in distinguishing impaired and unimpaired subjects was not demonstrated. It was thought that this method would be unsuitable to distinguish normal from abnormal coactivation in our study because in our tracking tasks, especially step tracking, the agonist and antagonist would often overlap to act as a ‘break’ at the end of the movement (normal co-activation).

6. Correlation coefficient of agonist and antagonist EMG (Canning et al. 2000; Dewald et al. 1995; Hu et al. 2006)

This method selectively analyses abnormal simultaneous activation of the flexor (antagonist) when the extensor (agonist) is activated. The similarity in timing and shape of the agonist and antagonist activation curves are measured providing a meaningful index, a correlation coefficient ranging between +1 and -1, with positive values indicating simultaneous activation

(coactivation) and negative values alternating activation (reciprocal inhibition/activation). For these reasons, this method was chosen to be evaluated further in this programme of research.

Table 2-1: Summary of upper and lower limb stroke studies which measure coactivation. The methods used have been divided into measurement of coactivation during isometric contraction, during isokinetic contraction and during both.

During isometric contraction						
Authors	**Sample**	**Joints**	**Measurement Tool**	**Description of method**	**Method of analysis**	**Outcome**
Chae et al. 2002b	Stroke; N=26; 6 mth+	Wrist	Wrist rig; sEMG	MVC of wrist extensors and flexors for 3s and 5s	Ratio of RMS of the antagonist EMG : agonist EMG	Significantly greater coactivation in paretic than non-paretic limb
Dewald et al. 1995	Stroke N=10 1yr+ normal controls N=2	elbow, sh , forearm	load cell 3º of freedom; sEMG, fine wire EMG	1.5s MVC shoulder and elbow muscles against 5 to 8 different loads in 8 directions	Agonist EMG / antagonist EMG scatter plots and correlation analysis	Elbow agonist and antagonist coactivation in 3 of 10 subjects
Hammond et al. 1988a	Stroke N=9 1yr+; normal controls N=5	Wrist	Wrist rig; needle EMG	MVC of wrist flexion and extension at 3, 6, or 9 second duration	Ratio of antagonist activity to total (agonist + antagonist) activity. Compared stroke with normal group	Significantly greater coactivation in stroke than controls
Hu et al. 2006	Stroke N=116 mth+;	Wrist and elbow	Wrist rig; sEMG	5s MVC of wrist flexion and extension at 8 angles between -45º to 60º, hemiplegic and non-hemiplegic sides	Normalised EMG to maximum – resting baseline. Agonist EMG / antagonist EMG scatter plots and correlation analysis	Significant wrist extensor flexor coactivation found in affected limb at all angles
Neckel et al. 2006	Stroke N=16 1yr+; normal controls N=16	Hip, knee, ankle	load cell 6 degrees of freedom; sEMG	3s MVC of hip, knee and ankle muscles in 8 directions	Normalised EMG to % maximum. Agonist EMG x physiological cross sectional area (PSCA) / antagonist EMG x PCSA. Compared stroke with normal group	Significantly greater coactivation during ankle dorsiflexion and plantarflexion and knee extension
Yan et al. 2005	Stroke N=46 acute	Ankle	sEMG	MVC of dorsiflexors and plantarflexors for 3s	Ratio of antagonist activity to total (agonist + antagonist) activity normalised by MVC. Compared FES treatment group with non-FES control groups	Significant reduction in coactivation with FES treatment compared to control
Yan and Hui-Chan 2009	Stroke N=62 acute	Ankle	sEMG	MVC of dorsiflexors and plantarflexors for 3s	Ratio of antagonist activity to total (agonist + antagonist) activity normalised by MVC. Compared FES treatment group with standard rehabilitation and placebo stimulation control groups	Significant reduction in coactivation with FES treatment compared to control groups

During isokinetic contraction						
Authors	**Sample**	**Joints**	**Measurement Tool**	**Description of method**	**Method of analysis**	**Outcome**
Burridge & McLellan 2000	Stroke N=18; Normal controls N=12	Ankle	Ankle rig; sEMG	30˚sinusoidal tracking tasks at 1Hz and 2Hz	Calf Modulation Index - ratio of calf EMG relaxed (mid to dorsiflexion) to active (mid to plantarflexion). Compared stroke to normal controls	Calf coactivation in 10 of 15 subjects. Those with coactivation were more likely to respond to FES
Canning et al. 2000	Stroke N=16 1yr+ Normal controls N=10	Elbow	Elbow rig; sEMG	Semi-random tracking with 50˚ elbow flexion and extension	Cross Correlation and spectral analysis	Only 2 of 16 subjects had coactivation in both slow and fast tracking
Fellows et al. 1994	Stroke N=25 9m+ Normal controls N=15	Elbow	Elbow rig with pulley and weight system, sEMG	Tracking with 90˚ flexion extension at 100º/s, 200º/s, 300º/s, without resistance and resisted at 1.27 and 3.2 Nm. MVC at 90˚	Biceps /triceps IEMG for total activation, and activation prior to peak velocity as % of total. Compared stroke group with normal group.	Increased antagonist EMG during extension in one group of subjects (n=7), without load at low speeds.
Hu et al. 2007	Stroke N=7 1yr+	Elbow and Sh	Elbow rig (robot), sEMG	Robot-assisted tracking training of 90˚ elbow flexion / extension at 10˚/second.	Overlapping activity of normalised biceps /triceps, anterior / posterior deltoid IEMG	Coactivation increased during early training and significantly decreased by end of training
Lamontagne et al. 2000	Stroke N=30 <6m Normal controls N=17	Ankle	sEMG	Walking at preferred speed for stroke and slow speed for control participants	Overlapping activity of tibialis anterior and gastrocnemius (above 20 µV threshold) divided by duration of gait phase	Less coactivation on paretic side in single support, more coactivation on non-paretic side in double-support
Gowland et al. 1992	Stroke N=44 subacute; normal controls N=10	Sh and elbow	sEMG + movement analysis	6 Chedoke-McMaster stroke assessment tasks undertaken	Mean amplitude EMG of agonist and antagonist, compared those who could and couldn't achieve tasks with control group	No significant difference in antagonist activity between groups
Turk et al. 2008b	Stroke N=10 1yr+; Normal Controls N=12	Wrist	Wrist rig; sEMG	60˚ sinusoidal tracking task at 0.5Hz	Flexor Modulation Index - ratio of wrist flexor EMG relaxed (mid to full extension) to active (mid to full flexion). Compared stroke to unimpaired	No significant different between groups

During both isometric and isokinetic contractions						
Authors	**Sample**	**Joints**	**Measurement Tool**	**Description of method**	**Method of analysis**	**Outcome**
Davies et al. 1996	Stroke N=12 Normal controls N=12	Knee	Isokinetic dynamometer	Isometric and isokinetic MVC flexion and extension	RMS EMG activity of biceps and rectus femoris normalised by MVCmax. Compared stroke to normal controls	Coactivation was low or absent and similar between groups
Kamper & Rymer 2001	Stroke N=11 2yr+; Normal controls N=6	Fingers MCP joints	MCP Rig; sEMG	MVC; resisted flexion + extension, extensors - eccentric contraction during flexion, concentric contraction during extension; Non-resisted extension	Mean EMG of agonist and antagonist in flexion and extension, and compared stroke and normal control groups	Significantly greater normalised flexor and 1st dorsal interosseous EMG activity in stroke than control group

2.8. Muscle onset timing

Altered timing of muscle activation, such as delayed onset has been shown to relate to functional activity of the hemiparetic upper limb (Chae et al. 2002a; Hughes et al. 2010a; Wagner et al. 2007).

2.8.1. Pathophysiology of delayed muscle onset timing in stroke

Onset of muscle activation in stroke can be attributed to lesions causing specific impairments in three components of a simple motor task: signal detection, motor processing and selection of motor strategy, and task execution. Motor processing is mediated by the posterior parietal cortex and premotor areas, whereas selection of motor strategy and motor execution are mediated by the primary motor and premotor areas (Ghez 1991). However, the final motor output among stroke survivors can be modulated by changes in descending and propriospinal excitatory and inhibitory inputs into the spinal interneurons and alpha motoneurones (Cohen 1999) as well as neuroplastic changes consequent to brain injury (Nudo and Friel 1999).

2.8.2. Methods of determining muscle onset

Onset of muscle activation is commonly evaluated in both impaired and unimpaired movement and posture, though no standard method of determination of muscle activation onset is used in the literature. Furthermore, due to the random characteristics of the EMG signal, onset determination is prone to false detection, especially when the signal-to-noise ratio (SNR) is very low i.e. conditions where the surface EMG response is weak, subjects themselves have little EMG activity or there is high level background noise. Visual determination may be used; however this is subjective, dependent on the assessors experience and skill, and has shown to have poor inter-rater reliability (Di Fabio 1987). One study, however, suggested that using an experienced assessor, visual determination was highly repeatable between assessments(Hodges and Bui 1996), and this method has been used to determine EMG onset in the stroke literature (Chae et al. 2002a).

Computer analysis may increase the objectivity of onset determination, reduce observer bias and be less time consuming(Di Fabio 1987), though there is little agreement regarding the most appropriate method. Techniques referred to as single-threshold methods are based on the comparison of the rectified raw signals and an amplitude threshold whose value depends on the mean power of the background noise (Di Fabio 1987; Hedman et al. 1997). To improve detection accuracy more advanced techniques have been proposed such as generalised-likelihood ratios (Micera et al. 1998), statistical methods based on double-threshold detection (Bonato et al. 1998), wavelet template matching (Merlo et al. 2003), and more recently a Teager–Kaiser energy operation method (Li et al. 2007). These methods, however, are computationally intense and thus beyond the scope of this project. Furthermore

using these methods good detection analysis is often possible only when *a priori* knowledge of the processed signal is known or correctly estimated, which is limited for this application. A further advance of the techniques proposed to detect EMG activity is in the direction of a local analysis of the signal (Khalil and Duchene 2000). Global properties are replaced by local properties, whose degree of change is measured on the basis of their recent values. This approach leads to an increase of accuracy, since the threshold level can be more precisely and adaptively set.

Other methods compare a low-pass filtered version of the rectified signal (the signal envelope) with a threshold based on the noise related (baseline) envelope(Hodges & Bui 1996). This method has an advantage in that it requires relatively uncomplicated processing algorithms, but is criticized for not being based directly on the raw (i.e. physiological origin) of the signal. Furthermore if the time delay introduced by the filtering is not taken into account a methodological bias will result. Differing criteria for the algorithms have been used in the literature to determine onset, such as the degree of smoothing the EMG signal (the frequency of the low pass filter (LPF)), the width of the sample window (in ms) for a moving average filter (MAF), and the magnitude of the deviation from the baseline required to indicate a threshold (number of standard deviations (SD)). An EMG study of unimpaired subjects performing arm movements compared the relative accuracy of a variety of these criteria for the computer determination of EMG onset against visually determined EMG onsets from the rectified raw signal (Hodges & Bui 1996). They showed that the LPF/SD/MAF parameter combinations of 50Hz/3 SD/25ms and 50 Hz/1 SD/50 ms respectively did not significantly vary from visually derived data for both subject groups divided by low background activity (high SNR) and high (low SNR). This method is therefore proposed for the current research, and different parameter combinations, as well as the use of global versus local baseline, will be evaluated against visual determination of EMG onset.

2.9. Non-neural stiffness and contracture

2.9.1. Pathophysiology of stiffness

The resulting hemiparesis and emerging spasticity from a CNS lesion causes limbs to be immobilised with muscles in a shortened position, which leads to stiffness and contracture. The increased stiffness experienced when stretching a limb of patients with spasticity can be attributable to 1) an increase in the stiffness mediated by the stretch reflex (neural response), 2) an increase in the intrinsic stiffness (muscle fibres contracting prior to stretch), and 3) an increase in the passive stiffness of tendons joints or muscles (Sinkjaer and Magnussen 1994). The non-neural (or non-reflex) stiffness in response to passive stretch is the sum of the intrinsic and passive components. The biomechanical changes that contribute to stiffness

are loss of sarcomeres and accumulation of intramuscular connective tissue and fat (Gracies 2005a). Another possible cause of muscle stiffness is thixotrophy. This term has been applied to substances which can be changed from gel to solution after being stirred. Muscles behave as a thixotrophic substance which is thought to be due to the formation of titin filaments in the relaxed muscle (Vattanasilp et al. 2000). This can be seen clinically with stroke patients when resistance to passive movement is initially increased when a paralysed limb has been sustained for some time in a shortened position, but decreases after stretch. When tested at the ankle joint, however, patients with spasticity after a stroke did not exhibit any higher thixotrophic response than neurologically normal subjects, suggesting that although thixotrophy may produce enough immediate resistance to impede movement in those who are very weak, it is not a substantial contributor to long-term muscle stiffness (Vattanasilp et al. 2000).

2.9.2. Measurement of non-neural stiffness

When measuring spasticity it is important to distinguish the reflex (neural) contribution to resistance to passive movement from the non-neural contribution due to biomechanical changes in muscles tendons and joints. Researchers have used different methods to make this distinction. Sinkjaer and colleagues measured total torque (sum of neural and non-neural torque) around the ankle joint during a voluntary contraction and non-neural torque during a contraction elicited by electrical stimulation of the tibial nerve which eliminates the stretch reflex (Sinkjaer et al. 1988; Sinkjaer et al. 1993; Sinkjaer & Magnussen 1994). Other researchers have investigated stiffness by measuring perturbations at various joints and used a complex model, described as a parallel-cascade, non-linear system identification technique, to separate overall stiffness into neural and non-neural components (Kearney et al. 1997; Mirbagheri et al. 2001; Mirbagheri et al. 2007). Another study (Kamper et al. 2003) measured stiffness at the metacarpophalangeal (MCP) joints of the fingers before and after administration of a local anaesthetic, blocking the median and ulnar nerves at the elbow. The anaesthetic was administered to reduce the activity of the muscles flexing the MCP joints, in order to distinguish mechanical from neuronal resistance to imposed MCP rotation. These methods measure and distinguish between neural and non-neural components in the same or matched conditions, however, they are complex and difficult to replicate in terms of practicality in a clinical setting.

Other researchers have distinguished non-neural torque from total torque using different speed conditions as the stretch reflex is not apparent at very slow speeds. Non-neural stiffness during extension was measured at the wrist joint (Pisano et al. 2000), with the fingers strapped in flexion around a handle, by ten repeated 50˚ passive range displacements in a torque motor controlled rig using constant velocity movements at 10˚/second. Only19 of

the 48 subjects were included for analysis as they exhibited no flexor EMG activity during the test. An intrinsic stiffness index was derived by calculating the slope of a torque angle regression curve, and statistically significant differences were found between unimpaired and impaired groups.

In our preliminary testing with the Southampton wrist rig, we measured non-neural stiffness during extension using manual slow passive displacements with range and speed controlled by tracking a target with a 0.04Hz sinusoidal waveform. The force angle index (FAI) was derived as the slope of an average force-angle curve calculated over the angles of 0˚ to 30˚ wrist extension. Unexpectedly, however, there was considerable overlap of FAI values between the impaired and unimpaired groups with no statistically significant difference. Although samples were examined during the test to ensure that there was no EMG activity, more detailed inspection of the EMG showed that in spite of clear instructions and encouragement, some subjects appeared to be unable to entirely avoid any flexor and extensor muscle activation in phase with passive wrist movement, which may have contributed to the large overlap in FAI between unimpaired and hemiplegic subjects.

To account for thixotrophy when measuring stiffness, using a ramp and hold method may be better than a constantly moving sinusoidal movement. It may be important to perform more than one displacement and calculate an average stiffness value. Prior to the test being carried out it may be important to control the number and range of stretches applied to the wrist for each subject.

This literature review has so far identified key motor impairments and identified and critically appraised methods of measuring these. The section that follows describes the tool that has been used in Southampton to neuromechanically measure motor impairments in the hemiplegic upper limb.

2.10. Tool used to measure upper limb motor impairments

There are a variety of different ways to measure motor control and other impairments of the upper limb after stroke. The choice of measurement method may include: the use of kinematics (movement analysis), accelerometers or other movement sensors, EMG, angle and torque sensors; measurement of multi-joint movement that is free and un-supported (Zackowski et al. 2004), or supported in a rotatory jig or robot (Hughes et al. 2010a); or measurement of single-joint movement in a rig designed for that joint (Kamper & Rymer 2001; Turk et al. 2008b). In this research, measurement of single-joint movement through the use of EMG and angle and torque sensors was used. This was because we thought that

neuromechanical methods would provide a better understanding of the underlying neural and biomechanical mechanisms that affect people post-stroke. Multi-joint movements were not chosen because, although they are closer to functional activity, the variability in movement is more than in uni-joint movement which adds to the already considerable variation in EMG.

It was therefore decided to use a wrist rig that had been previously researched by our group. In a small preliminary validation study, we used the wrist rig and active and passive sinusoidal tracking tasks to develop neuromechanical measures of motor control (sinusoidal tracking accuracy), muscle activation patterns (modulation of the flexors during active sinusoidal tracking), weakness (maximal voluntary isometric force), spasticity (reflex response to fast passive stretch), and non-neural stiffness (force angle relationship to slow passive stretch) (Turk et al. 2008b).

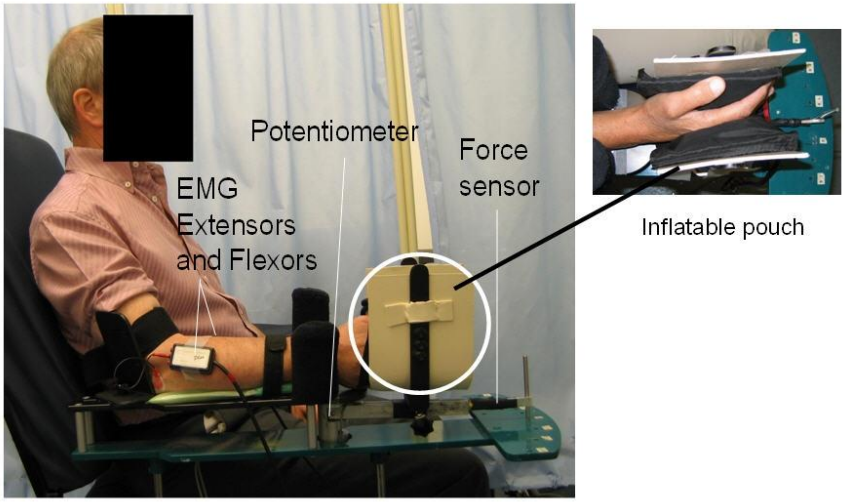


Figure 2-3: The version of the wrist rig that was used in the previous validity and FES studies (Turk et al. 2008a; Turk et al. 2008b)

The impairment measures were evaluated for reliability, sensitivity to distinguish between people with and without stroke induced hemiplegia (Turk et al. 2008b), and relationship with upper limb activity (Burridge et al. 2008). The within session test-retest reliability was excellent for these measures in the impaired group (ICC = 0.88-0.98) and Bland-Altman statistics showed no bias between two assessors for interrater reliability. Of all the measures, the sinusoidal tracking index was found to relate most closely with upper limb activity ($r=0.710$, $p=0.003$, and 56% of the variance in the Action Research Arm Test (ARAT) score). The wrist rig was then used as tool to measure impairment changes in a clinical study testing the feasibility of implanted microstimulators to improve upper limb functional activity post-stroke (Turk et al. 2008a). It was found that the sinusoidal tracking index and extensor muscle weakness were more sensitive measures of change than the ARAT.

2.11. Assessment of upper limb activity limitations

An extensive review of standardised upper limb functional activity measures was undertaken the aim of which was to choose the measure for this research according to set criteria. The search strategy was undertaken in two stages: firstly standardised upper limb functional activity measures were identified from a literature search and secondly each measure was assessed according to set criteria that were important to this study. Electronic databases were searched, including: Medline, CINAHL, AMED and EMBASE. The search strategy used the following keywords in combination: outcome measure$; upper limb / arm; function / activity; and with and without: Stroke / CVA; hemiparesis / hemiplegia. Other sources were reference lists from papers identified, books and book chapters. Table 2-2 shows the results of this review with the criteria listed on the left hand. The criteria that were thought to be most important for this research were:

- the measure is at the activity level and includes everyday tasks using whole arm reaching and hand manipulation of real life objects;
- there is both a scale of functional ability and a timing score;
- the measure has been used in stroke studies and is appropriate for elderly patients i.e. can be completed within 30 minutes;
- the measure is sensitive to differences in patients especially at the higher and lower levels of activity;
- construct validity and test-retest reliability have been tested and there is a correlation with an impairment measure.

Five measures which show the greatest fit with the criteria were short listed for the final decision: Action research arm test (ARAT), the arm motor ability test AMAT; the Wolf motor function test (WMFT); the CAHAI Chedoke Arm and Hand Inventory (CAHAI) and the Test d'Evaluation des Membres supérieurs des Personnes Agées (TEMPA).

The ARAT is quick to perform, the researcher of this thesis has been trained and is experienced in conducting this test, and the equipment is already available at the University of Southampton. However, the test contains some tasks more at the impairment level and does not have any everyday tasks using real life objects. The AMAT, CAHAI and TEMPA include tasks solely at the activity level. The CAHAI and TEMPA tasks however involve bilateral tasks and therefore do not focus on the ability of the impaired limb and therefore were not considered appropriate for this research. The AMAT is not appropriate as it takes too long to complete especially for older more frail patients. The WMFT, although it includes some tasks that could be considered more at the impairment level, it also has everyday tasks using real life objects that specifically test different grips and includes reaching at high and low levels, in sitting and standing positions. The modified WMFT (Whitall et al. 2006) is more

valid for use with moderately affected patients than the original and is more sensitive than the ARAT in that it includes easy and more difficult tasks with the same object. The functional scoring is more sensitive because there is 1 more point on the scale. The tasks are timed, with a set time if a task is not completed. Overall it was decided that the Modified WMFT should be chosen for the study.

Table 2-2: Review of upper limb functional activity measures

Criteria	ARAT (Lyle 1981; Platz et al. 2005)	Box and Block (Mathiowetz et al. 1985a; Platz et al. 2005)	AMAT (Chae et al. 2003; Kopp et al. 1997)	WMFT (Modified) (Morris et al. 2001; Whitall et al. 2006; Wolf et al. 1989)	CAHAI (Barreca et al. 2005)	SHAP (Light et al. 2002)	Jebsen (Hackel et al. 1992; Jebsen et al. 1969)	TEMPA (Desrosiers et al. 1995; Feys et al. 2002; Platz et al. 2001)	Frenchay Arm Test (Heller et al. 1987)	Motor Assessment Scale (Carr et al. 1985)	Nine Hole Peg Test(Mathiowetz et al. 1985b)
Impairment / Activity	Imp-> Activity	Activity	Activity	Imp-> Activity	Activity	Imp-> Activity	Activity	Activity	Activity	Imp-> Activity	Activity
Whole arm activity	✓	×	✓	✓	✓	×	×	✓	✓	✓ also LL and trunk	×
Hand manipulation	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓ also LL and trunk	✓
Real life objects/tasks	×	×	✓	✓	✓	✓	✓	✓	✓	✓	×
Timed	✓	✓	✓	✓		✓	✓	✓	×	×	✓
Functional scoring Scale (not Y/N)	✓	×	✓	✓	✓	×	×	✓	×	✓	×
Complete in <30 mins	✓	✓	×	✓	✓	✓	✓	✓	✓	✓	✓
Used with stroke	✓	✓	✓	✓	✓	×	✓	✓	✓	✓	✓
Construct Validity	✓	✓	✓	✓	✓ ARAT	×	✓	✓ ARAT	✓	✓FMA	✓
Test re-test reliability	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Standardised protocol	✓	✓	× not published	× not published	✓	✓	✓	✓	✓	✓	✓
Normal data	✓	✓	× not published	✓(unaffected side)		✓	✓	✓	N/A	✓	✓
Correlation with impairment measure	✓FMA / MAS / MI	N/A	✓ FMA	✓FMA	✓ CMSA	×not published	?	N/A	✓ Motricity Index	✓	?
Sensitivity at upper and lower limits	✓	N/A	✓	✓	✓	?	?	× lower limits	× lower limits	× lower limits	?

ARAT Action Research Arm Test; AMAT Arm motor ability test; WMFT Wolf motor function test; CAHAI Chedoke Arm and Hand Inventory; CMSA Chedoke-McMaster Stroke Assessment; SHAP Southampton hand assessment procedure; TEMPATest d'Evaluation des Membressuperieurs des Personnes Agee

2.12. The relationship between impairments and function – what we know so far

Historically it was assumed that spasticity was the major cause of activity limitations, and some therapeutic treatment approaches were based on the importance of reduction of spasticity. Recent studies, however, suggest that there is a poor relationship between spasticity and motor performance of the upper limb after stroke. Katz et al found a correlation between the upper limb Fugl Meyer assessment (FMA) score and elbow stiffness measured by ramp and hold tests (Katz et al. 1992), though the neural component was not distinguished from non-neural components, whereas no correlation was found between the FMA and stretch reflex measure using the H-reflex test. Others have also investigated spasticity at the elbow joint and found that although it contributed to contracture in the first four months after stroke, there was no significant contribution to motor performance measured using the upper limb tests of the motor assessment scale (Ada et al. 2006). This latter finding was corroborated in our preliminary study investigating impairments at the wrist, which found that both spasticity (stretch response) and non-neural stiffness did not relate to activity limitations measured using the ARAT (Burridge et al. 2008). As has been mentioned already (see coactivation section) there is a debate whether coactivation is related to spasticity and whether it is an important contributor to activity limitations, though it is clear that inconsistent timing of agonist and antagonist activation as well as delay in activation and termination may well be related to poor motor performance (Canning et al. 2000; Chae et al. 2002a).

Recent studies are suggesting that negative impairments may be more responsible for poor motor performance. Weakness, whether measured as torque (Ada et al. 2006; Burridge et al. 2008), or EMG activation (Chae et al. 2002b; Leonard et al. 2006), in particular has been found to be a major contributor to poor motor performance measured using the FMA (Chae et al. 2002b; Leonard et al. 2006) Arm motor ability test (AMAT) (Chae et al. 2002b), motor assessment scale (Ada et al. 2006) and ARAT (Burridge et al. 2008). Weakness has also been shown to contribute to reaching deficits, but more to velocity of upper limb reaching, whereas joint individuation (the ability to isolate flexion and extension movements at the wrist, elbow and shoulder) strongly contributes to variance in reach path and accuracy of end-point (Zackowski et al. 2004). Loss of dexterity measured using tracking tasks may also have a major contribution (Burridge et al. 2008), but less so than weakness (Canning et al. 2004). These studies included participants of wide age range but the mean age was 63 years or less. It is important to evaluate impairments in the older age group as patients with stroke are predominantly over 65 and it has been found that motor impairments may be affected by increasing age (Jagacinski et al. 1995).

2.13. Research questions

Through conducting the previous studies with the wrist rig as described in Section 2.10, further questions were raised related to the tests used, the indices derived from the tests, and the relationship between the impairment indices and functional activity, specifically:

- Would different forms of tracking tasks, such as those with more random waveforms, those using discrete rather than rhythmic sinusoidal movements, and those with some resistance applied, better characterise motor control dysfunction in post-stroke hemiplegia?
- Would different methods of measuring muscle activation patterns, in particular coactivation, provide more understanding of how spasticity affects active movement?
- What are the differences in the relationship of motor impairments to functional activity between the acute phase and chronic phase after a stroke?

It was these questions that informed the aims and objectives for this current research.

2.14. Aims and Objectives

The primary aim of this research was to advance understanding of the physiological and biomechanical mechanisms associated with normal and impaired function and recovery and the relationship between motor impairments and loss of activity in the upper limb of older adults, early and late post-stroke. The findings of the research were then used to make recommendations on measurement of impairments related to upper limb activity.

The objectives were:

1. Development of a system of measuring and characterising motor impairments using the instrumented wrist rig; including the development of appropriate signal processing and data analysis techniques.
2. a) Characterisation and derivation of indices for key elements of motor impairments at the wrist early and late after stroke;
   b) Evaluation of the validity impairment indices i.e. their ability to distinguish impaired from unimpaired and repeatability.
3. a) Evaluation of relationships between motor impairments grouped into negative, positive and secondary impairments early and late after stroke;
   b) Evaluation of the associations between motor impairments and motor control accuracy early and late after stroke;
   c) Evaluation of relationships between motor impairments and functional activity (using a standardised assessment of upper limb activity) early and late after stroke.

2.15. Hypotheses

2.15.1. Null hypotheses (H_0):

1. Negative impairments will not relate more to loss of functional activity than positive and secondary impairments, especially in acute participants.
2. Positive and secondary impairments will not relate to loss of functional activity in some individuals, especially in the chronic group.
3. Motor control accuracy and coactivation measures from step tracking (discrete movements) will not relate more to upper limb functional activity than the same measures from sinusoidal (rhythmic) tracking.
4. Negative impairments will not relate more with each other rather than with positive and secondary impairments
5. Positive impairments will not relate more with each other and with secondary impairments

2.15.2. Alternative hypotheses (H_1):

1. Negative impairments will relate more to loss of functional activity than positive and secondary impairments, especially in acute participants.
2. Positive and secondary impairments will relate to loss of functional activity in some individuals, especially in the chronic group.
3. Motor control accuracy and coactivation measures from step tracking (discrete movements) will relate more to upper limb functional activity than the same measures from sinusoidal (rhythmic) tracking.
4. Negative impairments will relate more with each other rather than with positive and secondary impairments
5. Positive impairments will relate more with each other and with secondary impairments

2.16. Summary

This Chapter has given a review to date of the relevant background literature related to this doctoral research. The neurophysiology of normal motor control has been considered, followed by a section on motor impairments of the upper limb post-stroke. Specifically, methods of measurement have been reviewed and critiqued, in order to inform the tests and impairment indices used for this research. The wrist rig, used in previous work as a measurement method, has been detailed. A review of standardised upper limb activity measures has been discussed, and has informed a decision regarding the most appropriate functional activity measure for this research. Lastly, a summary has been given of the literature which is found to date on the relationship between motor impairments and upper limb functional activity. The research questions and hypotheses, and more detailed aims and

objectives have been presented, which lead on to the methodology used in this research, which can be found in the following Chapter 3.

3. Development of the wrist rig

3.1. Introduction

This chapter describes the development of the wrist rig measurement system prior to trialling in the Pilot Studies Figure 3-1. The wrist rig was re-designed and re-built incorporating a new pivot joint system with the ability to add resistance, a new tracking target display and a new system for signal acquisition. Bench testing and calibration were carried out and safety tests passed. Using MatLab a novel human-computer interface software programme was developed; then new tracking tests were designed.

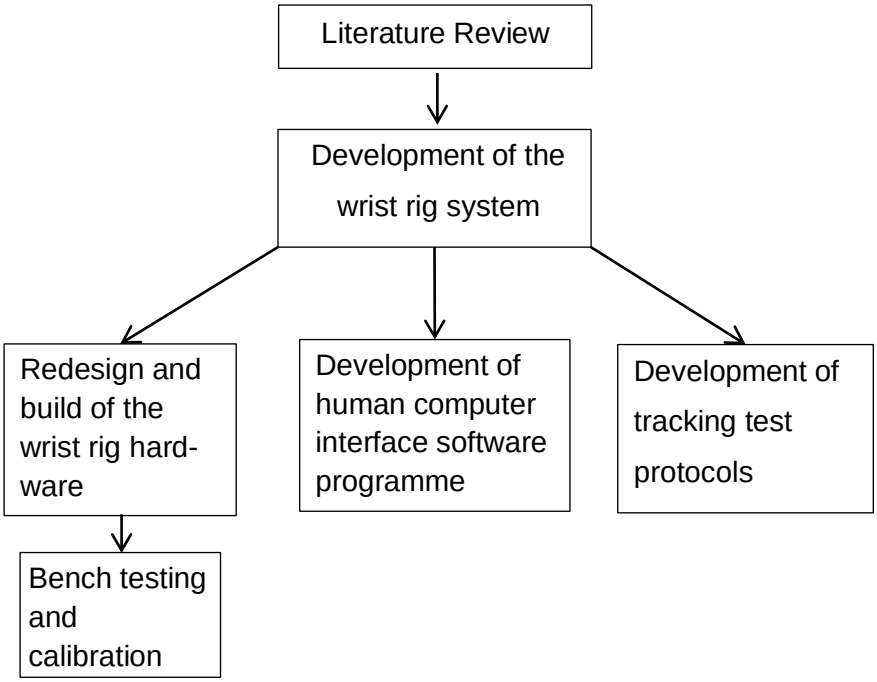


Figure 3-1: Flowchart to illustrate the initial development work undertaken on the wrist rig measurement system in preparation for testing with participants in the Pilot Studies.

3.2. Redesign and build of the wrist rig

The original wrist rig consisted of an instrumented arm rest attached to a chair, with a potentiometer (angle sensor) and strain gauges (force sensors) combined with electromyography (EMG) as described previously in the Literature Review Chapter 2, Section 2.10 and shown in Figure 2-3. The redesign described above was undertaken by collaboration between Ruth Turk (PhD researcher) and Dr David Simpson (ISVR Engineer and Supervisor) with advice from Prof Jane Burridge (Supervisor). Following extensive preliminary considerations of a) former designs, b) experience from previous related work, and c) cost and time constraints, a new design based around previous components was devised. The build was undertaken by ISVR technicians: a Mechanical Engineer Technician plus three

Electronics Engineer Technicians. This process involved a number of iterations of designs and test mock-ups, bench testing of new components and modifications to arrive at the final design. The main innovations included:

- **An LED array display designed for the tracking tests**: Previously the target was displayed as an ellipse on a computer screen placed at eye height and during the tracking test participants' wrist movement was represented on the screen as a cross (similar to the movement of a mouse on a computer screen). Thus, the previous tracking tests involved not only control of movement, but also, considerable visuo-perceptual demands and hand-eye coordination; all of which may be problematic for participants with stroke. In order to reduce the visuo-perceptual demands of the tracking tests, an LED display was fixed to the front the armrest; purposely placed so that participants could simultaneously watch the tracking target and see their hand moving. The LED array consisted of 80 LEDs placed on eight vertically mounted circuit boards, located on an arc from 80˚ flexion to 80˚ extension, one LED for every 2˚, as shown in Figure 3-2.

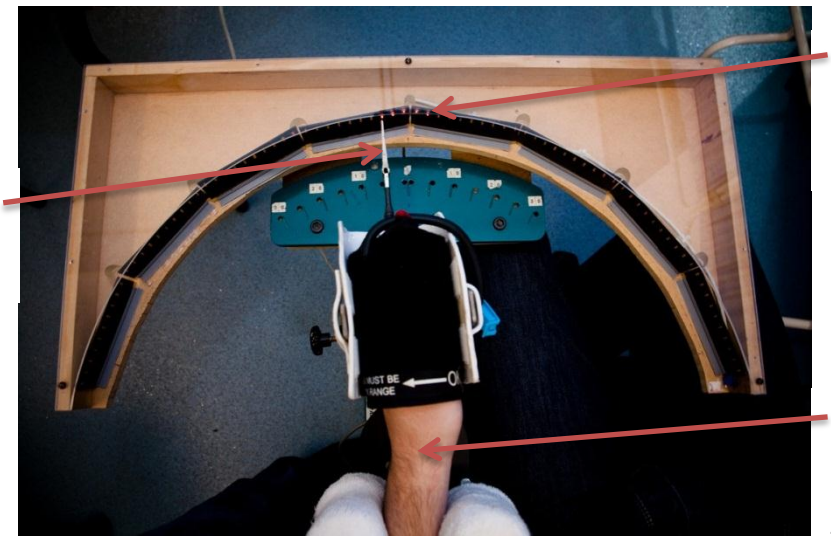


Figure 3-2: The LED display fixed to the front of the rig shown from above. The LED display consists of 80 LEDs (red when lit) placed on eight vertically mounted circuit boards, located on an arc from 80˚ flexion to 80˚ extension, one LED for every 2˚.

- **Development of four methods of hand positioning for pilot testing**: In our previous work, the wrist rig was designed with the hand supported by an air splint – an inflatable cuff within a U-shaped thermoplastic splint. Previous wrist rig designs in the literature have used a variety of finger positions from being held in flexion (Chae et al. 2002b; Yarosh et al. 2004), extension (Pandyan et al. 1997), or allowed to move freely (Kamper et al. 2006a; Pisano et al. 2000). Due to the close biomechanical relationship between the wrist and fingers, finger position was thought to be crucial when measuring a combination of motor impairments at the wrist. An adjustable foam covered handle, and a

thermoplastic full hand splint and palm splint, both of which were fixed to the handle, were developed to be compared with the air splint (see Chapter 4, Pilot Studies 2 and 3 for further details).

- **Development of a system to apply resistance to movement of the lever arm when required:** A commercially available slip clutch (Vari-Tork adjustable friction clutch, Huco Dynatork, Hertford, UK) was incorporated in the pivot joint, which, when turned 'off', allowed the pivot joint to be virtually friction-free, and which, when tightened, applied increasing resistance to the pivot joint.
- **Redesign of the pivot joint**: A new configuration for within the pivot joint mechanism was designed which allowed the slip clutch to be positioned at the bottom and the potentiometer for measuring angle at the top (Figure 3-3); rather than being located at the bottom, as previously designed. A new strain gauge arrangement was designed and built on a new pivot joint axle, in order to monitor changes in resistance applied by the slip clutch.

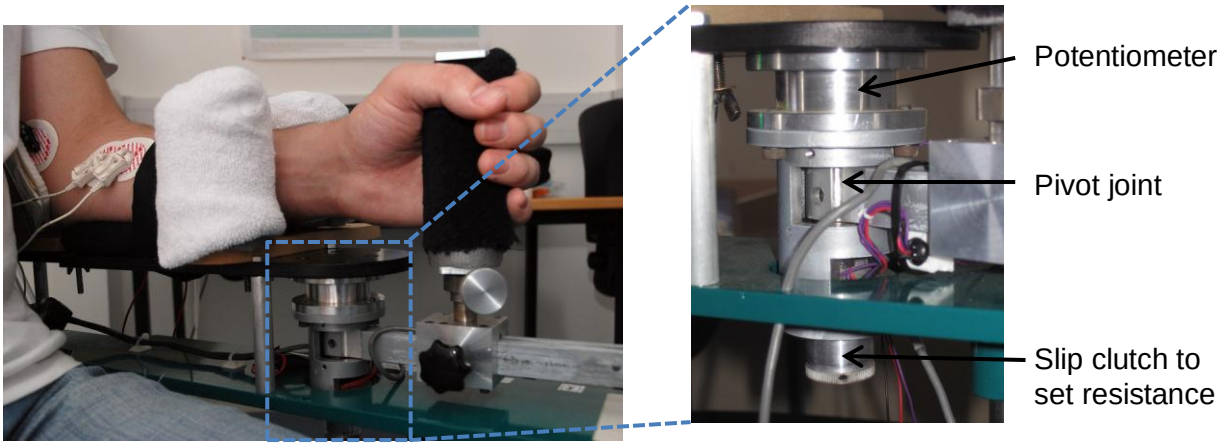


Figure 3-3: Configuration of the pivot joint mechanism

- **Development of electronics and connections for signal acquisition**: The EMG, strain gauges, potentiometer and LED display were connected to newly designed electronic circuits and housed in a box also containing A/D and D/A convertors (USB-1408FS and USB-1608FS, respectively, Measurement Computing, Norton, MA, USA) and a power supply (OFM100, Powerbox, Gnesta, Sweden). An optical USB link (Rover 200, Amplicon, Brighton, UK) provided an electrically isolated interface between the electronics box and the laptop computer (XPS M1330, Dell, Bracknell, UK) where the data is recorded and stored (see Wrist rig block diagram in Appendix A)
- **Development of a new elbow restraint, forearm support and strapping**: These restraints and support were designed to prevent movement of the elbow, upper arm and forearm during tests, so that movement and muscular effort was restricted to the wrist.

3.3. Bench testing and Calibration

In order to test the system and its outputs and calibrate the measurements, bench tests on the rig components were carried out by the researcher and Dr Simpson with the assistance of ISVR technicians. This process involved iterative testing, (modification and retesting) to ensure that the rig system and output data were valid and reliable. For details on the bench testing and calibration see Appendix B. The calibration coefficients for each output (angle, torque, EMG) were calculated and inserted into a customised Excel spread sheet (Appendix B, Table B1). This Excel spread sheet was read by the specially designed Matlab® wrist rig software when processing signals and representing signals on graphs in appropriate units of measurement (degrees/ Nm/ mV).

The calibration coefficients for most outputs remained stable throughout the duration of the project. However, the lever torque calibration coefficients were found to have changed following the pilot study. As these had remained stable through repeated assessments during the bench testing and calibration process, and changes to the pivot joint and electronics were also made following the pilot study, the source of the change in lever joint calibration was not clear. Because the accuracy of the calibration of this sensor was very important, it was decided to recalibrate before and after each testing session in the main study. As it became clear that the calibration coefficients were remaining stable, recalibration then occurred after every second testing session.

3.4. Safety testing

To ensure the wrist rig complied with medical safety standards, testing was carried out by an independent assessor at the Medical Physics and Bioengineering Department at the Southampton General Hospital. This initial test raised issues that could be partly corrected by ISVR technicians, but further specific advice was sought from Clinical Engineers at the Hospital to ensure compliance with the standard BS EN 60601-1. A final test was carried out and passed (30/3/2009).

3.5. Design and development of rig software programmes

3.5.1. Development of the human computer interface software programme

A new Matlab® software programme (Figure 3-4), easily adjustable for the needs of the system and application of new test protocols, was developed by Dr Oliver Baumann, a signal processing Engineer at ISVR, in close collaboration with the researcher (RT) and Dr Simpson.

The software was written in accordance with the testing protocol (Appendix C) developed by the researcher, informed by past experience and the literature review. This specified the tests to be included, and the parameters associated with, and signal outputs needed from, each test. The software was tested and modified iteratively until it was ready to be used for data collection.

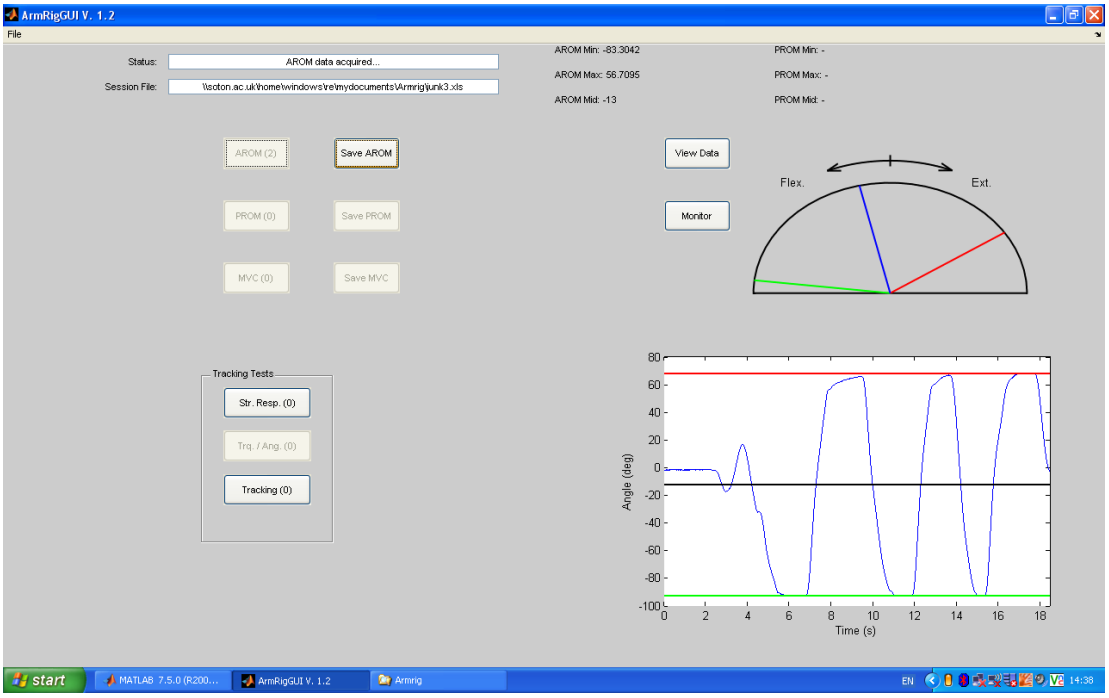


Figure 3-4: Software user interface showing the test programmes on the left and online signal display (in this case AROM test with flexion / extension ranges and mid-point) on the right

3.5.2. Development of the tracking tests

The tracking tests were either active, to measure motor control accuracy and muscle activation patterns, or passive, to measure spasticity or non-neural stiffness. The active tracking tests involved the participant pointing the lever arm, by flexing or extending their wrist, at a moving LED target (Figure 3-2), using a sinusoidal waveform for rhythmic movements and a random square waveform for discrete movements. In the passive tests, the assessor flexed and extended the participant's wrist in the rig to track the LED target. A range of possible tracking tests, with different specifications based on the intended measurement objective, were designed during this development phase and later evaluated during the Pilot Study phase (see Chapter 5, Section 5.3):

3.5.2.1. Active sinusoidal tracking (rhythmic movements):

Sinusoidal tracking, used in the previous studies with the wrist rig, was used, and employed a sinusoidal waveform (Figure 3-5) of ±20˚ displacement around the participant's midpoint of their active range of movement (AROM). The reason for using each individual's midpoint was because muscle function is maximal around the mid-range (Saladin 2004), and as each

participant's mid-range will vary (stroke participants are likely to be in more flexion than unimpaired participants), it is important that the tracking tasks are standardised to each individual. The frequency was set at 0.5Hz (both impaired and unimpaired participants in previous research have found this a moderately easy tracking speed) and 0.25Hz (a slower speed for training purposes).

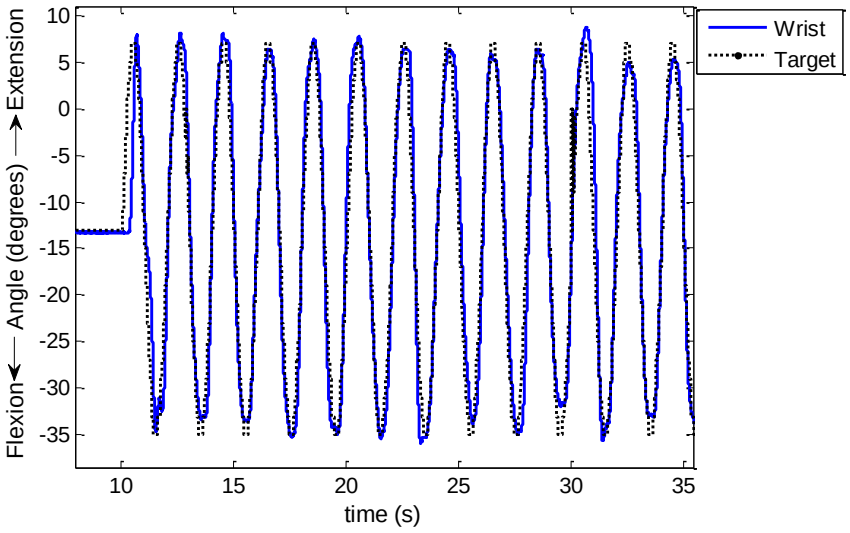


Figure 3-5 Example of unimpaired sinusoidal tracking at 0.5Hz frequency ±20˚ around the participant's midpoint (approximately 13º flexion) showing the target (black dotted) and unimpaired wrist movement (blue) signals.

3.5.2.2. Active step tracking (discrete movements):

The newly developed step tracking test used a square waveform (Figure 3-6). The target was visible as an individual LED lighting up at different positions on the LED array representing varied angles of displacement around a participant's midpoint of their active ROM and the target does not move during the plateau phase. The intention was that this would be a task demanding a higher level of voluntary engagement than sinusoidal tracking, where subjects may follow the rhythm and anticipate the target movement. Therefore both the time the LED stayed on (duration of the plateaus) e.g. between one and four seconds, and the displacement (step-size) changed randomly. The displacement was purposefully designed, starting with small ranges e.g. between 0˚ and 5˚ around the subject's midpoint, increasing in a series of 15 second blocks, up to ±40˚ (Figure 3-6) in order that stroke participants with low movement ability could at least perform the first part of the test, but that the last part of the test would be more challenging for those with higher ability. Different tests were designed with a variety of plateau phase times, ranges of displacement, and lengths of time blocks in order to determine the most appropriate combination of parameters. In the final protocol, all tests were carried out with an identical (random) sequence.

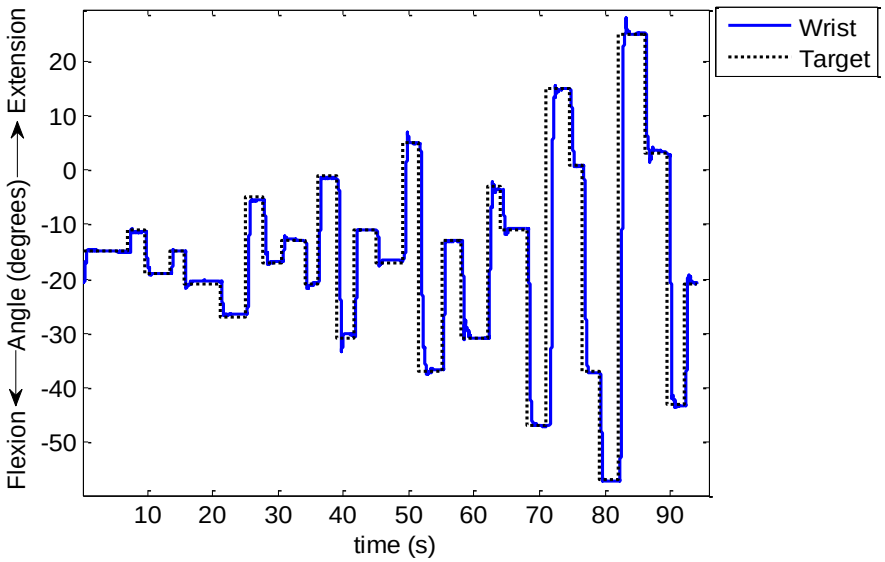


Figure 3-6 Example of square wave step tracking showing both target (black dotted) and unimpaired wrist movement signals (blue) with varying time intervals between steps and increasing displacement around the participant's midpoint. This is an unimpaired subject and the short delay in tracking is clearly evident.

3.5.2.3. Fast passive tracking (stretch response test)

A passive tracking test was developed using the same sinusoidal waveform of the active test at ±20˚ displacement around the participant's midpoint of active ROM but at a higher frequency (1.5Hz) to measure stretch response; the same frequency used in our previous studies (Turk et al. 2008a; Turk et al. 2008b).

3.5.2.4. Slow passive tracking (torque angle test)

A second passive test was developed to measure non-neural biomechanical stiffness around the wrist joint. This used a saw-tooth waveform (Figure 3-7), with ramps in angles from full passive flexion to full extension (taken from the passive range of movement test) at a constant velocity of 5˚/second, a hold of ten seconds at full extension and five seconds rest between repetitions. Full passive extension range was defined as the pain-free end-block reached at the end of a passive extension stretch. This protocol was based on previous research (Pisano et al. 2000). It should be emphasized again that, in the passive tasks, the experimenter guided the hand of the participant in accordance with the target.

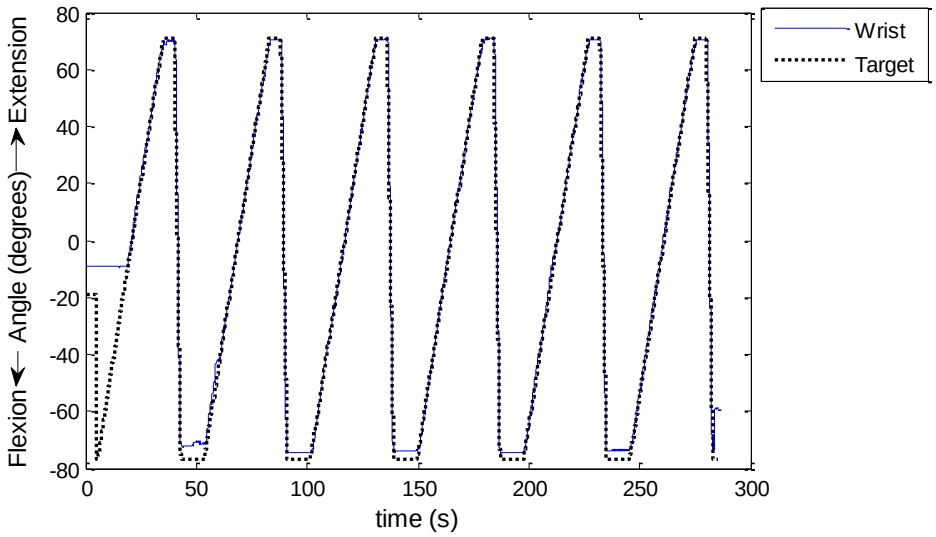


Figure 3-7 An example of slow passive tracking (torque angle test) using a saw-tooth waveform with ramps at 5˚/second over the full passive range of movement with a hold of five seconds at full extension and ten seconds rest between repetitions.

3.6. Summary and conclusions

This Chapter has detailed the development work undertaken prior to the start of wrist rig and functional activity tests with participants in the Pilot Study.

1. The wrist rig redesign and build involved much iteration before bench testing was completed and safety tests were passed. It involved a number of new innovations, was more extensive and complex than originally expected and took up the first year of the research project (from April 2008 to March 2009). However it was critical that the wrist rig was 'fit-for-purpose' to ensure the validity of the data generated and therefore the usefulness of the research.
2. The new software user interface using Matlab software was more flexible, and enabled easier adjustment as new tools facilities were required, and for the application of new tests.
3. New tracking tests requiring a higher level of voluntary engagement were designed and written in MatLab code.
4. At the end of this phase the system was ready to be piloted with participants in the Pilot Studies which follow in Chapter 4. The aim of the pilot work was to optimise the design of the rig, to test the methodology of data collection proposed for the Main Study, and to develop and evaluate methods for deriving the impairment indices.

4. Methodology

This chapter presents the methodologies used in the Pilot and Main Studies. The study design, participant samples, confounding factors, clinical assessments, wrist rig testing protocol, modified Wolf motor function test protocol, impairment measure indices, and statistical analyses are described and justified.

4.1. Study design

An observational measurement design was used in both the Pilot and Main Studies. The Pilot Studies, with impaired participants in the chronic stroke phase and unimpaired participants, involved one testing session comprising wrist rig tests (see Section 4.8) and the modified Wolf Motor Function Test (mWMFT) (Section 4.10). Repeated measures were taken in the rig to trial tests with different parameters (such as frequency of target tracking movements and range of displacement), and to test the effect of different hand supports (see Pilot Studies Chapter 5 for further details).

The Main Study was a cross-sectional observational study, with impaired participants in the acute and chronic phases post-stroke (see Section 4.4.2, selection criteria). It involved two testing sessions for most participants. The first session comprised practice runs with the active wrist rig tests, followed by an assessment with these tests and also the mWMFT, and in the second session both the full wrist rig protocol (active and passive tests) and the mWMFT was completed. For the convenience of participants who were able to complete the full-testing protocol in a single session, testing was only conducted on one day.

4.2. Study sites

4.2.1. Pilot Studies

The Pilot Studies were predominantly conducted at the University of Southampton and, for some unimpaired participants, at a Farnham University of the Third Age (U3A) site in Surrey. Unimpaired participants were recruited from the Faculty of Health Sciences staff working within the ARM (Activity Rehabilitation and Measurement of the upper limb) research programme (age under 60), and from a local Southampton Church and the Farnham U3A group (age over 60). Impaired participants were recruited from the Faculty of Health Sciences' Participant Register.

4.2.2. Main Study

Testing for the Main Study took place at four sites: in the Therapy departments of the Western Community Hospital in Southampton, Milford and Farnham Community Hospitals in Surrey and at the ARM research laboratory at the University of Southampton. Recruitment of

acute and chronic impaired participants was from two NHS centres: a community-based stroke service in Southampton (Solent NHS Trust) with a 25-bedded stroke unit, community and outpatient neurological therapy services; and community stroke services in South-West Surrey (Surrey Community Health) which comprises two inpatient stroke units, community and outpatient stroke therapy services and two day hospitals. For the chronic group, participants were also recruited from the Faculty of Health Sciences' Participant Register.

4.3. Ethics and Research Governance approval

Ethical approval for the Pilot Studies was given by the Faculty of Health Sciences Ethics Committee (SoHS-ETHICS 08-002), and sponsorship and insurance approval from the University of Southampton Research Governance Office. The Main Study was granted ethics approval by the Southampton and South West Hampshire Research Ethics Committee (Reference number: 09/H0504/21). This study gained research governance approval from the two NHS sites: Solent NHS Trust and Surrey Community Health; and sponsorship and insurance approval from the University of Southampton Research Governance Office (see Appendix D).

4.4. Study Sample

4.4.1. Sample size

This exploratory study examined a large number of impairment variables, relationships between them and a functional activity measure; we did not therefore have a primary outcome measure on which to estimate sample size. However, using data from the previous wrist rig development study (Turk et al. 2008b) with 10 unimpaired participants and 10 participants with hemiplegia following stroke, a power calculation was made based on the between group difference for one impairment measure. Taking motor control, measured by the sinusoidal tracking index, as the example impairment measure, (unimpaired mean = 192.6, impaired mean = 120.4) and the larger standard deviation (66.3), it was calculated that, to detect a difference between groups, fourteen participants per group were required to achieve an 80% power in a 2-sided 5% test. To allow for drop-out, non-compliance and anticipated smaller between group differences for other impairment measures, it was planned that 20 acute stroke participants, 20 chronic stroke participants and 20 age-matched unimpaired older adults would be recruited for the Main Study.

4.4.2. Recruitment and selection criteria – impaired and unimpaired participants

For recruitment of the Pilot Studies participants, convenience sampling was used, the advantage being that participants were easy to recruit, near at hand and likely to respond (Bowling 2002). For recruitment of impaired participants to the Main Study, a pragmatic,

clinically-based approach was used. Impaired participants were recruited into two groups: i) acute – stroke was between 2 and 17 weeks prior to recruitment (as most recovery occurs up to 4 months post-stroke in 95% of even the most severe strokes (Jorgensen et al. 1995)) and ii) chronic – stroke was more than one year prior to recruitment, as used in other studies (Canning et al. 2000; Kamper et al. 2003). For the acute group, consecutive sampling was used over a period of eight months for the three NHS centres, the advantage of this being ease of recruitment and retention of sample participants (Bowling 2002). Participants were identified by therapy staff as being suitable for the study, invited by their therapist to take part and given a participation information sheet (see Appendix I). For the chronic group, all discharged patients from the three centres over the previous two year period (2008 – 2009), who fit the selection criteria were identified by therapy staff through their patient records, and were sent an invitation and information sheet by letter from the lead therapist of the stroke service. invited to take part. A further convenience sample was recruited from the Faculty of Health Sciences participant database. These participants were identified by the database Manager and invited by letter or e-mail to participate. Those who expressed an interest in participating to their therapist or the researcher were recruited following an interview with the researcher (either in person or over the phone) with an explanation of the study and the opportunity to ask questions. Informed consent was obtained and documented by the researcher.

The validity and reliability of the findings is enhanced by the fact that the recruitment of patients was from two sites – Southampton and Surrey. Expanding the recruitment to further sites was not feasible within the scope of this project.

The selection criteria for the impaired group for both studies were as follows:

Inclusion criteria

1. Diagnosis (MRI/CT scan) of first stroke
2. Between 2 and 17 weeks (four months) post-stroke (acute group) or over one year post-stroke (chronic group)
3. Aged 60 or over (for the main study)
4. Upper limb movement deficit: with a minimum of some perceivable activity in the wrist (at least 5˚ active flexion/extension movement in the rig), with a maximum of some remaining gross movement deficit i.e. those with only hand dexterity problems were excluded
5. Able to transfer to a chair either independently or with the assistance of one person
6. Informed written consent.
7. Participants with all levels of spasticity, including those on antispasticity medication

Exclusion criteria

1. Upper limb sensory, perceptual or movement deficits attributable to non-stroke pathology;

2. Unilateral visuo-spatial neglect (star cancellation test score less than 51 (Wilson et al. 1987)) or other, non-corrected, visual deficits likely to compromise ability to attend to the tracking target;
3. Skin allergy to alcohol wipes and sticky tape;
4. Medical, psychological, language or cognitive impairment that, in the opinion of the treating therapist and/or researcher would compromise ability to undertake the testing protocol.

Unimpaired participants were selected if they were age 60 or over (for inclusion into Pilot Study 3 and 4 and the Main Study) and without any neuromusculoskeletal condition that impaired movement of their dominant arm, and visual deficiencies that were not corrected by contact lenses or glasses.

4.5. Confounding factors

A confounding factor can be defined as an extraneous factor (a factor other than the variables under study), not controlled for, which distorts the results (Bowling 2002). Possible confounding factors that were identified in this research were:

- Age
- Gender
- Hand dominance
- Side of cortical stroke
- Current and previous use of anti-spasmodic medication
- Sensory deficit (loss of proprioception)

The data for all these factors was collected at baseline and recorded. These characteristics are detailed in the Results Chapter Main Study Chapter 6, Table 6-1, and will be considered further in the Discussion Chapter 7. In the Main Study, age was controlled for to a degree by the inclusion of participants only over 60 for both the impaired and unimpaired groups. It was recognised that gender may have an effect on impairment measures such as muscle strength between the impaired and unimpaired groups but was more difficult to match due to the practicalities of the study.

4.6. Clinical assessments undertaken at baseline

Two clinical assessments were undertaken with impaired participants prior to data collection with the wrist rig and the functional activity test.

4.6.1. Neglect

Cancellation tests are paper and pencil tests that measure neglect in peri-personal space. Participants with a history of unilateral neglect were tested using the star cancellation test (Wilson et al. 1987). If a participant scored less than 51 stars cancelled during the test (which indicates presence of unilateral neglect) they were excluded from the study.

4.6.2. Spasticity

The Tardieu scale was used in this study to clinically assess the level of spasticity at the wrist joint because it is the most valid and reliable scale available (see Literature Review Chapter 2, Section 2.6.1.1. The specific protocol used for this study was based on that described by Morris (Morris 2002) and is shown in Appendix E, Table E-1.

4.6.3. Proprioception

Although the focus of this research is motor impairments, the prevalence of somatosensory deficits after stroke is as high as 35-60% (Carey 1995) and the somatosensory system has an important role in motor control, and could be considered a confounding factor. Proprioception sensation was tested at the wrist joint using a protocol described in a recently revised version of the Nottingham Sensory Assessment (Stolk-Hornsveld et al. 2006) and is described in Appendix E, Table E-2.

4.7. Protocol for data acquisition in the wrist rig

The following protocol was common to the Pilot and Main Studies.

EMG protocol:
Participants were seated comfortably in the chair and the skin of the forearm was rubbed with an alcohol wipe. Two pairs of active surface EMG electrodes (Biologic snap electrodes, Biosense Med Ltd) were applied with skin preparation according to standard guidelines (Hermans et al. 1999) with an inter-electrode distance of 1.5 cm. The flexor (flexor carpi radialis (FCR)) EMG electrodes were positioned on a line from the medial epicondyle of the elbow to the FCR tendon at the wrist, 7-9 cm distal to the medial epicondyle (Leis and Trapani 2000). The extensor (extensor carpi radialis longus) EMG electrodes were positioned on a line from the lateral epicondyle of the elbow to the 2nd metacarpal, 5-7cm distal to the lateral epicondyle (Leis & Trapani 2000) (Figure 4.1). Reference electrodes were placed over the medial and lateral epicondyles of the elbow. The electrodes were held in firm contact with the skin using tape. EMG signal quality was checked visually in every subject by testing for clear evidence of an EMG response to voluntary muscle contractions of flexor and extensor.

Positioning of participants:

The hemiplegic arm of impaired participants was tested, whereas the dominant arm was tested for the unimpaired group. This was because it was considered important to measure 'best performance', and thus a more consistent unimpaired reference value was obtained. Furthermore, due to the practicalities of the study, it was difficult to match the hemiplegic and unimpaired participants in terms of hand dominance. The set-up of the rig can be seen in Figure 4-2 4.2. The arm to be tested was placed on the armrest and the forearm supports were adjusted for the correct height so that the shoulder was relaxed. With the wrist positioned over the pivot point, the forearm was strapped onto the arm rest and the upper arm strapped to an elbow restraint positioned behind the elbow so that the arm was held firmly but comfortably.

EMG electrode positions for flexor carpi radialis

EMG electrode positions for extensor carpi radialis

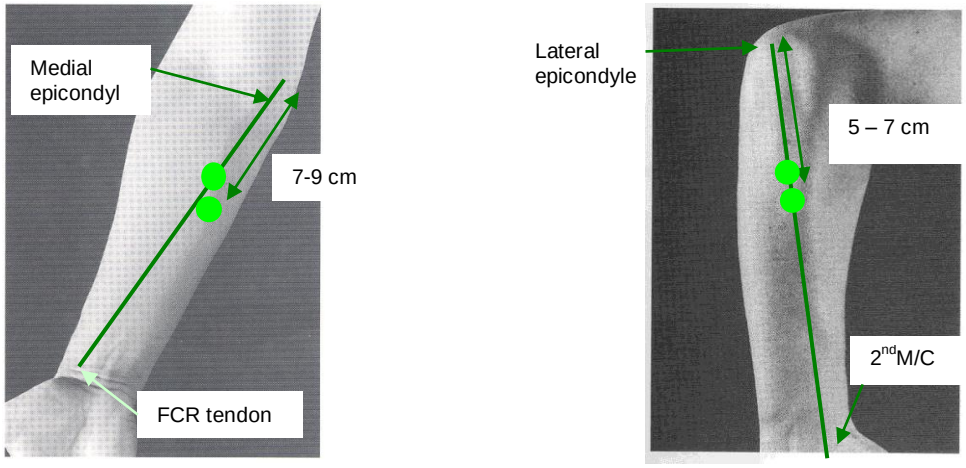


Figure 4-1 Positions of the wrist flexor and extensor EMG electrodes

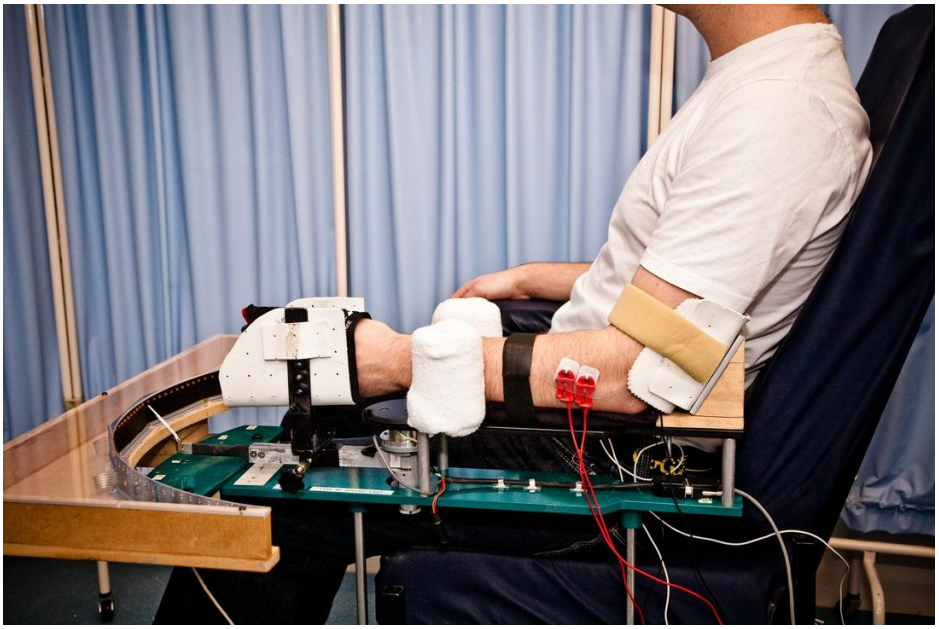


Figure 4-2: The wrist rig with participant positioned ready for testing

4.8. Wrist rig testing procedure

The following tests were performed in the rig. Further details of how the tests are performed are in Appendix C (Rig testing procedural protocol).

- Active range of movement (AROM): Three maximal active flexion and extension movements from which the active mid-point is also calculated.
- Passive range of movement (PROM): Three maximal passive flexion and extension movements conducted by the assessor. End of passive extension range was defined as the point where resistance from tissues increases either to a block or where further movement is difficult but remains pain-free. In this research, PROM was measured in the hemiplegic wrist only, whereas others have quantified it using the intact side minus the hemiplegic side (Ada et al. 2006). Measuring the intact wrist was not considered practical in this study bearing in mind the number of other tests that needed to be completed within the data collection time.
- Flexion and extension maximal voluntary isometric contractions (MVC) at the 0˚ and 20˚ flexion position on the rig. The 0˚ position is commonly used in research and the 20˚ position was chosen as it was thought to be within the mid-range of active movement where muscle contraction is strongest (Saladin 2004). Three five second contractions were performed into extension and flexion (Canning et al. 1999; Chae et al. 2002b; Colebatch et al. 1986).
- Torque/angle test - slow passive ramp movements from full passive flexion to extension (defined from the PROM test) at 5˚/s, and hold at full extension for 5 seconds, and rest at full flexion for 10 seconds.
- Stretch response test - fast passive sinusoidal movements with ±20˚ displacement around the active mid-point at 1.5 Hz, and ±5˚ at 3.5Hz, to calculate the stretch response at a high velocity, and ±20˚ 0.5 Hz to compare passive stretch response with muscle activation during the active sine tracking task
- Active tracking tasks without resistance then with resistance set at a percentage of participants' extension MVC force
    - sinusoidal tracking
    - step tracking

  Prior to the final performance, participants practised each tracking task until they reached their maximal performance (3 to 6 practice sessions depending on the participant's ability and their rate of learning).

4.9. Data Processing

The EMG signals were amplified and low pass filtered (2nd order, with a cut-off frequency of approximately 500 Hz) and digitized (1608FS, Measurement Computing, Norton, MA, USA) at a sampling rate of 2000 Hz. All the signals were acquired simultaneously to the laptop

computer which also controlled the target, using the customized software program developed in Matlab® (Natick, MA, USA). The angle and flexor and extensor EMG and torque raw data were analysed visually to check for subjects' compliance with the protocol, noise and artefacts. All signals were decimated reducing the sampling rate from 2000Hz to 200 Hz (following anti-alias filtering with a third order Butterworth filter, applied in forward and reverse direction). For the EMG signals a notch filter was applied to remove 50Hz mains noise and its harmonics. The flexor and extensor EMG envelope was then extracted by first removing the mean from the signals, and then rectification and smoothing (Butterworth low pass filter, 5 Hz cut-off, applied in the forward and reverse direction to cancel phase-shift). The cut-off frequency was chosen based on visual analysis of the signals, and a best compromise between smoothness and time-resolution.

4.10. Modified Wolf Motor Function Test (mWMFT) procedure

4.10.1. Development of testing and scoring manual

The modified version of the WMFT (Whitall et al. 2006) was chosen for this research because it is more valid for use with moderately affected patients than the original. However, as there was no published protocol guidelines of the mWMFT, and as the researcher needed to learn how to administer and score the WMFT, a manual with clear testing administration and scoring guidelines was developed in collaboration with a research therapist based at the University of East Anglia. The authors of the Whitall et al (2006) study were contacted. Their study WMFT manual was received and reviewed and further clarity was sought from the authors where necessary. A further manual of the original WMFT that was found on the internet (iCSP neurology section) and which was written in 2000 by the Constraint-Induced Movement Therapy Research Group, (University of Alabama and Birmingham Veteran's Administration Medical Center, USA) and used in a reliability study (Morris et al. 2001), further informed the testing and scoring guidelines. The following additions to the mWMFT manual were made for this study (see Appendix F, WMFT instruction manual):

- A template was added for precise positioning of objects as well as a list of required materials and equipment,
- Standardisation of table height and chair position to each participant has been included with the aim of accommodating all sizes and heights of participants,
- Practise of each task first with the non-paretic arm was allowed (not included in previous guidelines),
- The instructions have been changed to UK English,
- Specific guidelines for each task on scoring have been added.

Lastly, the modified WMFT materials were prepared, and through the process of reviewing previous WMFT manuals and forming a new UK-based version, the researcher familiarised herself with the test prior to piloting with patients in Pilot Study 3 (Chapter 5, section 5.4).

4.11. Data analysis

4.11.1. Data management and storage

The signals recorded during the wrist rig tests were automatically saved as Matlab files on the laptop computer. After checking and pre-processing of the signal data as described in Section 4.9, indices were derived from the signals, as described in 4.11.2.2, and saved in Excel spread sheets on a password protected computer. Access to the data was restricted to the researcher, and when necessary for analysis, to the research team. All data on the computerised data sheets was coded without using participants' names to ensure anonymity. Data collected on case record forms also was coded to ensure confidentiality, and stored in a locked filing cabinet within the Faculty of Health Sciences building. Data from the Excel spread sheets were transferred to SPSS for statistical analysis see (Section 4.11.3.).

4.11.2. Derivation of indices

4.11.2.1. Introduction

In our previous research the wrist rig and sinusoidal tracking tests were used to develop neuromechanical measures of motor control (sinusoidal tracking accuracy), muscle activation patterns (flexor modulation index), weakness (MVC force), active range of movement, spasticity (neural response to passive stretch), and stiffness (force angle relationship to non-neural passive stretch). Using this experience, and knowledge from the literature review, common post-stroke motor impairments were identified which could be measured using the proposed tests conducted in the wrist rig (Table 4-1).

For some of these impairments, measurement is straight forward, for example weakness can be simply and adequately quantified by measuring force during a maximal voluntary contraction (MVC), and active range of movement by recording maximal angle. Measurement of other impairments, such as movement tracking performance and altered muscle activation, is more complex, as these are derived from angle and EMG signals recorded during controlled tasks, which require signal processing and interpretation. The tracking tests were undertaken with and without resistance. However, the system for applying resistance did not work as well as anticipated - the backlash was too big and the resistance was not 100% smooth across full angle (see Table 5-3 in Pilot Study Chapter 5). The resisted tracking data was therefore not included in the analysis.

Table 4-1: The motor impairments that were identified as important to measure in the wrist rig

Motor Impairments	Impairment measurement	Rig Test	Signals needed for measurement or index
Active range of Movement	AROM	AROM	Wrist movement angle
Passive Range of Movement	PROM	PROM	Wrist movement angle
Weakness	Isometric Force	Flexor and extensor MVC	Lever arm torque
Movement tracking performance	Overall tracking accuracy	Sinusoidal / Step Tracking	Target and wrist movement angle
	Accuracy at target end point	Step Tracking	Target and wrist movement angle
	Corrective overshooting at target end point	Step Tracking	Target and wrist movement angle
Muscle activation patterns	Coactivation	Sinusoidal / Step Tracking	EMG; target and wrist movement angle
	Muscle onset timing	Step Tracking	EMG; target and wrist movement angle
Spasticity	Neural response of flexor to passive stretch	Fast passive tracking	Flexor EMG; target and wrist movement angle
Non-neural stiffness	Non-neural resistance to passive stretch	Slow passive tracking	Lever arm torque; wrist movement angle

4.11.2.2. Calculation of the indices

The software to pre-process the data and calculate the indices from the signals was written by Dr D. Simpson in Matlab, in accordance with specifications provided by the researcher's (RT) review of the literature and clinical knowledge. The researcher then applied this software to the wrist rig signal data to extract the impairment indices. All the results were checked in accordance with visual inspection of signal plots. Where the analysis of the signals indicated the need for modifications in the indices, this was discussed jointly, considering relevant aspects of physiology and physiotherapy as well as signal processing, before specifying and testing the new indices. The researcher made minor modifications to the software (e.g. to provide different plots or change timing parameters) and also wrote part of the Matlab programme for calculating muscle onset timing.

4.11.3. Data entry

For all studies, the participant characteristics and measurement data was entered onto the SPSS (PASW v18) data sheet by the researcher who carried out all statistical analyses. All the data sets were examined using histograms or dot plots to identify any outliers that may have occurred due to incorrect data entry.

4.11.4. Checking for normal distribution

All data was checked for normal distribution prior to any further statistical analysis. Histograms with normal distribution curves overlaid, as well as the z-score for skewness, were examined. Finally the impairment and activity measure was tested for normal distribution using the Kolmogorov-Smirnov and Shapiro-Wilks tests. If one or both of the tests were found to be significant (p=0.05), then the variables in question were taken as being not-normally distributed and non-parametric statistics applied.

4.11.5. Descriptive statistics

The demographic and clinical characteristics of participants in the Pilot and Main Studies are presented as means, standard deviations (SD) and ranges.

4.11.6. Pilot Studies statistical analysis

All variable data in the Pilot Studies was found to be normally distributed, therefore parametric tests were used with the statistical significance level set at p=0.05. The following tests were used:

4.11.6.1. Differences between impaired and unimpaired

Descriptive statistics (mean SD and range) for each measurement index for the impaired and unimpaired groups are presented. Differences between the impaired and unimpaired groups were tested using two sample t tests and 95% confidence intervals.

4.11.6.2. Differences between hand positions

Differences between hand positions for each of the impairment variables and between impaired and non-impaired groups were determined using repeated measures ANOVA. Where statistical significance was found a t-test and 95% confidence intervals were calculated to determine specifically where the statistical significant difference lay.

4.11.7. Main Study statistical analysis

Some of the impairment measures were found not to be normally distributed in the Main Study (see Appendix G Table G-2). It was therefore decided to use non-parametric tests for all the impairment measures; a p-value of 0.05 was accepted as statistically significant. The following tests were used:

4.11.7.1. Validity (ability to distinguish between impaired and unimpaired)

The purpose of evaluating the ability of the impairment indices to distinguish between impaired and unimpaired was to confirm the findings in the Pilot Studies with a larger sample of older impaired participants in the acute as well as chronic phase post-stroke.

4.11.7.2. Between-days test-retest reliability (active tests)

Reliability is commonly assessed using the intraclass correlation (ICC) (Kirkwood and Sterne 2003), however the ICC is estimated using a one-way analysis of variance and thus is a parametric test and assumes normal distribution of data. Bland Altman methods (Bland and Altman 1986) were used to evaluate between-days agreement for the impairment measurement indices. The 95% limits of agreement, were calculated and examined with respect to the within and between-group range of values for each index. The 95% limits of agreement are given by the mean difference between the day 1 minus the day 2 readings plus or minus twice the SD of the differences. If the differences are normally distributed then approximately 95% of the differences lie in this range. Again, this analysis assumes normal distribution of data, but no other more appropriate test appears to be recommended in the literature. Bland and Altman plots for each of the differences between the day 1 and day 2 readings against the mean value for each participant were examined. The repeatability coefficient (Bland & Altman 1986) was calculated as $\pm 1.96\sqrt{\frac{\sum(d_1-d_2)^2}{n}}$ using the readings from day 1 (d1) and day 2 (d2), and gives a 95% range about a true change that might be expected from measurement error alone. Changes larger than the value of the repeatability coefficient can be considered to be due to a real change in underlying values, rather than random variations. The repeatability coefficient has thus also been termed the smallest real difference, SRD (Beckerman et al. 2001).

4.11.7.3. Within-test repeatability (active and passive sinusoidal tests)

Within-test repeatability of the impairment indices was assessed to understand how movement tracking, muscle activation patterns, flexor EMG stretch response and isometric force may change within the period of the tests concerned. This could be assessed with the sine tracking index and coactivation index but not with the step tracking indices because the active sine tracking test involved repeated identical cycles whereas the step tracking consisted of random movements through the test. Similarly the stretch index could be assessed because the passive stretch response test involved repeated identical cycles. The mean torque test also involves five identical cycles, but repeatability could not be assessed because in the calculation of the mean torque index only cycles where the extensor and flexor activity were below a threshold were accepted, and this was often not the case for all cycles.

For the within-test repeatability, data from each of the tests were divided into three sections of equal number of target cycles. The sine tracking test was divided into three sections of eight target cycles: beginning (section 1), middle (section 2) and end (section 3), and the mean tracking index and coactivation index for those sections were calculated. Similarly the passive sine tracking test (stretch response test) at 3.5Hz was divided into three sections of 44 target cycles, and at 0.5Hz into three sections of six target cycles. Mean stretch index for each

section was calculated. Changes were examined between sections one and two, and two and three, and tested for statistical significance using the two related samples Wilcoxon test.

4.11.7.4. Differences between acute impaired, chronic impaired and unimpaired groups

These results are presented to show how the impairments differ at the acute and chronic phases post-stroke compared to unimpaired. Differences between the three groups were determined using a Kruskal Wallis Test, the non-parametric equivalent of a MANOVA, which takes account of the number of variables, and thus reduces the risk of a type I error, where there is a false claim of statistical significant difference due to the number of tests conducted. Post hoc tests are not provided with this test, so in order to determine the chronic vs. unimpaired and acute vs. unimpaired differences for each impairment variable, Mann Whitney U tests were also used. To show how individuals differ across the three groups, data for each participant across the three groups are presented as dot plots.

4.11.7.5. Association between impairment indices and motor control accuracy (tracking performance)

To determine the contribution of the motor impairments to good and poor motor control accuracy (MCA) differences in the motor impairments between high and low motor control accuracy (MCA) groups were evaluated. The impaired participants were assigned to high and low MCA groups based on their step tracking performance. Visual inspection of step-tracking performance indicated a suitable threshold for separating between the groups. To compare differences between the three groups (low MCA, high MCA and unimpaired) for all the impairment measures, a Kruskal Wallis Test was first conducted followed by Mann Whitney *U* tests to determine where statistical significance lay (see section 4.11.7.4 for justification of these tests). The individual participants who had low MCA and high MCA shown on the dot plots of step tracking performance were identified and their values in other impairment dot plots were compared.

4.11.7.6. Inter-relationships between negative, positive and secondary motor impairments

To examine the inter-relationships between all the impairments, separately for the acute and chronic groups, Spearman's correlation was used and statistical significance presented as *p*-values. Because of the number of variables tested (12 impairments) a Bonferroni correction was added, which although very conservative (Field 2000), highlighted the most important relationships within the data.

4.11.7.7. Relationships between impairment indices and functional activity measure

To examine the relationships between the impairment measures and functional activity (mWMFT), separately for the acute and chronic groups, Spearman's correlation was used, *p*-values calculated, and statistical significance assessed with and without Bonferroni correction (see Section 4.11.7.6 for justification).

To examine the importance of impairment measures in explaining performance of the functional activity measure (mWMFT), separately for the acute and chronic groups, a multiple linear regression was calculated using SPSS (PASW statistics v18). Statistical analysis of linear regression is based on the assumption that the data are normally distributed, and because some of the main study data did not fit this assumption, a quantile regression was also run using Stata (StataCorp LP) by a Statistician with expertise in Stata (Peter Nicholls) to compare and verify the results.

Not all the impairments could be tested all together, because the number of predictors and how they are entered into the regression analysis can have a great impact on the resulting regression coefficient values (Field 2000). Selection of predictors for the regression analysis was even more important because of the small sample size, which was further reduced as the acute and chronic groups were considered separately. The impairments were therefore grouped into negative, positive and secondary features in each patient group, and a series of two regression analyses were performed to determine the most important (statistically significant) contribution of an individual predictor in each feature group and each patient group. Firstly, an individual linear regression of each impairment measure was applied and those that were statistically significant were chosen as important predictors for each feature impairment group in the next multiple regression analysis, as recommended by Field (Field 2000). For each impairment feature group, where there were two or more significant predictors, these predictors were entered into a forward stepwise analysis, which revealed the predictor that accounts for the most variance in mWFMT and made a statistically significant contribution to the power of the model.

4.12. Summary

This Chapter has presented the methodologies used in the Pilot and Main Studies of this research programme in order to achieve the research objectives outlined at the end of Chapter 2 Literature Review. Further details of methods specific to the Pilot or Main Studies are included in those Chapters (Chapter 5 and 6). The following Chapter, Chapter 5, reports the Pilot Studies undertaken, the aims of which were to finalise the testing protocols and derive the impairment measure indices in preparation for the Main Study.

5. Pilot studies and derivation of indices

5.1. Introduction

Following the development of the wrist rig described in Chapter 3, the aim of the pilot work was to optimise the design of the rig, to test the methodology of data collection proposed for the main study and develop and evaluate methods for deriving impairment indices Figure 5-1 5.1.

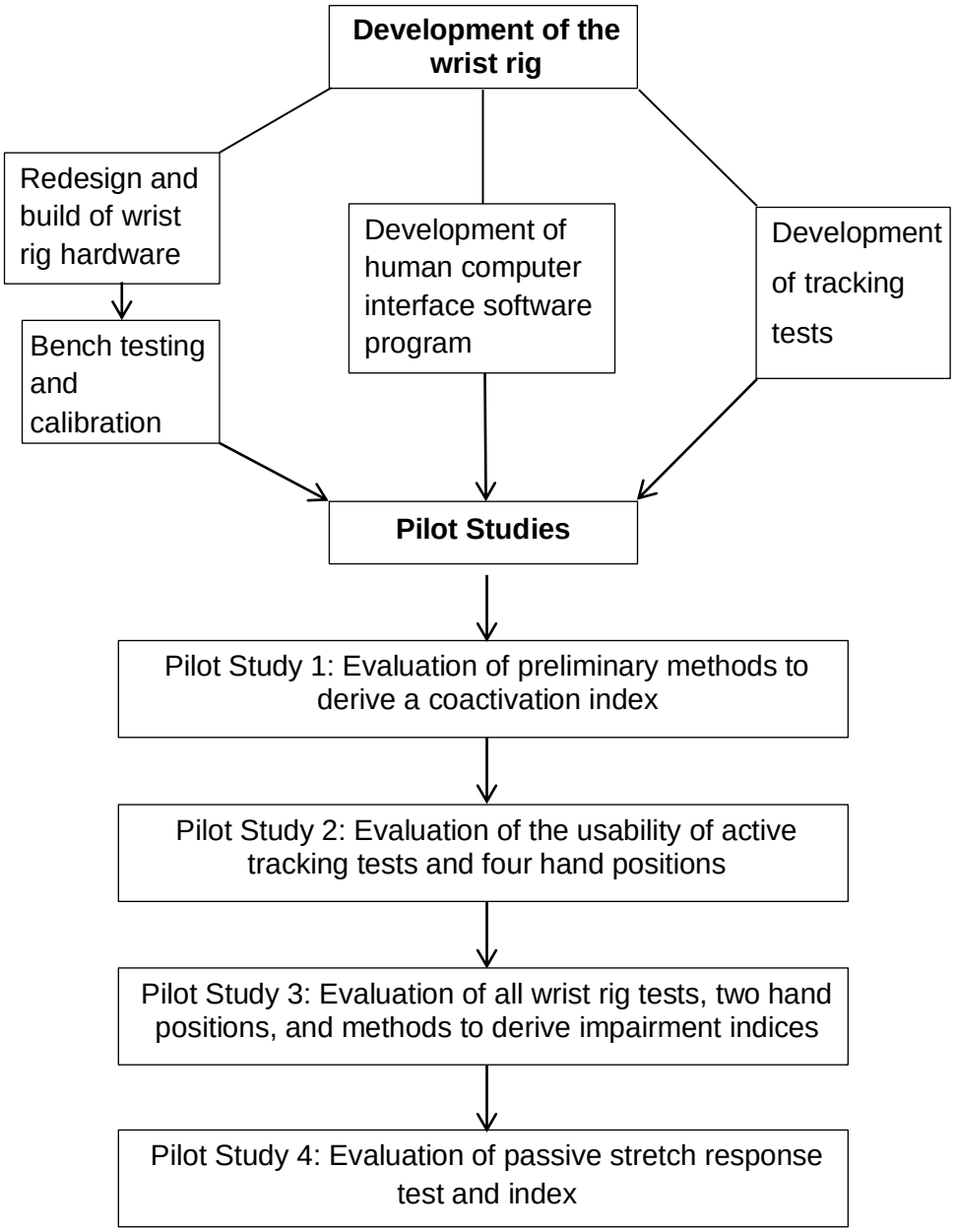


Figure 5-1 A flowchart to illustrate how the four pilot studies with the overall objectives follow on from the development of the wrist rig described in Chapter three.

A series of four pilot studies was conducted and, using an iterative process, the following overall objectives were addressed:

1. Define protocols for conducting the tests in preparation for the main study
    a. Test parameters – frequency of target tracking movements, range of displacement, length of baseline recording and resistance applied during the tests
    b. Application of the modified Wolf Motor Function Test (WMFT) protocol
2. Optimise usability and comfort of the rig from the participants' perspective in terms of:
    a. Comfort of the chair and arm in the rig
    b. Performance of the tracking and strength tasks in terms of speed, rest time intervals, range of displacement and visualisation of the target
3. Derive impairment indices using existing data from a previous study and data from the pilot studies
    a. Develop and define methods of analysis to generate the most physiologically and clinically relevant indices to characterise motor impairments – considering a wide range of options.
    b. Evaluate how the measurement indices differentiate between those impaired from stroke and neurologically intact controls
4. Determine the optimal hand positioning in the rig in terms of:
    a. Differences for each of the impairment variables between hand supports
    b. Differences between impaired and non-impaired groups for each of the impairment variables measured using different hand supports
    c. Usability and comfort of different hand supports

5.2. Pilot Study 1

5.2.1. Introduction

The aim of this study was to develop and evaluate methods to measure coactivation during sinusoidal tracking. Focus was placed on coactivation because this index was needed for Pilot Study 2 (see section 5.3) to answer an important question; does different positioning of the fingers affect the amount of coactivation recorded?

The literature review identified seven methods to measure co-activation in stroke and, of these, the method that was chosen was correlation of the agonist and antagonist EMG (Canning et al. 2000; Hu et al. 2006) because this method can selectively analyse abnormal simultaneous activation of the antagonist (flexor) when the agonist (extensor) is activated, by measuring the similarity in timing and shape of the agonist and antagonist activation curves. The measure provides a correlation coefficient ranging between +1 and -1, with positive values indicating simultaneous activation (coactivation) and negative values alternating

activation (reciprocal inhibition/activation). To investigate correlation, EMG, target and wrist angle data was used that had been recorded during a 0.5Hz sinusoidal tracking test from a previous wrist rig study (Turk et al. 2008b). To investigate validity of this measure, the relationship with wrist tracking accuracy (motor control) and upper limb activity limitation (the ARAT described previously in Chapter 2 section 2.11), was evaluated.

5.2.2. Methods

Data from ten participants impaired from stroke and 12 unimpaired participants who had taken part in a previous study (Turk et al. 2008b) was used (Table 5-1). Participants had undertaken a sinusoidal tracking test at 0.5 Hz and ± 20º around their active mid-range, and performed the ARAT.

Table 5-1 Demographic characteristics of participants from a previous study (Turk et al. 2008b) whose data was evaluated in Pilot Study 1

		Impaired (N=10)	Unimpaired (N=12)
Age (years)	Mean (SD)	62.9 (11.6)	50.5 (19.5)
	Min - max	44 - 78	22 - 72
Gender	Male	6	6
	Female	4	6
Time from stroke (years)	Mean (SD)	5.6 (3.8)	N/A
	Min - max	1 - 13	
Side assessed	Right	3	10
	Left	7	2
ARAT score (normal value = 57)	Mean (SD)	18.8 (11.5)	N/R
	Min - max	3 - 37	

N/A = not applicable; N/R = not recorded; ARAT = Action Research Arm Test

The target, wrist angle and EMG data between 5 and 60 seconds were selected for analysis. The raw flexor and extensor EMG data were rectified and smoothed using a low pass filter at 2 Hz to produce an EMG envelope. To aid visual analysis of the data, the peak flexion of the wrist angle signal was detected and ensembles of the wrist angle, flexor EMG envelope and extensor EMG envelope were made centred on each flexion peak with 2 seconds of data before and after the peak (Figure 5-2). Coherent averaging was used to calculate an average of the ensemble of signals.

For the analysis, the graphical results for each correlation method were visually analysed as flexor/extensor EMG plots (Results Section Figure 5-3). Correlation of the extensor and flexor EMG envelopes was then calculated using four different criteria for selecting which segments of the flexor and extensor EMG envelope samples to be included in the analysis:

1. Correlation of the whole sample (the EMG envelopes during both flexion and extension movements)

2. Correlation during extension movement only, based on the angle data from peak flexion to peak extension. This can be seen on Figure 5-2 a) between zero and one seconds.
3. Correlation based on the extensor EMG signal when the extensor EMG was increasing (Results Section Figure 5-4). In order to avoid the inclusion of periods with small fluctuation in extensor EMG amplitude, only the periods when there was an increase in greater than half the standard deviation of extensor EMG (calculated over the duration of the task) were included.
4. Correlation based on the extensor EMG signal during peak extensor EMG. Segments were included when the extensor EMG samples were greater than 50% of the peak extensor EMG

Correlation based on angle data when there was acceleration into extension was also considered, but was found to be unsuitable as this would include the flexion phase if the movement was in a true sinusoidal pattern.

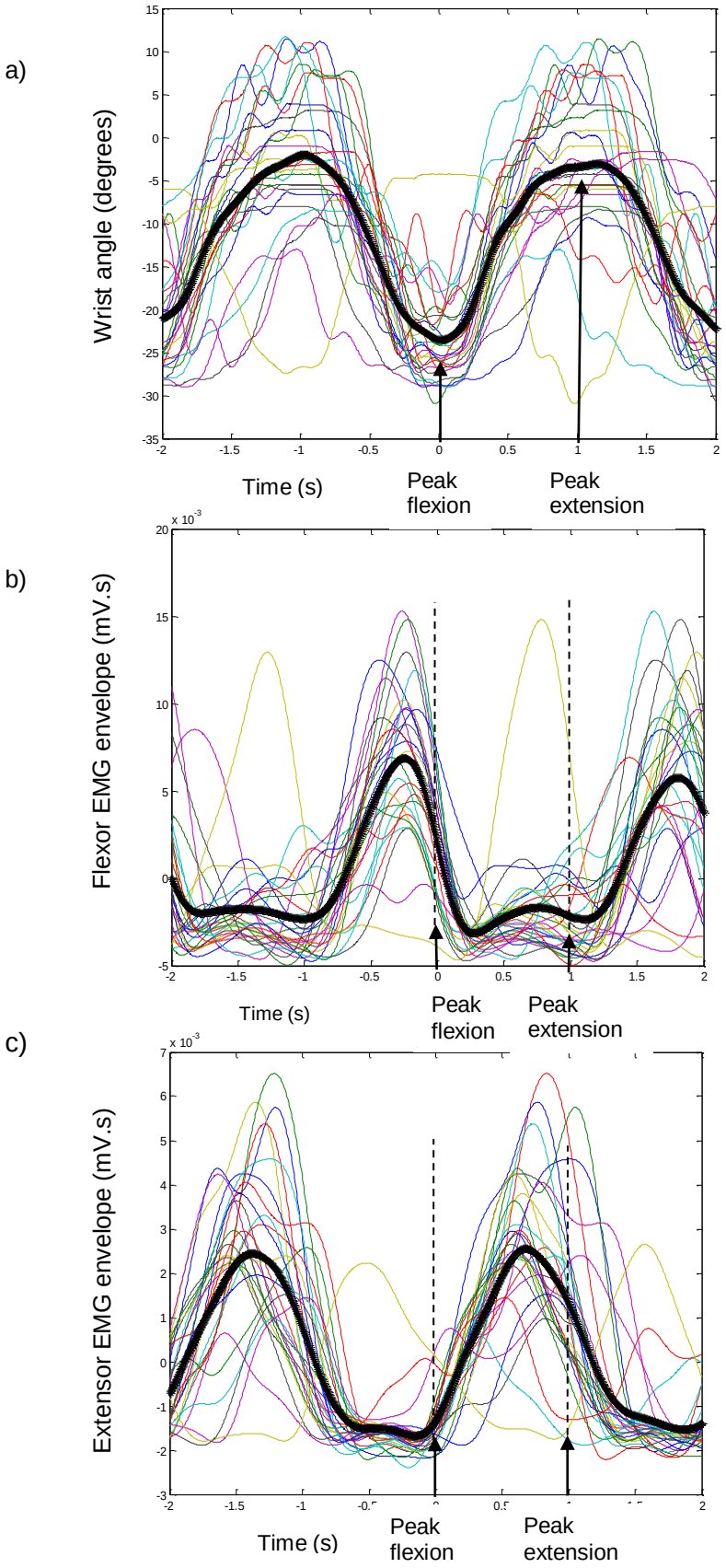


Figure 5-2: Ensembles (thin lines) and average (bold line) of a) wrist movement, b) flexor and c) extensor EMG envelopes from one impaired participant performing a sinusoidal tracking test (0.5Hz, ±20˚). The extension phase is shown between 0 and 1 seconds; there is clear extensor activation and slight flexor activation during the extension phase.

5.2.2.1. Statistical analysis

The mean was removed from the EMG envelope signals and the simultaneous extensor and flexor EMG sample values, according to the four criteria above, were plotted (extensor on the x axis and flexor on the y axis) (Results Section Figure 5-5). A Pearson's correlation was then applied in MatLab to calculate the coactivation index values. Descriptive statistics (mean and SD) were calculated to compare mean differences between impaired and unimpaired activation for each coactivation measurement method. Dot plots were created to show individual differences between the impaired and unimpaired values. Interpretation of the strength of coactivation was based on recommended values for strength of relationship/ associations between variables (Pett 1997); these being: 0.00 to 0.25 no association to weak association, 0.26 to 0.50 a low degree of association, 0.51 to 0.75 moderate to strong degree of association and 0.76 to 1.00 very strong association. It should be pointed out that due to the correlation between successive samples in each signal, the degrees of freedom are smaller than the number of samples available, preventing the application of the usual test os statistical significance for the correlation coefficient. To investigate the relationship of the coactivation measure with motor control accuracy and functional activity, a two-tailed Pearson correlation analysis was performed using SPSS (PASW statistics v18) with a tracking index (accuracy of tracking a moving sinusoidal target calculated using cross correlation) (Notley SV et al. 2007) and with the ARAT performance score.

5.2.3. Results

Figure 5-3 shows two examples of muscle activation patterns seen in this study: an unimpaired participant with a classic reciprocal activation / inhibition pattern and good tracking performance, and an unimpaired participant with coactivation and poor tracking.

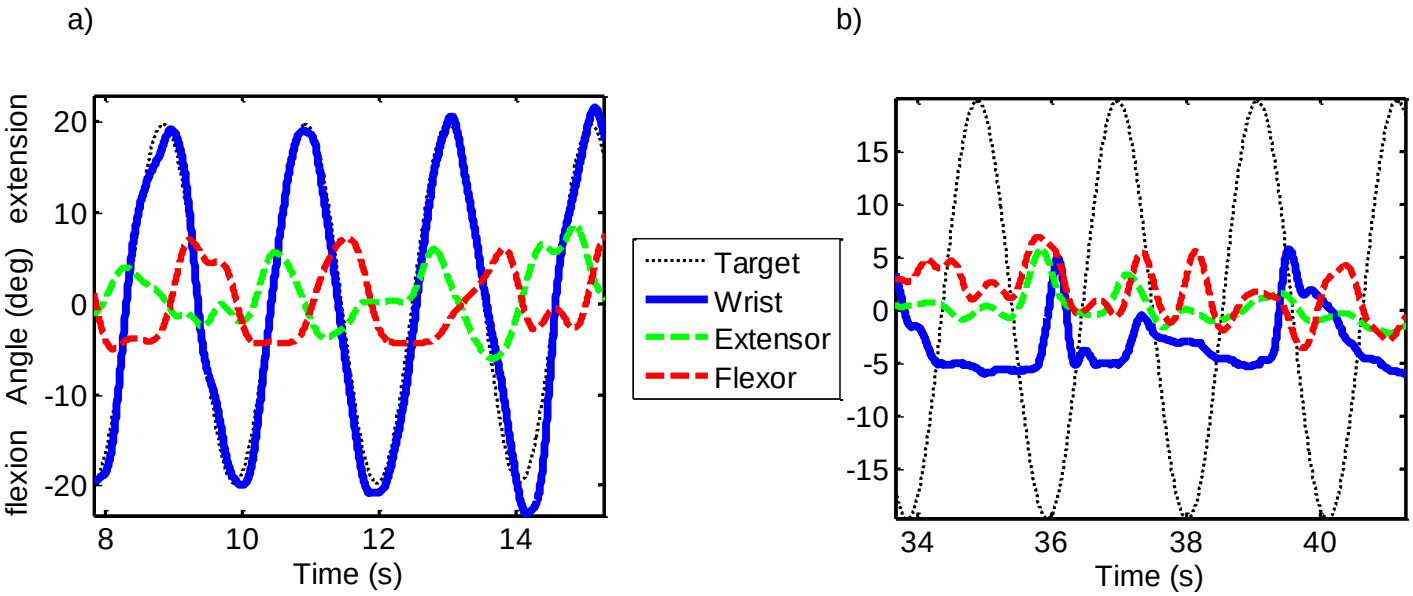


Figure 5-3 a and b: Two Individual examples of sinusoidal tracking showing the target (black dotted) and wrist movement (blue solid), together with rectified and smoothed flexor (red dashed) and extensor (green dashed) EMG. Example a) is an unimpaired participant with good tracking performance and reciprocal activation. Example b) is an impaired participant with poor tracking performance and coactivation.

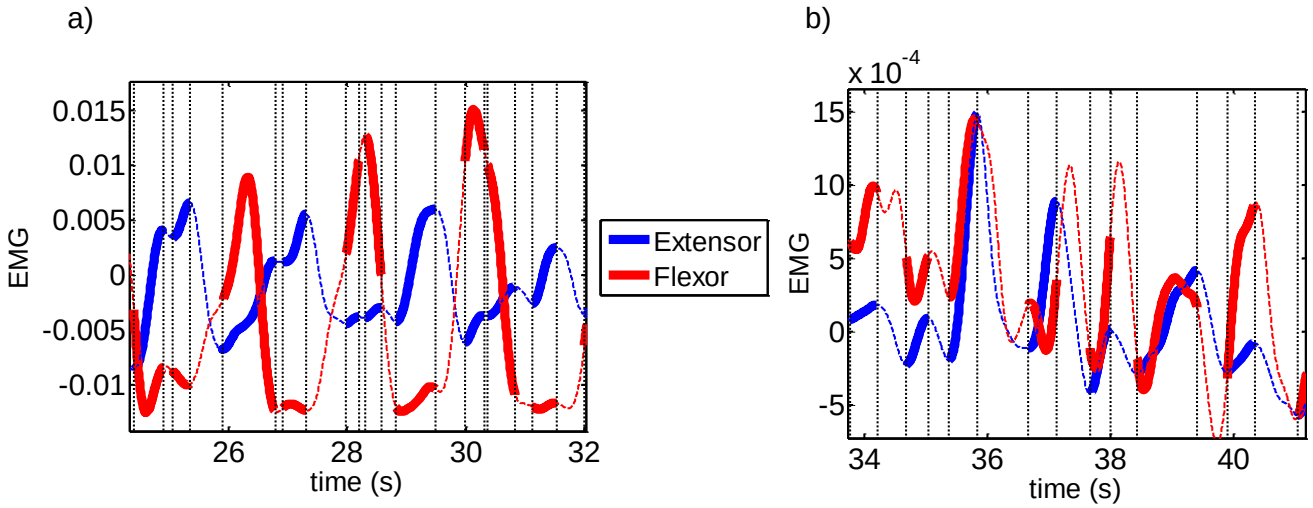


Figure 5-4 a & b: Two examples of rectified and smoothed flexor (red) and extensor (blue) EMG during sinusoidal tracking showing a) reciprocal activation (unimpaired participant in Figure **5-3**a) and b) coactivation (impaired participant in Figure 5-3b). Sections of bold between the dotted lines are the EMG samples included in the correlation analysis based on when extensor EMG is increasing (blue bold).

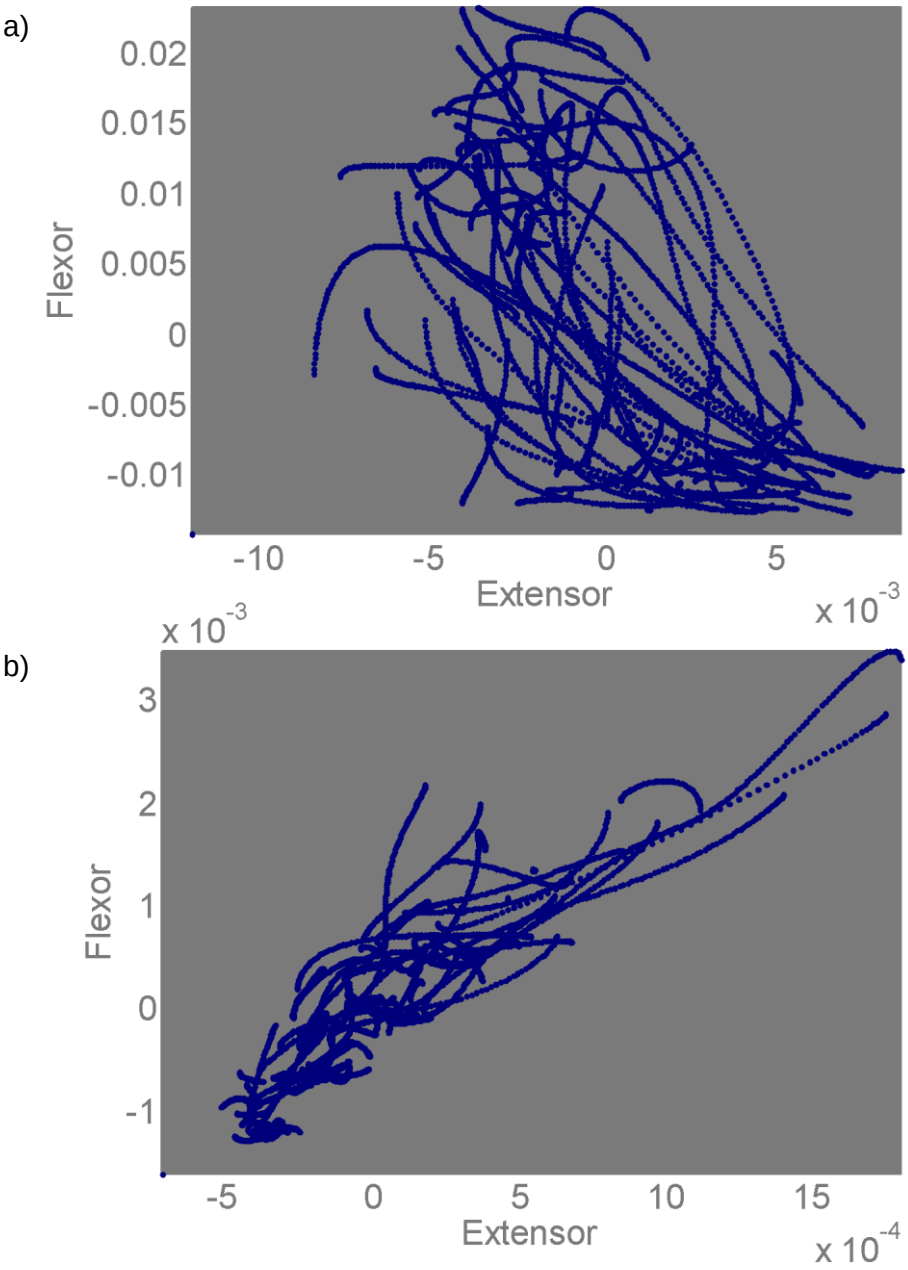


Figure 5-5: Individual examples of correlation analysis graphs of extensor and flexor EMG samples. Example a) is an unimpaired participant with good tracking performance and reciprocal activation (r=-0.64). Example b) is an impaired participant with poor tracking performance and coactivation (r=0.86).

The mean and SD of the impaired and unimpaired groups can be seen in Table 5-2. The mean impaired group values indicate low to no coactivation, though the SD and minimum to maximum ranges show the wide variation in the data.

Table 5-2: Mean (SD) of the coactivation measure (correlation coefficient) for the impaired and unimpaired groups comparing four different criteria for selection of data (none statistically significant P≤0.05)

Group	Measure of Coactivation (correlation) Mean (SD) and min to max			
	During flexion and extension movements	During extension movement	When extensor EMG is increasing	During peak extensor EMG
Impaired (N=10)	-0.08 (0.44)	0.35 (0.30)	-0.08 (0.43)	0.01 (0.38)
	-0.51 to 0.88	-0.24 to 0.85	-0.54 to 0.86	-0.32 to 0.79
Unimpaired (N= 12)	-0.29 (0.30)	0.29 (0.24)	-0.28 (0.35)	-0.06 (0.22)
	-0.62 to 0.42	-0.01 to 0.64	-0.64 to 0.63	-0.32 to 0.36
Mean Difference	0.21	0.06	0.20	0.06

Although not reaching statistical significance, greater mean differences between impaired and unimpaired were found in two criteria for selection of data: during the whole test (flexion and extension movements) and when extensor EMG was increasing. The other two criteria, during movement into extension and during peak extension, tended to have more positive correlation coefficients for both groups with only small differences between impaired and unimpaired performance. To investigate this, visual analysis of the data showed that for some participants in both groups there was some flexor EMG activation towards the end of the extension movement, presumably acting as a break (see Figure 5-2b between zero and one seconds for an example from the stroke group). Coactivation analysis during extension movement and during peak extension includes this section of the data where both the extensor and flexor EMG are activated. This did not reflect abnormal coactivation as when the whole pattern was observed it can be seen that the flexor EMG was at low activation levels during extension compared to flexion, and there was clearly reciprocal activation. Correlation analysis based on when extensor EMG is increasing, however, includes the section of data before the movement starts and at the beginning of the movement, resulting in better distinction between normal and abnormal coactivation. Two examples illustrating this method of analysis can be seen in Figure 5-4 a) and b).

Specifically correlation of the flexor and extensor envelopes during an increase in extensor EMG was selected for further analysis as it most reflected the part of the cycle where abnormal coactivation may be detrimental to the action of the extensor to produce extension movement. Comparison of the individual impaired and unimpaired values using this measure is shown in the dotplot in Figure 5-6 and the wide spread of values can be seen. In the unimpaired group most correlation coefficient values lie near to zero or are negative indicating reciprocal activation/inhibition, except for one outlier with strong coactivation (r=0.63) which was also evident from visual analysis of the tracking and EMG plots. In the

impaired group, the majority of values also lie near to or below zero, also indicating that these participants used reciprocal activation/inhibition during tracking movements. However one participant showed low coactivation (r=0.43) and another very strong coactivation (r=0.86).

For the impaired group a moderate to strong and statistically significant negative correlation was found between coactivation and tracking accuracy (r=-0.675, p=0.032) (Figure 5-7); there was a moderate but non-significant correlation with functional ability (r=-0.621, p=0.055). The two strongest co-activators also showed the worst performance in the tracking test and lowest function scores.

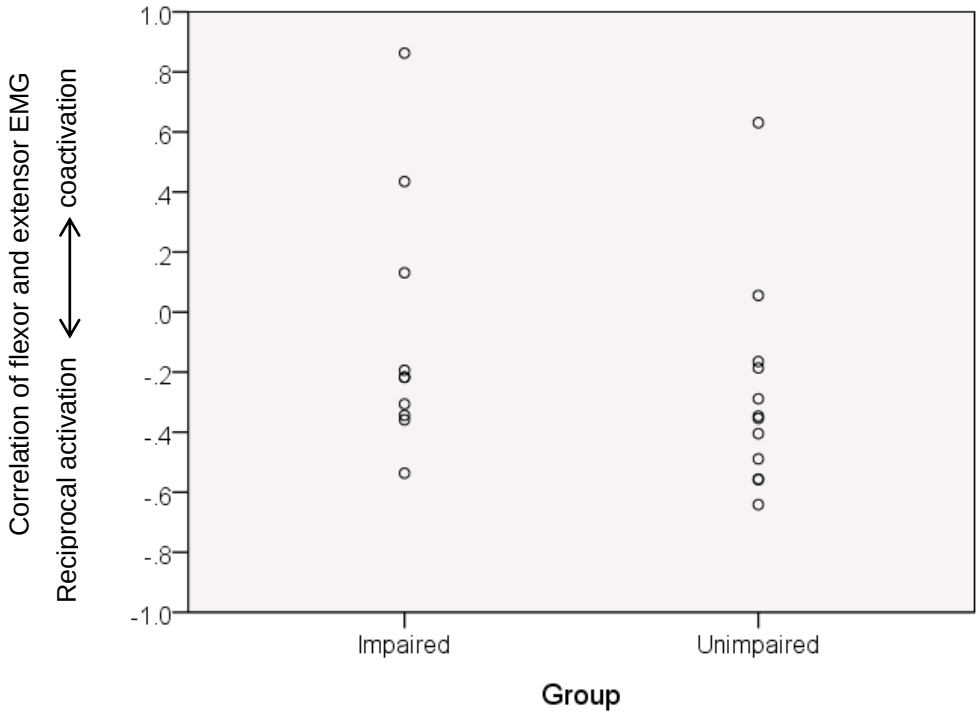


Figure 5-6 Dotplot of coactivation measurement values for the impaired and unimpaired groups using correlation of extensor and flexor EMG when extensor EMG is increasing

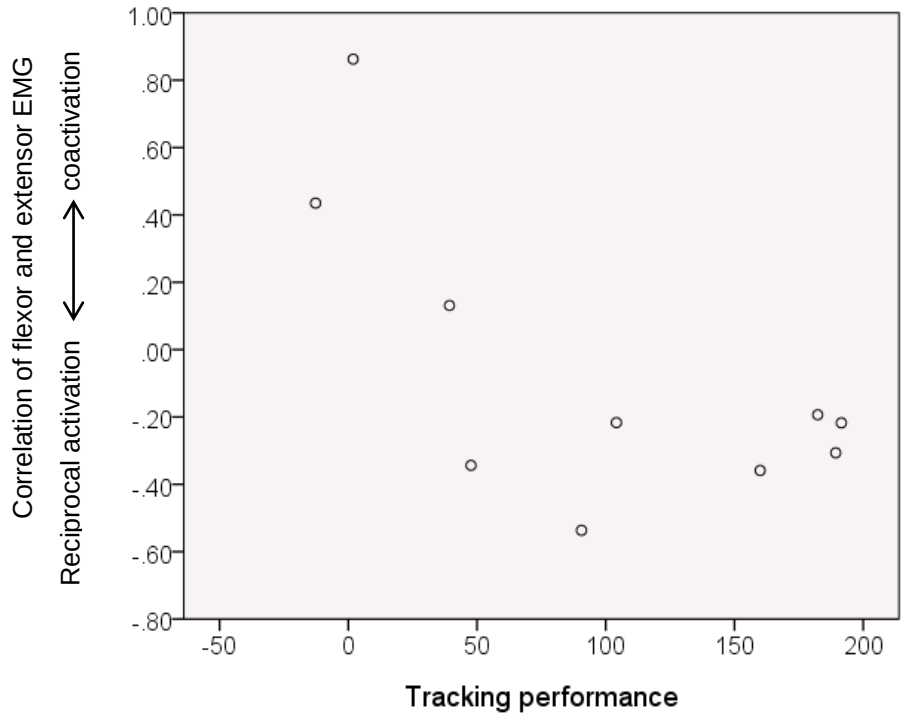


Figure 5-7 Scatter plot to show correlation between a coactivation measurement (correlation of extensor and flexor EMG when extensor EMG is increasing) and tracking performance

5.2.4. Discussion and conclusion

In Pilot Study 1 we have used correlation of the flexor and extensor EMG to quantify coactivation during a sinusoidal tracking test. A limitation of using correlation as a method is the assumption that the two variables have a linear relationship, and with flexor and extensor EMG this is not the case. However, previous methods used to quantify coactivation have been found unsuitable as they neither evaluate the co-activation relationship between the antagonist with the agonist, nor attempt to distinguish between abnormal coactivation from normal co-activation that stabilises a joint and ensures end-point movement accuracy.

Coactivation has previously been quantified during a random tracking test at the elbow using correlation of EMG through the whole test (flexion and extension movements) (Canning et al. 2000). In our study four methods of correlation of flexor and extensor EMG envelopes were compared. Two methods of correlation better distinguish normal coactivation from abnormal coactivation due to stroke: correlation of EMG through the whole test (flexion and extension movements) and when extensor EMG is increasing. The latter method may be more useful clinically as it most reflects the part of the cycle where abnormal coactivation may hinder the action of the extensor to produce extension movement. Visual analysis of the traces suggested this approach was able to exclude more sections of the data where there is 'normal' coactivation to stabilise a joint and ensure end-point movement accuracy.

Using this correlation method, coactivation was found in two of the ten patients in this small sample suggesting it was not the main cause of disability for the group, but is present in some individuals. This is similar to findings of other upper limb studies where coactivation during tracking has been evaluated (Canning et al. 2000; Turk et al. 2008b). Coactivation was also found in one unimpaired participant showing that even in the unimpaired whose tracking performance is excellent a variety of muscle activation strategies can be used.

Coactivation in this study was found to be associated with poor tracking performance (r=-0.675, p=0.032) and (less) with functional performance (r=-0.621, p=0.055). This is unlike the findings of our previous study where coactivation was measured using a flexor modulation index (ratio of flexor activity as an antagonist and agonist) and no association was found with sinusoidal tracking performance (r=0.380, p=0.162) and upper limb functional activity using the ARAT (r=0.217, p=0.438) (Burridge et al. 2008).

This initial investigation of coactivation analysis methods would enable further investigation in Pilot Study 3 with both sinusoidal and step tracking data.

5.3. Pilot Study 2

5.3.1. Objectives

The purpose of this study was early evaluation of the modified wrist rig components and proposed test variables. The objectives were as follows:

5.3.1.1. Define tests

- Evaluate the newly developed step tracking test with varying visual feedback and random timing
- Evaluate sinusoidal and step tracking with resistance set at a fixed % of participants' MVC

5.3.1.2. Evaluate wrist rig usability and comfort

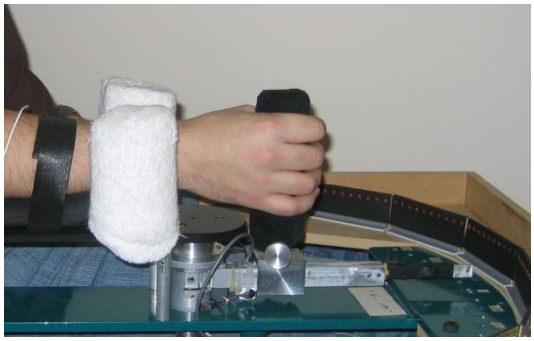
- The comfort and usability of the wrist rig from participants' perspective was evaluated.

5.3.1.3. Evaluate four hand splints

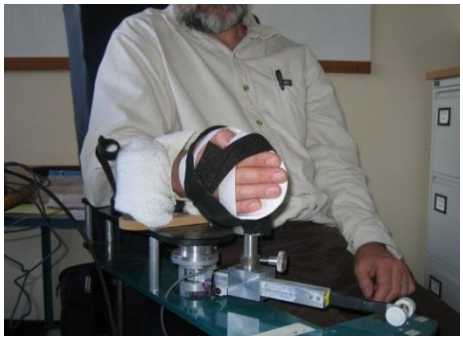
The importance of hand positioning in the wrist rig has been discussed in the development Chapter (Section 3.2). The four different hand splints, designed and built during the development phase (see Section 3.2 and Figure 5-8 a-d) were evaluated specifically to:

- Evaluate the usability of the hand splints when conducting active tests – sinusoidal and step tracking and MVC
- Evaluate the effect of the hand splints on muscle activation (using a coactivation index developed in Pilot Study 1 section 5.2). It was hypothesised that positioning the fingers in flexion, for example around a handle during the active tracking tasks may increase normal coactivation patterns in the forearm muscles due to the fingers gripping the handle, especially in resisted tracking.

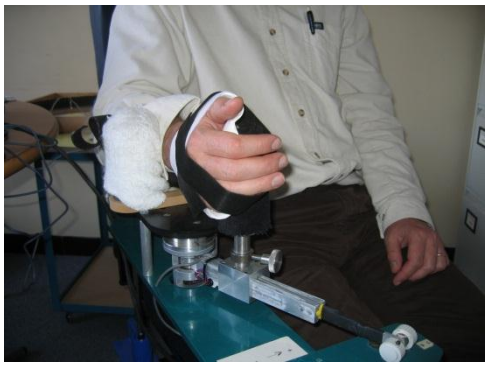
a) Handle (the fingers are in flexion)



b) Full hand splint (the fingers are in relaxed extension)



c) Palm Splint (the splint reaches to the metacarpophalangeal joints allowing flexion of the fingers



d) Air splint (the fingers are in relaxed extension) where the hand is held by an air-filled cuff

Figure 5-8 a – d: Four different hand positions tested during Pilot Study 2

5.3.2. Methods

5.3.2.1. Participants

Participants were recruited for this study who were able to tolerate repeated procedures without fatigue, had an understanding of the project and were able to give informed feedback. Four unimpaired participants, two female and two male with a mean age of 40

years (30 to 57 years), were recruited from staff in the Faculty of Health Sciences ARM research programme.

5.3.2.2. Data collection

Following set up in the rig as described in Chapter 4 Methodology Section 4.7, the hand was initially positioned around the handle with the wrist joint in vertical alignment with the pivot joint (Figure 5-8 a) and the following tests were carried out:

- Participants provided feedback after practicing the following tests:
    - Sinusoidal tracking at 0.25Hz and 0.5Hz, ± 20˚
    - Random step tracking with varying rest time intervals and increasing displacements.
    - MVC of wrist flexors and extensors at the 0˚ and 20˚ flexion position on the rig.
- Resistance at approximately 5% and then 10% of participants' extensor MVC was trialled with :
    - Sinusoidal tracking at 0.5Hz ± 20˚, for 60 seconds
    - Step tracking with random 1-4 second rest intervals between movement of the target, increasing displacement of the target from 5˚ to 40˚ in 15 second blocks for a total of 90 seconds.
- Resistance was set at 10% of MVC and three further hand supports were tested in the following order: full hand splint, palm splint, and air splint (see Figure 5-8 b, c and d). Participants performed:
    - Sinusoidal tracking test as above
    - Random step tracking test as above
    - MVC of flexors and extensors

To determine the usability of the rig and active tests, each participant was asked the following questions at appropriate times throughout the testing process:
1. How comfortable did you find the wrist rig when you performed the tasks? a) The forearm and elbow support, b) Each hand support, c) The straps that secure the arm and hand
2. How easy did you find it to track the lights on the LED display? a) Without resistance, b) with resistance
3. How easy did you find it to perform a maximal contraction using each hand support?
Answers were recorded on the participant record form (Appendix H).

5.3.2.3. Analysis of coactivation

The flexor and extensor EMG envelopes were visually analysed. A section from 25 to 60 seconds of the data from both the step and sine tracking tests was selected for analysis because in step tracking only small movements are made prior to 25 seconds and

coactivation was easier to observe and measure in the larger movements. In order to select the EMG data where there was movement i.e. exclude data during no movement but where there is still some EMG activity, a moving standard deviation of the wrist angle in windows of 0.5 seconds was calculated and only the parts of the data where the standard deviation was greater than the median value were selected for analysis.

To calculate coactivation, a correlation coefficient between the flexor and extensor EMG envelope during both flexion and extension movements was used. It was measured during both flexion and extension because normal coactivation may occur in both phases of movement, so with unimpaired participants it is not so important to measure only during the extension phase of movement as is the case for stroke impaired participants. Due to the small sample size, descriptive statistics were used to describe differences in coactivation between the hand splints for the two tracking tests. Interpretation of the strength of coactivation was based on recommended values for strength of relationship/ associations between variables (Pett 1997) as described in Pilot Study 1 section 5.2.2.

5.3.3. Results

5.3.3.1. Usability of wrist rig and tracking tests

Issues that affected the ability of participants to perform the tracking tasks and modifications made are outlined in Table 5-3.

Table 5-3 Issues encountered during the pilot testing process with unimpaired participants and modifications made

Subject	Usability issues	Modification
LED target display	Tracking accuracy was variable depending on participant height due to a parallax problem	A pointer was designed and attached to the end of the lever arm to point close to the LEDs
	The hand supports obscured vision of all the LEDs; LED display board is too close to participant's lap	Height of LED display board was increased; size of the air splint was reduced
Sinusoidal tracking	When tracking at 0.5Hz, there was blurring of the LED target (appearance of 3 LEDs activated at the same time) due to the rapid sequential activation of successive LEDs, which makes it difficult to be accurate in tracking.	The software for the task was redesigned so that each LED was on for a shorter length of time (with approximately 20ms gap before the next LED was activated) which ensured that the eye saw only one LED lit at any time during the cycle.
Rest period of tracking tests	Too short rest period (2 seconds) before start of tracking tasks	Rest period increased to 4 seconds

Subject	Usability issues	Modification
Step tracking	Different strategies used during step tracking: if accuracy is the main focus for the participants, movement is slow, and when speed of tracking is the main focus accuracy is compromised.	Instructions to participants clarified with speed being the priority – 'track the target as quickly and accurately as possible'
	Random rest time interval between target changes: 1-3 seconds was challenging for unimpaired and likely to be too difficult for impaired group. Time intervals longer than 4 seconds seemed very easy and may not be challenging enough for some impaired participants	2-4 seconds was still challenging for unimpaired but allows some slower times for impaired participants. This will be trialled with impaired participants in Plot Study 3.
Resistance applied using the slip clutch	Challenge of setting resistance as accurately as possible to 5% and 10% of extensor MVC as speed of moving the lever arm altered the torque (Nm) recorded at the torque sensor.	It was important when setting the resistance manually to use a 0.5Hz ±20º sinusoidal tracking task, to standardise the speed and range of movement of the lever arm. When this was used, accuracy in setting the level of resistance altered between cycles by approximately ±0.02Nm
	When resistance was applied at 5% the task was too easy; at 10% of MVC the resistance was felt but the task was still easy to perform.	Resistance was set at 10% and trialled with impaired participants in Plot Study 3.
	With resistance applied there was 'play' in the lever arm due to the backlash effect of the slip clutch. This affected target end-point tracking accuracy during step tracking causing greater overshoot and undershoot movements.	This was a limitation of the slip clutch that could not be modified at this stage. This issue may be a confounding factor when investigating target end-point accuracy with resisted tracking

5.3.3.1. Usability of the hand supports

All the participants found the handle easy to use for the tracking tasks, but found the extensor MVC task difficult as all the pressure is applied through the thumb. The participants found the palm and full hand splints insecure especially when force was applied during the MVC. The air splint was easy to use and the hand felt secure and 'connected' to the rig. One participant found it easier than the handle as the fingers are pointing at the target. In summary, the handle with a minor modification and the air splint seemed most usable.

5.3.3.2. Effect of hand supports on muscle activation patterns

Correlation coefficients of flexor and extensor EMG envelopes during the two tracking tests and for the four hand positions can be seen in Table 5-4. For sinusoidal tracking reciprocal activation / inhibition was seen in all participants. For step tracking, three participants have negative correlations i.e. reciprocal activation / inhibition, and have similar correlation values for the hand positions. The reciprocal activation / inhibition could be seen on the tracking and EMG plots (see Figure 5-9 for an example). Further observation showed agonist activation (AG1) at the start of movement with antagonist activation (ANT1) at the end of the movement

in order to accurately reach the target or make a correction for overshooting the target with further agonist activation to stabilise the position (AG2) (Figure 5-9). One participant (#1) showed moderately strong coactivation (r=0.65) when using the handle which was evident from the plot (Figure 5-10). The correlation value for this participant reduces with subsequent tests to weak coactivation with the full splint (r=0.33), and no appreciable coactivation with the palm splint (r=0.28) and air splint (r=0.23). When comparing the group means for each of the different hand support conditions there is little difference between the means for both tracking tasks.

Table 5-4 Correlation coefficients of flexor and extensor muscle activity during random step and sinusoidal tracking tasks with four different hand supports; Positive correlation = more coactivation, negative correlation = reciprocal activation.

Participant	Resistance 10% Extensor MVC (Nm)	Tracking	Correlation Coefficients			
			Handle	Full splint	Palm Splint	Air Splint
1	0.18	Step	0.65**	0.33*	0.28	0.23
		Sinusoidal	0.01	0.05	-0.08	-0.22
2	0.24	Step	-0.11	-0.24	-0.36	-0.27
		Sinusoidal	-0.76	-0.82	-0.74	-0.61
3	0.61	Step	-0.13	-0.11	-0.03	-0.01
		Sinusoidal	-0.63	-0.64	-0.56	-0.53
4	0.5	Step	-0.23	-0.28	-0.19	-0.16
		Sinusoidal	-0.71	-0.68	-0.72	-0.62
Group Mean (SD)		Step	0.05 (0.41)	-0.08 (0.28)	-0.08 (0.27)	-0.05 (0.22)
		Sinusoidal	-0.52 (0.36)	-0.52 (0.39)	-0.53 (0.31)	-0.50 (0.19)

* weak coactivation; ** moderate to strong coactivation

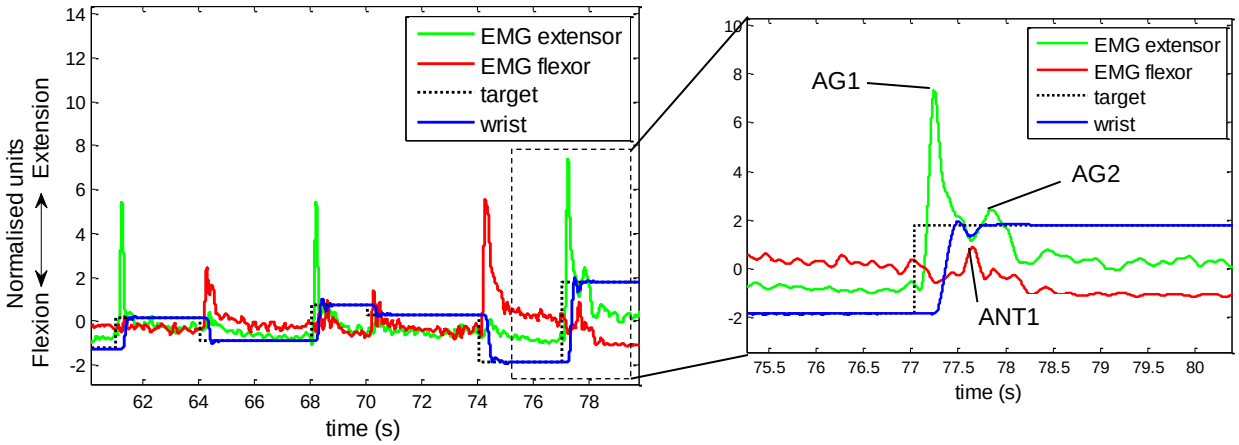


Figure 5-9 Example of unimpaired muscle activation during the step tracking task using the air splint showing reciprocal activation – alternating agonist activation of the extensor and flexor. The enlarged section is an extension movement showing a classic triphasic activation pattern of agonist (AG1) then antagonist (ANT1), then agonist again (AG2)

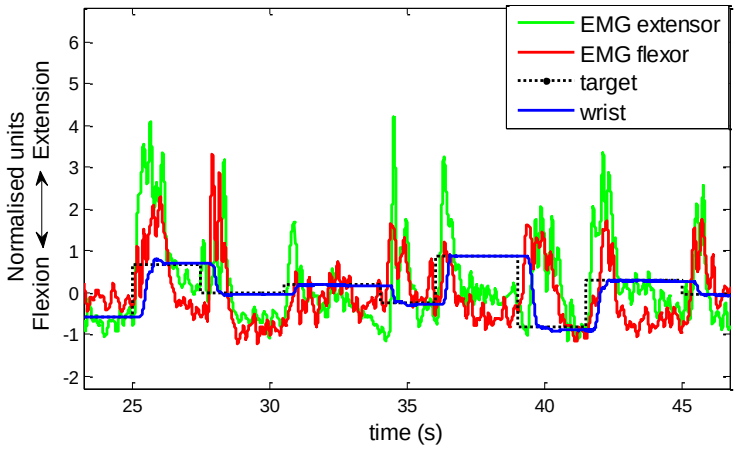


Figure 5-10 Example of unimpaired muscle activation during the step tracking task using the handle showing some coactivation of the extensor (green) and flexor (red)

5.3.4. Discussion

This was the first trial of the step tracking test and feedback from participants allowed decisions to be made on the timing parameters of the test - details of the final tests decided upon for the Main Study are defined at the end of this Chapter in Section 5.6 Table 5-19. As resistance setting was dependent on the speed at which the lever arm was moved, it was impossible to be accurate unless a tracking task was used to standardise the speed and range of movement when moving the lever arm. When this was used accuracy in setting the level of resistance at the slip clutch was approximately ±0.02Nm, which, although was not ideal, was considered suitable for this study as the 10% of extensor MVC mean for these unimpaired participants was 0.62 Nm and range 0.43 to 0.89. Older unimpaired and stroke impaired participants are likely to have smaller MVC torques, and this needed further investigation in Pilot Study 3.

5.3.5. Conclusions

1. Following usability testing with unimpaired participants, modifications made to the wrist rig system and tests will be further trialled in Pilot Study 3 with impaired and older unimpaired participants
2. The perspectives of the participants on the usability of the different hand supports suggest that the full hand and palm splints are not useable, but that the handle and air splint could be used with some modification to the handle to include an extra padded bar next to the dorsal surface of the hand against which participants can push when performing the extensor MVC.
3. There was little difference in mean coactivation values seen between the different hand positions during both tracking tasks, though this is limited by the small number of participants tested. Coactivation was seen in one participant during the random step

tracking task, though this reduced over time with each hand position tested. The difference seen between hand position conditions, therefore, may be a trend due to a learning effect.

4. Two of the four hand splints, the handle and air splint will be further tested with patients in the next Pilot Study using all the active and passive tests, in order to conclude which hand support should be used in the main patient and unimpaired studies.

5.4. Pilot Study 3

5.4.1. Objectives

The purpose of this Pilot Study was the evaluation of the modified wrist rig components and proposed test variables with a small group of impaired participants with chronic stroke who were able to tolerate repeated procedures and give feedback, and a group of older unimpaired participants. The specific objectives were as follows:

5.4.1.1. Define tests

- Evaluate the sinusoidal and step tracking tasks that were modified in Pilot Study 2
- Evaluate the level of resistance set at a percentage of participants' extension MVC force – 5% or 10%
- Evaluate the Stretch response test - passive sinusoidal movements of ±20º around the mid-point of each participant's active ROM at 1.5Hz and 0.5Hz. Whereas in a previous study the stretch response test was ±30º at 1.5Hz (Turk et al. 2008b), a displacement of ±20º was chosen because it was the same as the active sinusoidal test and therefore results could more easily be compared.
- Evaluate the speed and number of repetitions needed for the Torque/angle test – six slow passive ramp and hold movements at 5º/second (slow enough to exclude stretch reflex activation). The greater the number of repetitions, the more likely to get a number of cycles without neural activity and the more accurate the measurement. However a balance was needed with the length of time to undertake the test. At 5º/second speed the test time could be long (four minutes for six repetitions), an important factor to consider with older patients with acute stroke who fatigue easily.

5.4.1.2. Assess usability

As well as the usability of the tests described above, the comfort of the wrist rig as a whole was evaluated from the perspective of patients and older unimpaired adults.

5.4.1.3. Derive indices

In Pilot Study 1 methods to derive a coactivation index were considered (see Section 5.2). In Pilot Study 3 methods to derive indices to characterise the following impairments were assessed:

1. Active ROM
2. Passive ROM
3. Isometric Force of flexors and extensors
4. Wrist movement tracking accuracy – sinusoidal and step tracking
5. Coactivation – sinusoidal and step tracking
6. Timing of extensor muscle activation – step tracking
7. Stretch reflex response of the wrist and finger flexors
8. Biomechanical stiffness of the wrist and finger flexors (and other soft tissues)

Each impairment index was evaluated to determine how they differentiate between those impaired from stroke and neurologically intact controls.

5.4.1.4. Evaluate two hand positions

The effect of two different hand positions (the handle with fingers in flexion and the air splint with the fingers in extension) on the ability to conduct the tests and comfort was evaluated. Differences between hand positions for each of the impairment variables and how they differentiate between the impaired and non-impaired groups were evaluated

5.4.2. Methods

5.4.2.1. Participants

Participants with post-stroke hemiplegia (n=7) were recruited as a convenience sample from the Faculty of Health Sciences' Participant Register. Unimpaired participants (n=9) were recruited from a University of the Third Age group. Selection criteria for both groups are detailed in the Methodology Chapter 4 Section 4.4. Participant characteristics are shown in Table 5-5.

Table 5-5 Demographic characteristics of Pilot Study 3 participants

		Impaired (N=7)	Unimpaired (N=9)
Age (years)	Mean (SD)	60.43 (8.02)	75.89 (3.44)
	Min - max	49 – 74	71 – 81
Gender	Male	4	1
	Female	3	8
Time from stroke (months)	Mean (SD)	79.57 (52.35)	N/A
	Min - max	41 – 192	
Side assessed	Right	1	9
	Left	6	0

5.4.2.2. Data collection

Following set up in the rig as described in the Methodology Chapter 4 Section 4.7, participants were tested with their hand positioned around the handle (Figure 5-8a) and in the air splint (Figure 5-8d) in a random order. The following tests were carried out using both hand positions in the following order (for justification of tests and detail of how tests were conducted see Methodology Chapter 4 Section 4.8 and Appendix C):

- Active range of movement (AROM).
- Passive range of movement (PROM).
- Flexion and extension maximal isometric contractions (MVC) at 0˚ and 20˚ flexion.
- Torque/angle test: six repetitions of passive ramp movement from full passive flexion to full extension at 5˚/s.
- Stretch response test: passive ±20˚ displacement at 1.5 Hz to measure the stretch response at high velocity and 0.5 Hz to compare stretch response with muscle activation during the active tracking task.
- Active tracking tasks, first non-resisted then with resistance set at 5% and 10% MVC
    - Sinusoidal tracking test at 0.5Hz, ± 20˚, for 60 seconds
    - Random step tracking task with increasing displacement of the target from 5˚ to 40˚ in 15 second blocks for 90 seconds and random 2-4 second target rest intervals.

To determine the usability of the two hand splints and the tests conducted with participants, the questions asked previously in Pilot Study 2 (Section 5.3.2.2) were asked at appropriate times throughout the testing process. Answers were recorded on the participant record form (Appendix H).

Participants' activity was assessed using the modified WMFT (detailed in Methodology Chapter 4, Section 4.10 and instruction manual in Appendix F). The assessments were video-taped, viewed and rescored by the researcher to improve her scoring ability. They were also viewed and scored by a moderator, a research therapist at University of East Anglia. Where there was scoring inconsistency due to lack of clarity, instructions were added to the manual.

5.4.3. Derivation of impairment indices

5.4.3.1. Introduction

From our previous research and knowledge from the literature, common post-stroke motor impairments were identified, which could be measured using the proposed tests conducted in the wrist rig (see Methodology Chapter 4 Section 4.11.2, Table 5-6). The following sections in this Chapter describe how the indices were derived to characterise motor impairments.

Table 5-6: The motor impairments that were measured in the wrist rig

Motor Impairments	Impairment measurement	Rig Test	Signals needed for measurement or index
Active range of Movement	AROM	AROM	Wrist movement angle
Passive Range of Movement	PROM	PROM	Wrist movement angle
Weakness	Isometric Force (IF)	Flexor and extensor MVC	Lever arm torque
Movement tracking performance	Overall tracking accuracy	Sinusoidal / Step Tracking	Target and wrist movement angle
	Accuracy at target end point	Step Tracking	Target and wrist movement angle
	Corrective overshooting at target end point	Step Tracking	Target and wrist movement angle
Muscle activation patterns	Coactivation	Sinusoidal / Step Tracking	EMG; target and wrist movement angle
	Muscle onset timing	Step Tracking	EMG; target and wrist movement angle
Spasticity	Neural response of flexor to passive stretch	Fast passive tracking	Flexor EMG; target and wrist movement angle
Non-neural stiffness	Non-neural resistance to passive stretch	Slow passive tracking	EMG; Lever arm torque; wrist movement angle

5.4.3.1. Range of movement

Active and passive range of movement was taken as the maximum angle range of flexion and extension recorded during the AROM and PROM tests.

5.4.3.2. Weakness

Weakness was measured as the maximum flexor and extensor isometric force (IF) (Nm) from the three trials of the flexor and extensor MVC tests, as has been used in previous studies (Ada et al. 2003; Canning et al. 1999; Colebatch et al. 1986).

5.4.3.3. Tracking indices (motor control accuracy)

Tracking indices have been developed to measure accuracy, speed and smoothness of the wrist movement compared to the tracking target during the two different tracking tests:

a) Step tracking indices (TIstep):

The step tracking task involved a series of discrete movements from which the accuracy in attaining the target, as well as movement control at the target end points can be assessed. Sixty seconds of data was included for analysis which included 17 random flexion and extension movements. The same sequence was used for all subjects. Step tracking was divided into movement phases (movement of the wrist to the target and any corrective sub-movements that occur within 1.5 seconds of the target change), and target phases (from the end of the movement phase until the next target change) (Figure 5-11 and Figure 5-13).

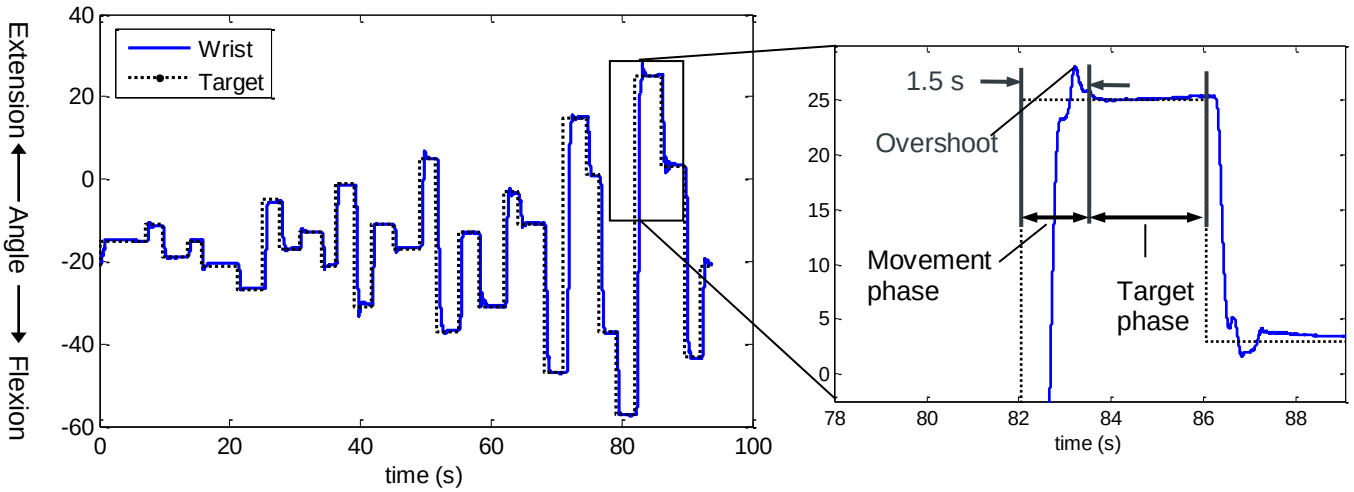


Figure 5-11: Example of step tracking undertaken by an unimpaired participant. The target (dotted line) moves in random steps of gradually increasing range of up to ±40° around the midpoint of the participant's active range of movement. The bold line represents wrist movement. The expanded section shows the movement phase (movement to target and slight overshoot lasting approximately 1.5 seconds) and target phase (holding target position) Visual analysis of impaired tracking data identified in different cases: inaccuracy during the movement phase and target phase, and range and number of corrective sub-movements (over- and under-shoot) during the target phase (see Figure 5-12 and Figure 5-13 for examples). It was thought important to assess the accuracy and smoothness of tracking for the total task (movement and target phases) and specifically to assess the ability to attain the target position and control the extent of corrective sub-movements at the target phase.

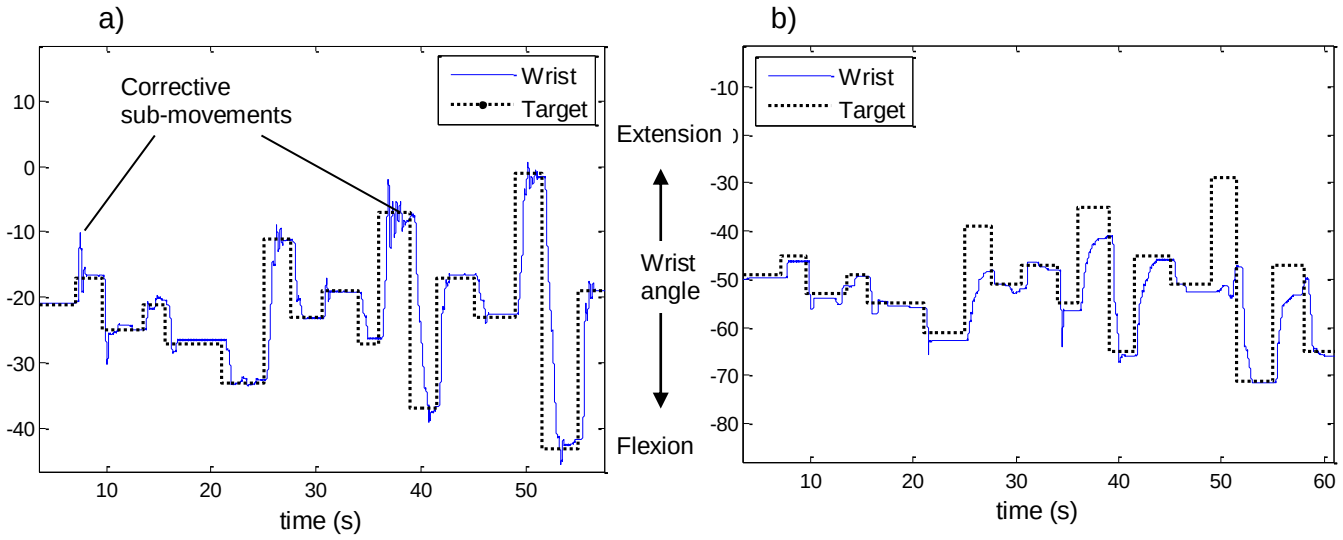


Figure 5-12 Examples of step tracking from two impaired participants: a) Participant has the ability to attain the target but has poor movement control at the target phase; b) Participant has difficulty attaining the target in extension which worsens with bigger amplitudes.

The following indices were derived:

The mean absolute error (MAE) between wrist movement and target was used to assess tracking accuracy (Miall et al. 2000; Weir et al. 1989).

$$\mathbf{TIstep(MAE)} = \frac{\mathbf{1}}{\mathbf{N}}\sum_{\mathbf{i-0}}^{\mathbf{N-1}}|\mathbf{w_i} - \mathbf{t_i}| \qquad \text{(Equation 1)}$$

where w_i is the wrist angle at sample i, t_i the corresponding target and the sum is taken over N samples in the recording selected for analysis. This index may be considered as measuring the area between the target and wrist, normalized by the duration of the recording selected for analysis. This is similar to the root mean square error (RMSE) used in other studies (Patten et al. 2003), but less sensitive to large errors, which are exaggerated by squaring. Two indices using MAE were derived:

1) MAE was calculated during the whole task i.e. all movement and target phases ($TIstep_{(totalMAE)}$). This index is a gross overall measure of tracking performance and does not quantify specific subtle differences between individuals in movement control such as speed of response, ability to attain the target and amount of over- and under-shoot at the target phases (corrective sub-movements).
2) MAE was calculated only at the target phase ($TIstep_{(targetMAE)}$). This index measures specifically the ability to attain and maintain the target position.

Other indices were derived to characterise the amount of corrective sub-movements (over- and under-shoot) specifically at the target phases (Figure 5-13):

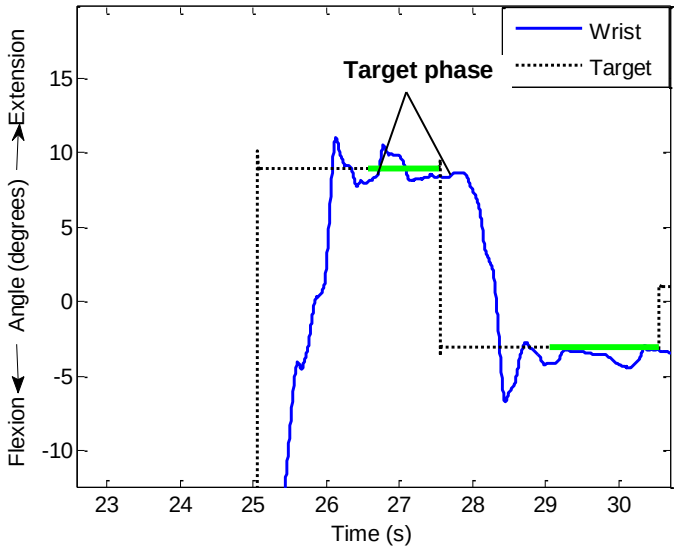


Figure 5-13 An example of impaired control during step tracking showing the target phase sections (bold green) during which the path lengths and standard deviation of the wrist angle are calculated then summed and averaged (greater over- and undershoot indicates larger path length and standard deviation).

3) The total variability of the wrist position during each end target position was measured using the path length of the angle data (i.e. the more over-and under-shoot from the target position, the longer the path length and the higher the variability). Path length has been used in previous motor control research using step tracking (Feys et al. 2006) and in this research was defined as the total distance of travel by the wrist, normalized by the length of the target phase recording:

$$\mathrm{TIstep(PL)} = \frac{1}{(N-1)} \sum_{i=1}^{N-1} \left| w_i - w_{i-1} \right| \qquad \text{(Equation 2)}$$

The path length was measured in units of degrees per sample (using the decimated sampling rate of 200 Hz) and the sum was taken over all the samples in the target phase. This index does not depend on how well subjects attain the target, but rather the extent of sub-movements at the target phase and is sensitive to the smoothness of fluctuations.

4) The range of variance at each end target position was calculated using the standard deviation (SD) of the wrist angle (i.e. the larger the range of over-and under-shoot displacement, the greater the standard deviation), as follows:

$$\mathbf{TIstep(SD)} = \sqrt{\frac{\sum(w_i - \bar{w})^2}{N-1}} \qquad \text{(Equation 3)}$$

b) Sinusoidal tracking index (TIsin):

Examples of unimpaired and impaired sinusoidal tracking performance can be seen in Figure 5-14. Prior to analysis the signals were visually analysed and the initial eight seconds of each test were removed to exclude the resting baseline and first two cycles which often showed poor tracking due to the need for initial adjustment to the test and were therefore unrepresentative of overall performance. In previous work (Notley SV et al. 2007) on sine tracking, we found that the RMS error did not correlate well with functional performance (Action Research Arm Test) and is therefore not reconsidered in this current work. Instead, our previous recommendation has been followed by using correlation:

$$\mathrm{TIsin} = \max\left\{ \frac{1}{N} \sum_{i=\tau}^{N-1} w_i t\langle_{i+\tau}\rangle \right\} \qquad \text{(Equation 4)}$$

where τ is a delay, which varies over a range of ±1.2 s (i.e. a little over half a cycle for the 0.5 Hz sinusoidal target). The maximum value of the correlation is used in order to disregard delay or target anticipation the subjects may show in tracking the periodically moving target. The mean value of w and t are removed prior to this analysis to disregard any offset in tracking. One can regard this parameter as a correlation coefficient between target and wrist movement, which has not been normalized to the range ±1, and is thus sensitive to the amplitude of wrist movement, as well as the shape of the movement. Normalized correlation is unsuitable since it only quantifies the similarity in signal shape of target and wrist movements, regardless of the amplitude of wrist deflections; the amplitude is clearly important in the assessment of patients' wrist control.

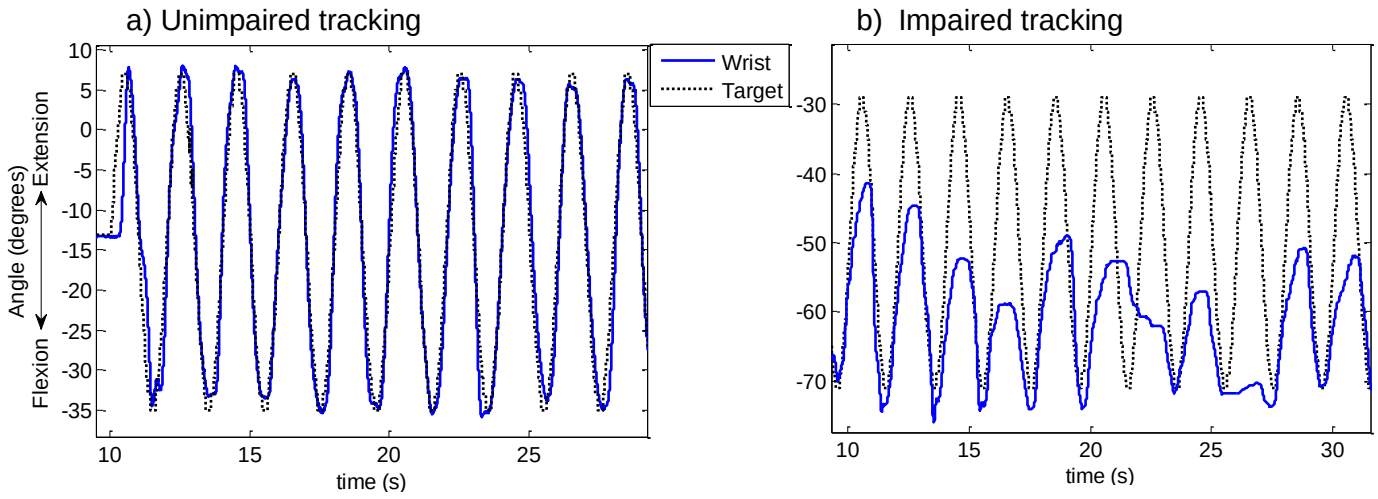


Figure 5-14 Examples of unimpaired and impaired sinusoidal tracking performance at 0.5 Hz ±20^{o} around the midpoint of the participant's active range of movement, showing target and wrist movement. The impaired tracking shows difficulty with extension movement which becomes progressively worse over time.

5.4.3.4. Coactivation index during both sine and step tracking

Following the initial evaluation of methods to measure coactivation during sinusoidal tracking in Pilot Study 1 (Section 5.2), further investigation of correlation analysis methods for the coactivation index was undertaken using both sinusoidal and step tracking data from Pilot Study 3. Sinusoidal tracking (5 to 55 seconds into the recording) and step tracking (5 to 65 seconds) data were selected. Three correlation analyses each related to the extensor phase were performed:

- CI $_{(extmovt)}$ - Correlation during extension movement only, based on the angle data from peak flexion to peak extension.
- CI $_{(incext)}$ - Correlation based on the extensor EMG signal when the extensor EMG was increasing.
- CI $_{(peakext)}$ - Correlation based on the extensor EMG signal during peak extensor EMG.

Correlation of the whole sample (the EMG envelopes during both flexion and extension movements) that was evaluated in Pilot Study 1 and 2 was not included because it did not quantify coactivation specifically during the extension phase, and this is what is most problematic to stroke patients. The graphical results for each of the three methods were visually analysed (for examples see Figure 5-22 and Figure 5-23 in the Results Section 5.4.4.2) and descriptive statistics were calculated and compared.

5.4.3.5. Extensor muscle onset time

Extensor muscle onset timing was calculated across all 11 discrete extension movements to attain the target in step tracking (Figure 5-15); it was not investigated during sine-tracking because movement was continuous and graded. Extensor muscle timing was chosen

because activating the extensors is commonly more problematic than the flexors in the upper limb for patients after stroke. In the literature review, computer-based methods to determine muscle onset timing have been discussed (Chapter 2, Section 2.8). Rather than using recent advanced techniques in this study which are computationally intense, beyond the scope of this project and too complex for a clinically-based measurement tool, muscle onset was detected by comparing the EMG envelope with a threshold based on the envelope during a baseline period (Hodges & Bui 1996). This method has an advantage in that it requires relatively uncomplicated processing algorithms, but is criticized for not being based directly on the raw (i.e. physiological origin) of the signal. Furthermore if a time delay is introduced by the filtering a methodological bias will result; however in this study the filtering method used corrects for this. All previous studies using this method have used a global resting baseline (typically before the start of the task) but differing processing parameter, such as the degree of smoothing the EMG signal (the frequency of the low pass filter (LPF)), the width of the sample window (in ms) for a moving average filter (MAF), and the magnitude of the deviation from the baseline selected as the threshold to define the beginning of muscle activation (number of standard deviations (SD)). Others have suggested that local analysis of the signal, where muscle onset is measured with respect to baseline EMG values taken from just before each individual movement starts, may lead to greater accuracy (Khalil & Duchene 2000).

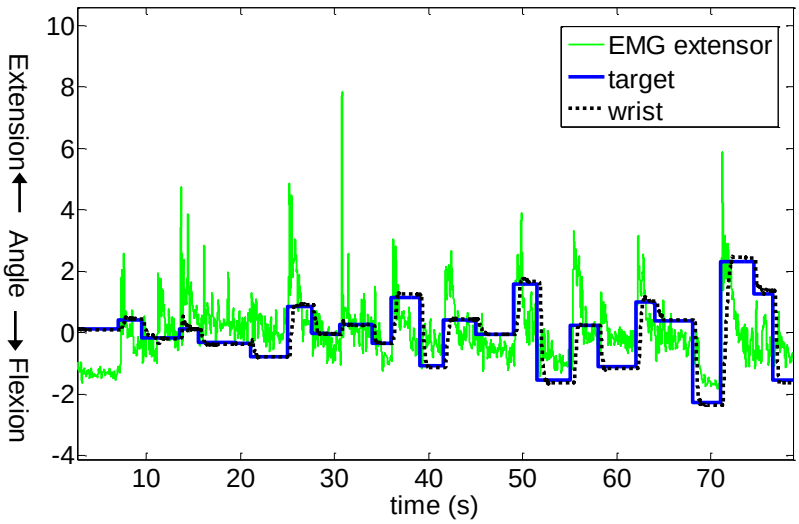


Figure 5-15: An example of the step tracking task conducted by an unimpaired participant and showing the extensor EMG envelope. Note the peaks of extensor activity in phase with each step movement into extension, and occasional smaller peaks during flexion, corresponding to corrective sub-movements.

The parameters for the muscle onset timing algorithm were chosen by methods used previously (Hodges & Bui 1996) where visually determined onsets of the rectified raw signal were compared with those from the algorithm. The global baseline method was compared

against the local baseline method. With the global baseline, the LPF/SD/MAF parameter combinations of 50Hz/3 SD/25ms and 50 Hz/1 SD/50 ms respectively were tested because in a previous study computer determination using these parameters did not significantly vary from visually derived EMG onsets (Hodges & Bui 1996). The 50Hz/3 SD/no MAF combination was also assessed in order to evaluate the usefulness of the using the MAF as well as the LPF. As no previous studies have used thresholds based on local baselines to determine EMG onset, the LPF in this analysis was chosen to be 50Hz as in the global conditions. Two, three and four SD from the baseline was trialed and it was found from visual evaluation of plots that the 4SD threshold level was nearest to visually derived onsets. For the final data analysis six different parameter combinations were compared, as seen in Table 5-7. The global baseline was given by the extensor EMG envelope during a three second window prior to the first target step. The local baseline was given by the extensor EMG envelope during a one second window prior to each movement of the target in the direction of extension.

These tests were carried out on data from four participants (two impaired and two unimpaired) purposefully selected from the study sample because they covered the full range of step tracking performances and amount of background EMG activity (SNR). Extensor muscle onset timing was calculated as the time-lag between the target moving and the detected EMG activation onset. For the six computer analysis conditions, each of the 11 muscle onset timings and the overall mean timing were recorded. To compare methods the mean timings, and differences between the mean computer-based timings and the mean visually determined onset timings, are presented. To compare the methods Bland Altman 95% limits of agreement, given by the mean difference between the visual minus each of the computer-based readings plus or minus twice the SD of the differences, were calculated.

Table 5-7: The six low pass filter / standard deviation / moving average filter parameter combinations for the computer-based analysis, three using a global baseline and three using local baselines

Baseline condition	LPF	SD	MAF
Global 1	50Hz	3SD	none
Global 2	50Hz	1SD	100 samples / 50ms
Global 3	50Hz	3SD	50 samples / 25ms
Local 1	50Hz	4SD	none
Local 2	50Hz	4SD	50 samples / 25 ms
Local 3	50Hz	4SD	20 samples / 10 ms

LPF – low pass filter; SD – standard deviation from the mean baseline for the threshold; MAF – moving average filter

5.4.3.6. Stretch index

The stretch index characterises the flexor EMG stretch response (SR) to passive movement. The target, angle and flexor EMG data from the 1.5Hz speed ±20˚ displacement test conducted in Pilot Study 3 were edited then analysed.

a) Method of editing data

The signals from each file were plotted and visually checked for any artefacts. As the passive tracking was undertaken manually, it was important to ensure that the data used for analysis corresponded to periods where the passive tracking was most accurate to the set target. Data were included from four to 40 seconds (36 seconds, corresponding to 54 cycles of data for analysis) of the task. Extension cycles (from maximum flexion to maximum extension) were excluded where displacement was more than ±5˚ of the target extension peak and/or more than ±10˚ of the target flexion peak. Greater accuracy was deemed necessary at the extension peak as the peak stretch response lies between zero crossing and peak extension. Less accuracy at full flexion was accepted due to physical restrictions of the rig and participant comfort (size of abdomen).

b) Method of analysis

The flexor EMG envelope in the section of each extension cycle was detected for analysis. Where a stretch response was seen it started approximately at the start of wrist extension, or just after (see Figure 5-16 and Figure 5-17).

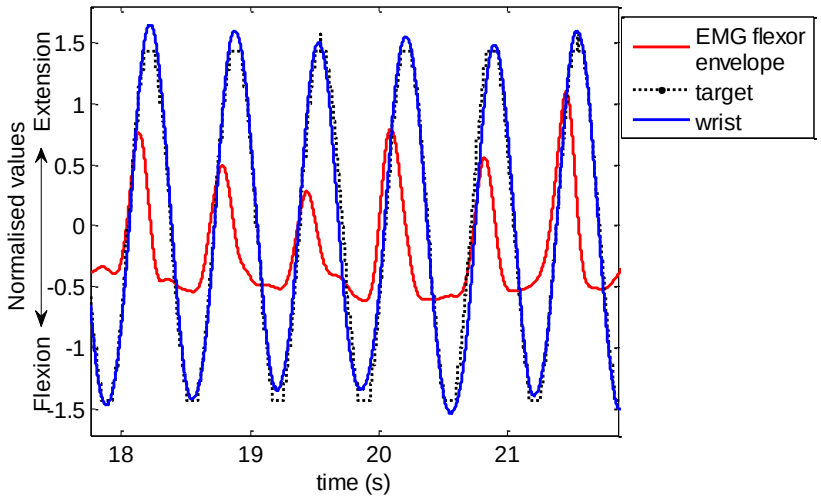


Figure 5-16 Passive sinusoidal tracking at 1.5 Hz showing target (black), wrist movement (blue) and flexor EMG envelope (red). This is an example of an impaired participant with a flexor stretch response during the extension phase.

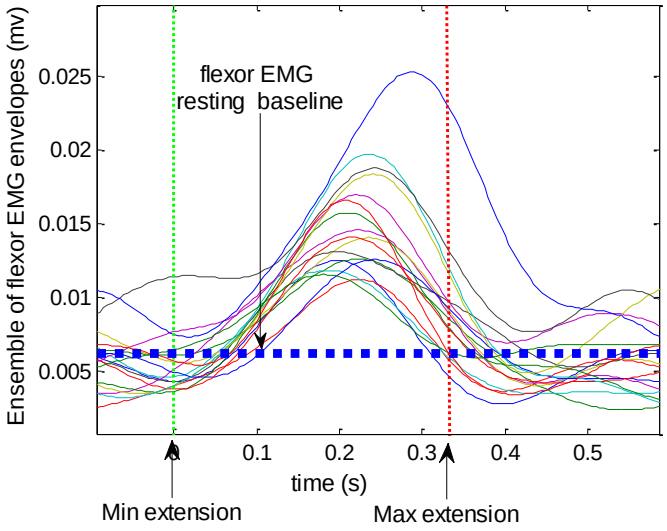


Figure 5-17 Plot to illustrate the method used to calculate stretch response showing data from an impaired participant with a stretch reflex response. The index was calculated as the area under the flexor EMG envelope curve normalised by the length of the extension phase for each cycle, minus the resting baseline.

To quantify flexor response the stretch index was calculated (Figure 5-17), as follows:

$$\mathbf{SI(area-BL)} = \frac{\mathbf{1}}{\boldsymbol{M}}\sum_{\boldsymbol{i}}\left(\boldsymbol{EMG_{fe}(i)} - \overline{\boldsymbol{EMG_{fe}}}\boldsymbol{(baseline)}\right) \qquad \text{(Equation 5)}$$

where $EMG_{\mathrm{fe}}(i)$ is the flexor EMG envelope at sample i, and the sum is calculated over all samples from maximum flexion to maximum extension, for each of the M cycles, and $\overline{EMG_{\mathrm{fe}}}(baseline)$ is the average value of the flexor EMG envelope during the baseline period. This might thus be considered as the average area (per cycle) of the EMG above baseline. For the calculation of the baseline a moving average filter with one second window was applied from zero to four seconds of data (the period of rest before the start of the passive tracking). The baseline flexor EMG level was taken as the minimum of the moving average windows. Although this method does not involve normalisation of the EMG, it was appropriate for the purposes of this study to compare the stretch response within participants using two hand positions. Visual analysis of unimpaired stretch tests, however, showed that some participants, despite clear instructions and encouragement, appeared to be unable to avoid flexor activity during the extensor stretch Figure 5-18. This voluntary activity looked very similar to the stretch reflex response seen in some patients, but its presence was more variable, whereas if the stretch response was present it appeared in every cycle.

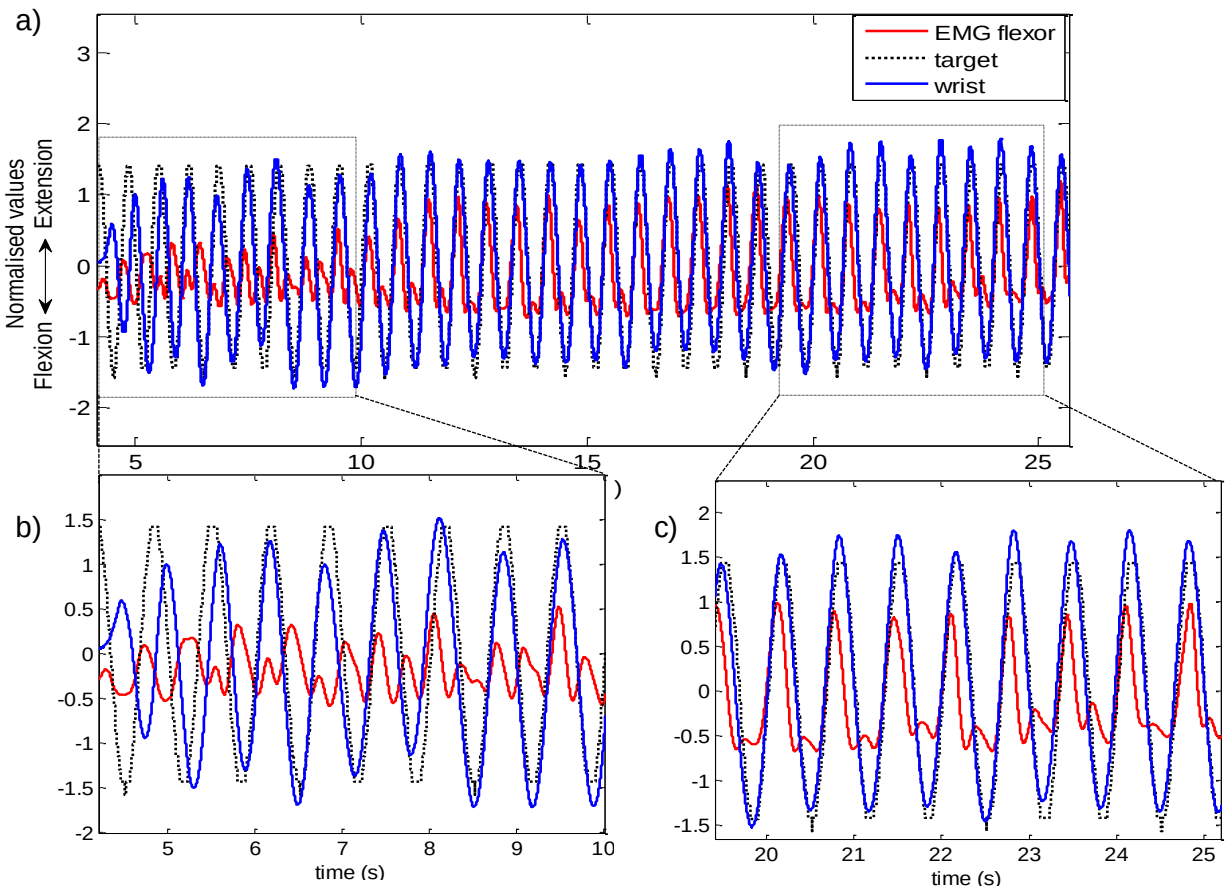


Figure 5-18 a-c: An example of unimpaired passive sinusoidal tracking at 1.5 Hz showing voluntary flexor activity from mid to end of the extension phase possibly as protection from the stretch. This activity was variable between cycles (compare section b and section c).

The stretch index calculation was therefore modified in an attempt to exclude the flexor activity in the unimpaired group. The area under the flexor EMG envelope curve minus the resting baseline EMG was determined during a -5º and 18º window of the extension phase for each cycle (rather than the full extension phase -20º to +20º), and the mean across cycles was then calculated (Figure 5-19). This window was where most stretch reflex response peaks occurred, whereas most unimpaired flexor activity peaks occurred after 18º.

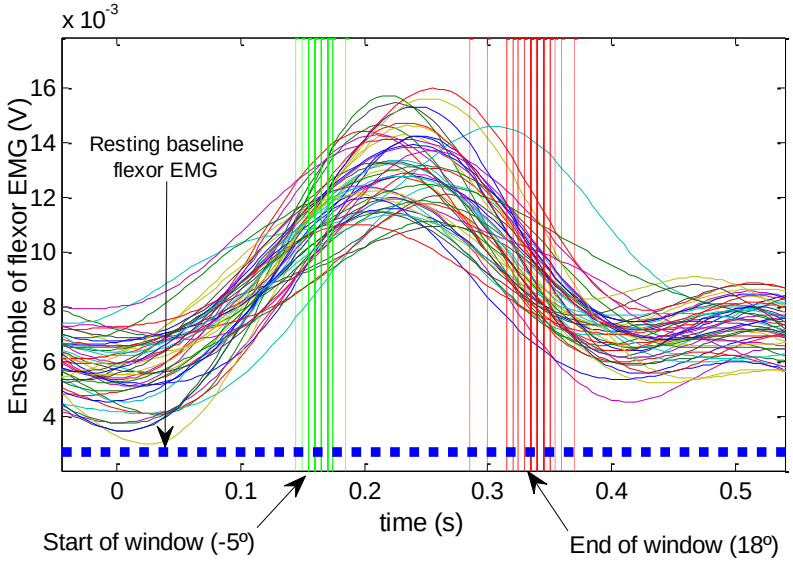


Figure 5-19 Plot to illustrate the modified stretch response calculation showing data from an impaired participant with a stretch reflex response. The area under the flexor EMG envelope minus the resting baseline EMG for each cycle was taken during a -5º to 18º window. The start and end points of the window varies slightly for each cycle because the timing of the manual tracking is slightly different.

5.4.3.7. Torque/angle index

Secondary, non-neural mechanical changes in the muscle and soft tissue may restrict voluntary movement. In deciding upon an intervention and measuring response, it is important for a therapist to know whether the stiffness experienced by the patient, or detected on passive movement, is of neural or non-neural origin. By measuring both the stretch response (neural) and the resistance to movement in the absence of EMG activity (non-neural) the relative importance of each can be examined. Passive non-neural stiffness was characterised by quantifying the torque around the wrist applied by soft tissues during the passive ramp and hold stretch tests at 10˚/s and 5˚/s speed. Target and wrist angle, flexor and extensor EMG, and torque data were used for this analysis.

c) Editing of data

This is a measure of non-neural passive stiffness and thus EMG activity during the passive stretch will affect the calculation. Flexor activity (voluntary or stretch reflex) may increase flexor stiffness and extensor activity (participant assisting the movement) may reduce stiffness. Prior to calculation of the torque the first cycle was automatically excluded in order to minimise initial thixotrophic effects and to allow participants time to relax and minimise EMG activation. However, inspection of EMG during the other cycles showed that, in spite of clear instructions and encouragement, some impaired and unimpaired participants appeared to be unable to consistently avoid flexor and extensor muscle activation in phase with

passive wrist movement. The data were therefore edited to exclude any cycles with flexor and/ or extensor EMG envelope amplitudes above a set threshold (Figure 5-20). Baseline flexor and extensor EMG values were calculated by applying a moving average filter with a one second window during an initial five second rest period and taking the mean value of the minimum window. When the flexor and extensor EMG envelope increased more than three standard deviations from the baseline, the muscles were considered to be active and the cycles automatically excluded (Figure 5-20). This threshold level has been used in other spasticity measurement research (Pisano et al. 2000).

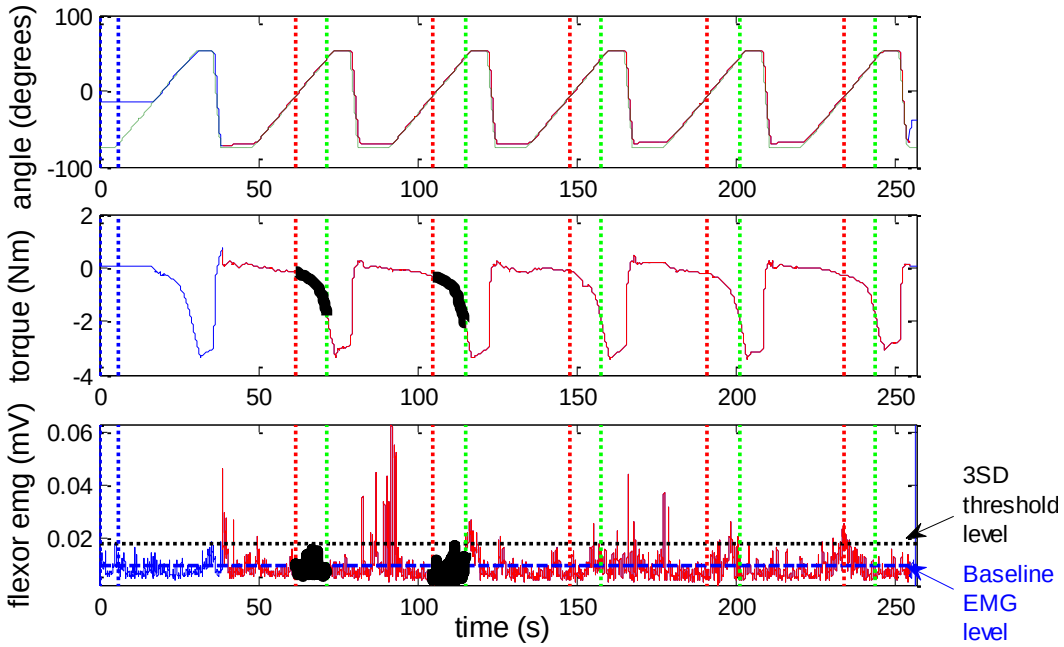


Figure 5-20 An example of torque-angle test data from an impaired participant. The top graph shows the wrist and target angle data, with six ramp and hold extension movements. The sections between the red and green dotted vertical lines represent the 50º period of data that was used for analysis. The middle graph is the torque which increases in magnitude with extension. The bottom graph is the flexor EMG with a resting baseline flexor EMG level (blue dotted) and a threshold 3SD above the baseline (black dotted). The two cycles that are included for the torque analysis (bold black) are those where the flexor EMG (and extensor, but not shown here) does not exceed the threshold.

d) Methods of analysis

For each cycle included for analysis, the torque angle curve was determined over 50˚ at the end of the passive extension range, ending 10˚ from the maximal extension angle to avoid a change in speed due to deceleration. Firstly an index that characterises the changes in torque with increasing extension angle was determined. The torque angle index (TAI) was calculated as the gradient of the torque angle curves for all cycles, as illustrated in Figure 5-21.

The torque-angle index assumes that stiffness linearly increases with increasing extension angle. However, on visualisation of the data it could be seen that a linear fit is only a rough approximation and furthermore for some patients the gradient of their torque angle curve was quite flat i.e. although their stiffness was high it did not alter much with changing angle. A second index was derived that simply measures the mean torque without taking into account changing angle. The mean torque index (MTI) was the centre torque value of the 50˚ regression line i.e. the mean torque, which is also the torque at the mean angle.

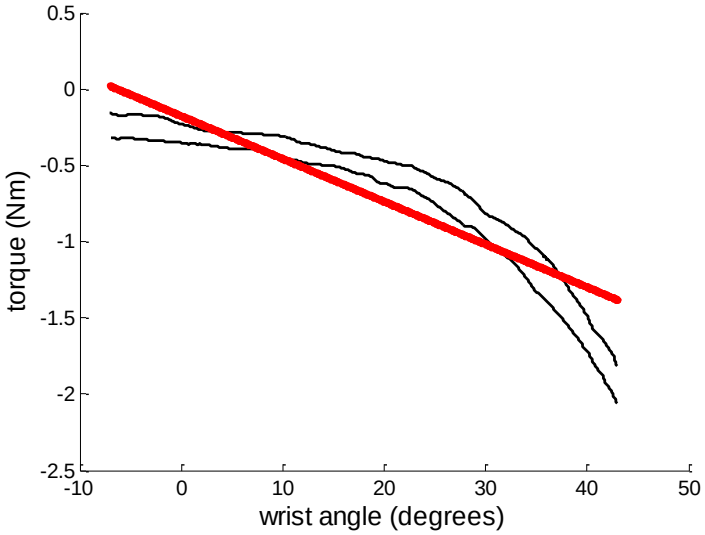


Figure 5-21 A line graph showing the two torque-angle curves over a 50º period included in the torque-angle analysis from the example in Figure 5-20. The red bold line is a regression line, and the torque-angle index is calculated as the slope of this line, whereas the mean torque index corresponds to the centre torque value of that distribution.

5.4.3.8. Statistical Analysis

- To evaluate how the measurement indices derived from the tests data differentiate between those impaired from stroke and neurologically intact controls descriptive statistics for each index for the impaired and unimpaired groups were calculated. Differences between the impaired and unimpaired groups were evaluated using two sample t tests with the statistical significance level set at $p<0.05$.
- To assess the effect of two different hand positions on the test results, descriptive statistics of a selected number of impairment indices were calculated. The impairment indices were selected depending on how well they differentiated between impaired and unimpaired. Differences between hand positions for each of the impairment variables and between impaired and non-impaired groups were determined using repeated measures ANOVA.

5.4.4. Results

Of the 16 participants recruited for Pilot Study 3, data was missing from one impaired participant for the tests using the handle because his high level of spasticity and contractures meant that he was not able to complete any of the tests (see Results Section 5.4.4.3). Due to technical problems data was missing for two unimpaired participants for the resisted tracking tests i.e. sine and step tracking and coactivation indices for handle and air splint positions.

5.4.4.1. Defining the tests

- The sinusoidal and step tracking tasks that were modified in Pilot Study 2 worked well with the participants in Pilot Study 3 and no further modifications were made
- When setting the level of resistance for the tracking tasks at a percentage of participants' extension MVC force, it quickly became obvious after testing the first few participants using 5% and 10%, that 5% MVC resistance was not challenging enough. The resistance was set at 10% for all further participants.
- Visual analysis of stretch response test data (passive sinusoidal movements of ±20º at 1.5Hz) showed that a number of unimpaired participants, despite encouragement, were unable to prevent voluntary activation of their flexors (as described in Section 5.4.3.6). As such their stretch index was almost as high as those patients with stretch reflex activity and it was difficult to distinguish between those with spasticity and those without – see Section 5.4.4.2 for data.
- Visual analysis of the Torque/angle test (passive ramp and hold movements at 5º/second) showed that six repetitions were needed to ensure that for most participants at least one cycle without neural activity could be included in the analysis. However, following editing of the data to remove cycles with neural activity, one impaired participant's data could not be included because a flexor reflex response was present at each stretch cycle; two unimpaired participants' data were excluded because despite encouragement they were unable to prevent extensor activity at each stretch cycle.

5.4.4.1. General Usability

All participants found the rig comfortable; skin contact with the straps, elbow stop and air splint caused minimal reddening which disappeared within 30 minutes.

5.4.4.2. Derivation of indices

A summary of the data for the derived impairment indices for both impaired and unimpaired groups, with between group mean differences, 95% confidence intervals and *P* values (where appropriate) are shown in Table 5-8 (ROM and isometric force), Table 5-9 (tracking

accuracy), Table 5-10 (coactivation), Table 5-11 and Table 5-12 (extensor onset timing) and Table 5-13 (stretch response and torque).

Range of movement and isometric force: Although flexion, extension and total ROM was recorded, only extension was presented (Table 5-8) as this is the direction of interest and flexion ROM was often not accurate due to the physical restrictions of the rig and size of the participant's abdomen. There were statistically significant differences between impaired and unimpaired participants in active ROM, but not passive ROM. Weakness was quantified by isometric force. With this sample of participants there was a statistically significant difference between impaired and unimpaired in extension IF, not flexion IF (Table 5-8).

Table 5-8 Differences in values for extension range of movement and isometric muscle force in the impaired (N=7) and unimpaired (N=9) groups. Statistically significant *P* values are in bold.

Test	Range of Movement (ROM) Isometric Force (IF)	Impaired Mean (SD) Min-max	Unimpaired Mean (SD) Min-max	Mean difference [95% CI]	*P*
Active ROM	AROM extension (degrees)	-0.63 (48.36) -58.3 - 64.1	57.41 (9.96) 41.5 – 70.9	58 04 [13.25, 102.83]	**0.019**
Passive ROM	PROM extension (degrees)	54.06 (20.79) 23.1 - 79	66.89 (9.62) 43.5 – 74.4	12.83 [-32.40, 6.74]	0.169
MVC	IF Extension (Nm)	1.91 (2.19) 0 - 5.51	4.95 (2.60) 1.84 – 10.05	3.04 [0.41, 5.67]	**0.027**
	IF Flexion (Nm)	7.16 (4.42) 0.94 – 12.25	6.66 (3.49) 2.09 – 13.04	0.51 [-3.73, 4.74]	0.801

Tracking accuracy: For tracking accuracy (Table 5-9) all the derived indices reach statistical significance between the groups, except TI (target MAE) which did not quite reach the *P*<0.05 significance level.

Table 5-9 Differences in values for tracking accuracy indices in the impaired (N=7) and unimpaired (N=9) groups. Statistically significant *P* values are in bold.

Test	Tracking accuracy Indices (TI)	Impaired Mean (SD) Min-max	Unimpaired Mean (SD) Min-max	Mean difference [95% CI]	*P*
Sine tracking	$TI_{(CC)}$ (degrees^2)	112.99 (85.70) 3.81-205.60	226.14 (18.45) 203.96-258.65	113.15 [33.78, 192.52]	**0.012**
Step tracking	$TI_{(total\ MAE)}$ (degrees)	8.07 (4.07) 3.89-12.94	3.81 (0.54) 3.14-4.65	4.27 [0.50, 8.03]	**0.032**
	$TI_{(target\ MAE)}$ (degrees)	5.41 (5.58) 0.31-12.53	0.30 (0.08) 0.19-0.45	5.11 [-0.06, 10.27]	0.052
	$TI_{(path\ length)}$ (degrees/sample)	0.015 (0.002) 0.012-0.017	0.007 (0.001) 0.005-0.009	0.008 [0.006, 0.009]	**<0.001**
	$TI_{(SD)}$ (degrees)	0.69 (0.44) 0.15-1.36	0.06 (0.02) 0.02-0.09	0.63 [0.21, 1.04]	**0.009**

Coactivation: Mean values for the different methods of calculating the coactivation indices are shown in Table 5-10. There was no statistically significant difference for any of the methods, though correlation when extensor EMG is increasing showed the greatest mean difference between impaired and unimpaired. Visual analysis of individual sine and step tracking and EMG plots confirmed the findings in Pilot Study 1 that the correlation methods based on extension movement and during peak extensor EMG included normal antagonist activation which often occurred towards the end of the movement phase acting as a brake, whereas correlation when extensor EMG is increasing included the phase of agonist activity before the movement starts, resulting in better distinction between normal and abnormal coactivation (see Figure 5-22 and Figure 5-23).

Table 5-10 Differences in values for coactivation indices in the impaired (N=7) and unimpaired (N=9) groups. *P* value not shown as none reached statistical significance.

Test	Methods of Coactivation Indices (CI) (correlation coefficient)	Impaired (N=7) Mean (SD) Min-max	Unimpaired (N=9) Mean (SD) Min-max	Mean difference [95% CI]
Sine	$CI_{(increase\ extensor\ EMG)}$	0.14 (0.43)	-0.19 (0.31)	0.32
		-0.43 – 0.73	-0.53 – 0.45	[-0.10, 0.75]
	$CI_{(extension\ movement)}$	0.24 (0.31)	0.12 (0.19)	0.12
		-0.12 – 0.65	-0.09 – 0.52	[-0.15, 0.39]
	$CI_{(peak\ extensor\ EMG)}$	0.16 (0.21)	0.05 (0.16)	0.11
		-0.11 – 0.47	-0.11 – 0.32	[-0.09, 0.31]
Step	$CI_{(increase\ extensor\ EMG)}$	0.09 (0.34)	-0.08 (0.22)	0.17
		-0.26 – 0.60	-0.53 – 0.45	[-0.13, 0.47]
	$CI_{(extension\ movement)}$	0.16 (0.43)	0.20 (0.41)	-0.05
		-0.53 – 0.58	-0.53 – 0.72	[-0.50, 0.40]
	$CI_{(peak\ extensor\ EMG)}$	0.11 (0.36)	0.02 (0.21)	0.09
		-0.43 – 0.52	-0.19 – 0.52	[-0.21, 0.40]

a) bold sections: extensor EMG increasing b) bold sections: wrist extension

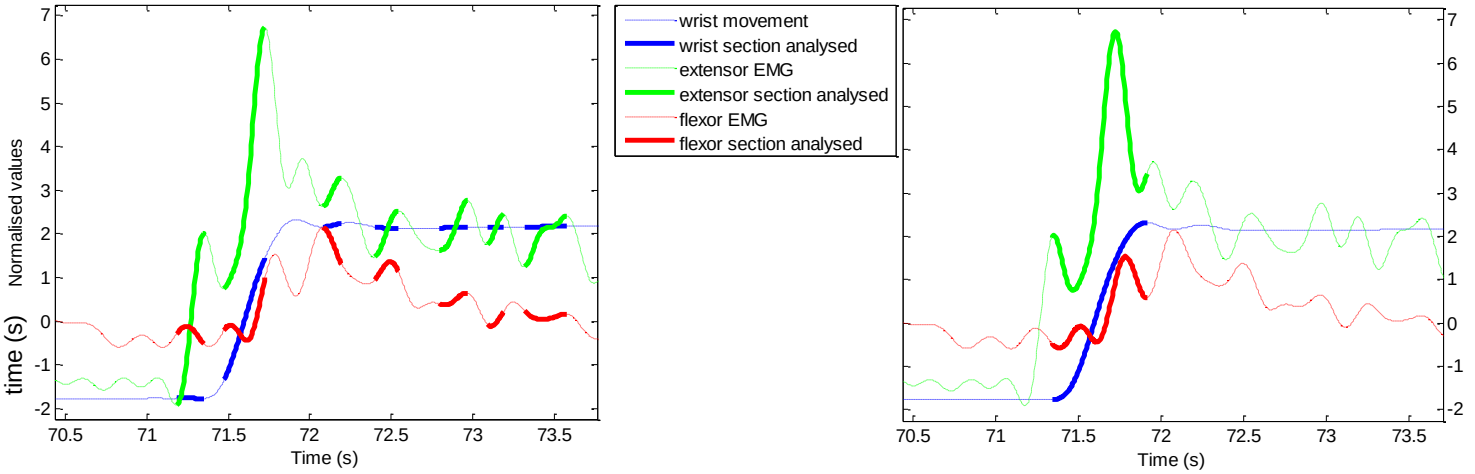


Figure 5-22 Example of unimpaired step tracking showing wrist movement (blue), extensor EMG (green) and flexor EMG (red). Lines in bold are sections of data included in the coactivation calculation based on: a) extensor EMG increasing; b) during wrist extension. This example shows the agonist extensor EMG increasing before and during extension to initiate and propel the movement, and the antagonist flexor EMG increasing towards the end of extension to act as a brake, while both muscles modulate with corrective sub-movements at the target position. The bold EMG curves in a) are graphically dissimilar and the resulting correlation coefficient, using this method, was r=-0.03 (no coactivation). The bold EMG curves in b) are similar and using this method the resulting correlation coefficient was r=0.72 (strong coactivation). This illustrates the ability of method a) to detect and exclude normal coactivation. Plots are displayed in arbitrary units in the vertical axis to facilitate visualization.

a) bold sections: extensor EMG increasing b) bold sections: wrist extension

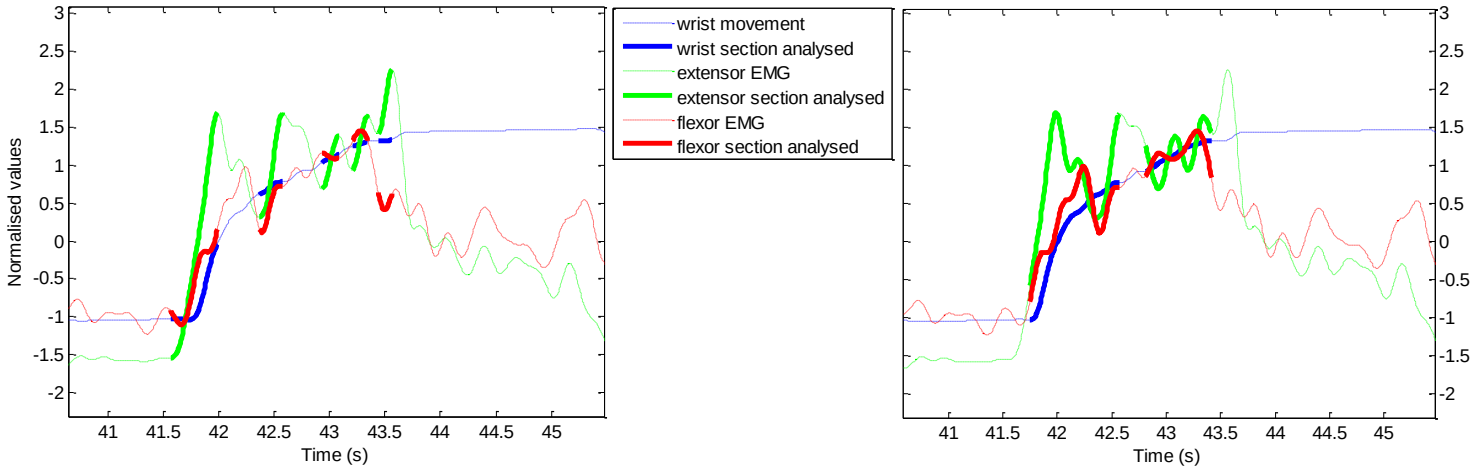
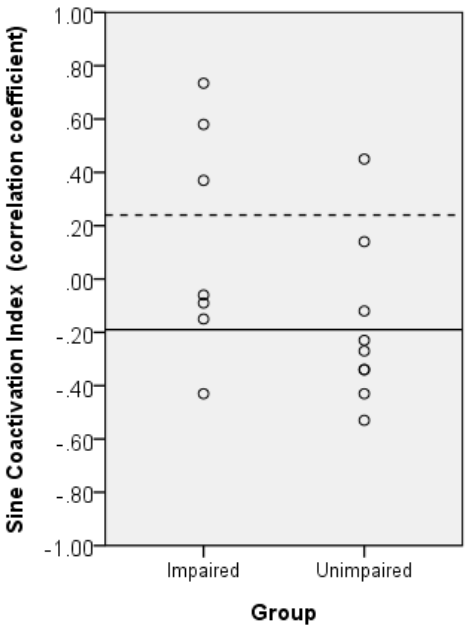


Figure 5-23 Example of impaired step tracking: bold lines are the sections of data included in the coactivation analysis based on: a) extensor EMG increasing; b) during wrist extension. In both a) and b) the EMG curves increase simultaneously (abnormal coactivation) and for each method the resulting correlation coefficients are similar (r=0.60, r=0.57 respectively).

Because no significant difference was seen between impaired and unimpaired groups, sine and step coactivation index values from the correlation during increase in extensor EMG method were further investigated at an individual level and can be seen in the dot plots in Figure 5-24 a & b. Values greater than two standard deviations from the unimpaired mean were taken as being beyond the normative range. For both coactivation indices there is much overlap between the groups though three impaired participants clearly lie outside the normative range. In particular it is interesting to note that there is an outlier in the unimpaired group in sine tracking with a coactivation index value as high as 0.45; visual analysis of the EMG traces confirmed their coactivation.

a)



b)

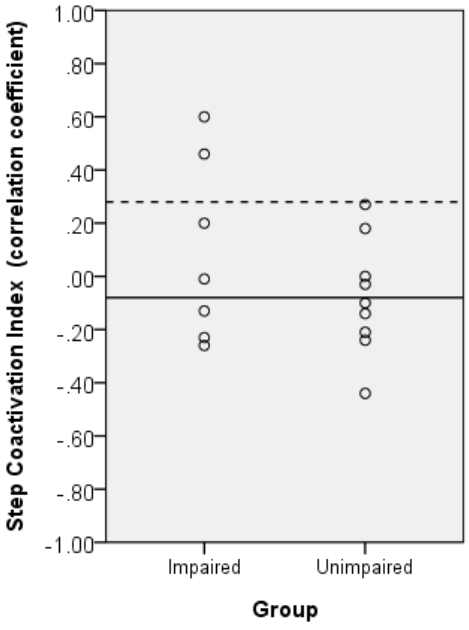


Figure 5-24: Dot plots for a) sine coactivation index and b) step coactivation index values based on when extensor EMG is increasing. Differences between participants in the impaired and unimpaired groups are shown. The horizontal line is the mean of the unimpaired group and the dashed line is the mean +2SD. Participants with values above this line are considered to have abnormal coactivation

Muscle onset timing: The mean differences and 95% limits of agreement between visually determined onsets (V) and the six computer based methods (G1-3 and L1-3) for each of the four participants and the group mean difference are shown in Table 5-11. The group mean difference between the visual determination and computer-based methods shows that the local baseline methods generally were more similar to the visual onsets than the global methods. The least difference was seen for method local 3 (LPF 50Hz / 4SD / MAF 10 ms).

Table 5-11: Mean differences and 95% limits of agreement between visually determined onsets (V) and the six computer based methods (G1-3 and L1-3) for each of the four participants and the group mean difference

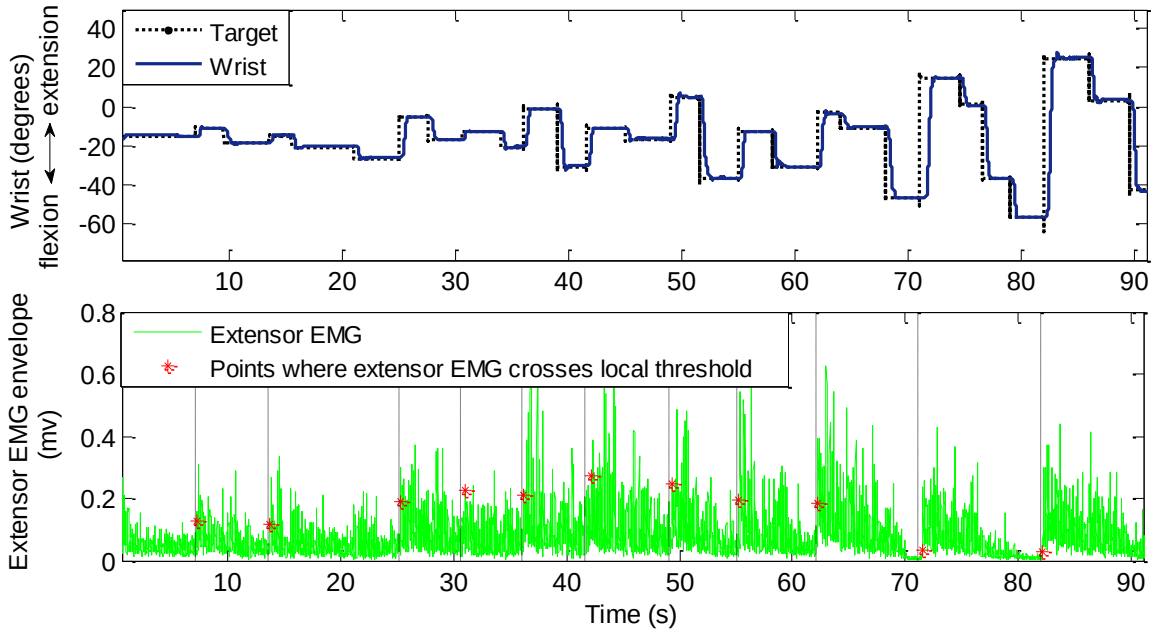
	Participant ID	053MB	057FR	016RO	021VS	Group Mean Difference (ms)
V vs. G1	Mean difference	168	-271	-57	23	-34.1
	Limits of agreement	(-266, 218)	(-274, 525)	(-113, 477)	(-136, 71)	
V vs. G2	Mean difference	115	-373	-62	-38	-89.4
	Limits of agreement	(-185, 332)	(-197, 596)	(-68, 475)	(-90, 105)	
V vs. G3	Mean difference	169	-236	-21	121	8
	Limits of agreement	(-267, 217	(-332, 404)	(130, 473)	(-367, 188)	
V vs. L1	Mean difference	91	-45	-52	25	4.9
	Limits of agreement	(-206, 163)	(-120, 276)	(-195, 133)	(-64, 40)	
V vs. L2	Mean difference	62	-57	-104	171	17.8
	Limits of agreement	(-449, 203)	(-184, 279)	(-539, 253)	(-300, 202)	
V vs. L3	Mean difference	116	-36	-90	24	3.7
	Limits of agreement	-(221, 152)	-(118, 264)	(-235, 142)	(-62, 41)	

The extensor muscle onset results, using the local baseline method 3 (LPF 50Hz / 4SD / MAF 10 ms) and applied to the seven impaired and nine unimpaired participant data, can be seen in Table 5-12. A difference between impaired and unimpaired onset timing can be seen, but that did not reach significance (p=0.09) in this small sample. Examples of impaired and unimpaired step tracking with the extensor EMG envelope can be seen in Figure 5-25, showing the points of activation onset as determined using local baseline method 3.

Table 5-12: Differences in values extensor muscle onset timing in the impaired (N=7) and unimpaired (N=9) groups

	Impaired Mean (SD) Min-max	Unimpaired Mean (SD) Min-max	Mean difference [95% CI]	*P*
Extensor muscle onset timing (seconds)	0.58 (0.36) 0.02 - 1.16	0.31 (0.06) -0.12 - 0.23	0.27 [-0.06, 0.60]	0.090

a) Unimpaired step tracking



b) Impaired step tracking

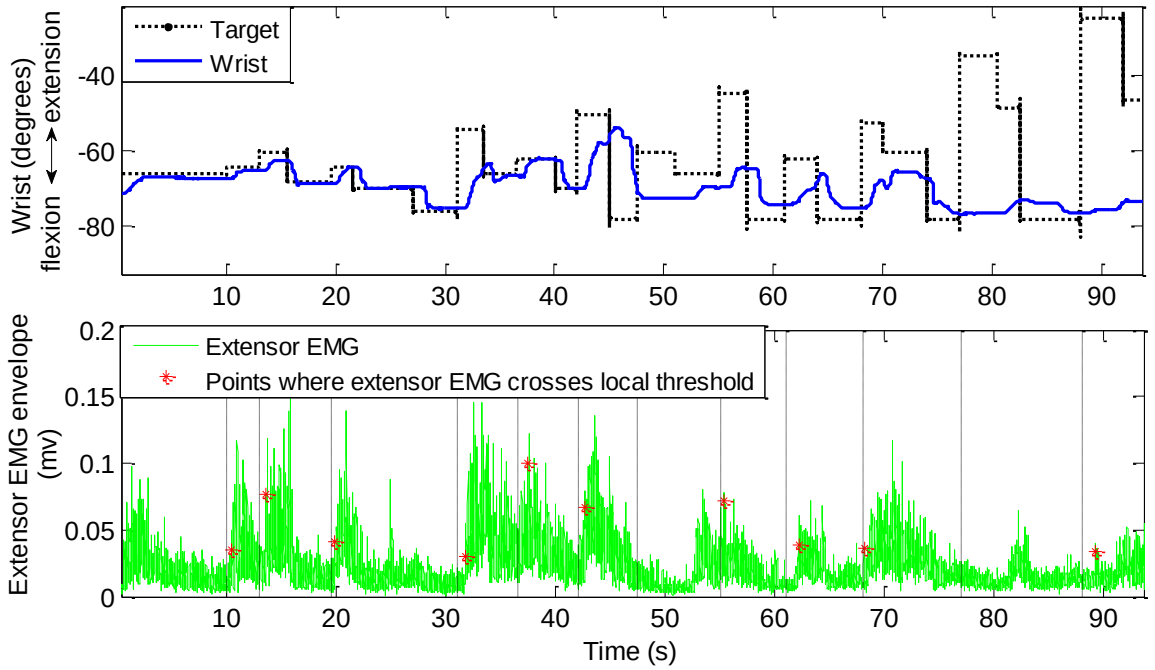


Figure 5-25: Step tracking and simultaneous extensor EMG activation from a) an unimpaired participant and b) an impaired participant. The dashed vertical line is where the target moved into extension and the red stars show the points at which muscle onset was calculated to occur, which was somewhat delayed in the impaired participant. In these examples, muscle onset was defined as the time at which the extensor EMG envelope exceeds the mean of the local baseline EMG plus four times its standard deviation (local baseline method 3). The local baseline was given by the extensor EMG envelope during a one second window, prior to movement of the target in the direction of extension.

Stretch response: The stretch index group results can be seen in Table 5-13. This shows a difference between impaired and unimpaired that did not quite reach significance (*p*=0.052). The stretch index calculation chosen was dependent not only on the area of flexor EMG activation, but also on a global resting baseline level. This was found to be problematic because visual analysis of flexor EMG data from the 1.5Hz and 0.5Hz stretch response tests and sine and step tracking tests showed that the amplitude of the global resting baseline within participants was often very variable; thus was likely to affect the accuracy and repeatability of the stretch response measure.

Table 5-13 Differences in values for stretch and torque indices in the impaired (N=7)* and unimpaired (N=9)* groups

Passive Tests	Stretch (SI) and Torque Indices	Impaired Mean (SD) Min-max	Unimpaired Mean (SD) Min-max	Mean difference [95% CI]	*P*
Stretch	Stretch index $_{(\text{mean area-BL})}$ (mV·s)	0.35 (0.39) 0.02 - 1.16	0.05 (0.12) -0.12 - 0.23	0.29 [-0.002, 0.59]	0.052
Torque	Torque-angle Index [a] (Nm)	0.023 (0.016) 0.007 - 0.048	0.015 (0.005) 0.009 - 0.023	0.008 [-0.009, 0.024]	0.284
	Mean Torque Index [a] (Nm/degree)	0.86 (0.39) 0.44 - 1.52	0.46 (0.11) 0.34 - 0.65	0.40 [-0.02, 0.81]	0.057

*Unless stated otherwise; [a] Impaired group N = 6, Unimpaired group N=7

T*orque:* Editing the data and detailed inspection of the EMG showed that, in spite of clear instructions and encouragement, three participants were unable to entirely avoid any flexor and extensor activation during all cycles of passive wrist extension and were excluded from the analysis. This included two unimpaired participants with voluntary extensor activity and one impaired participant with increasing flexor activity in phase with passive wrist extension (see Figure 5-26). This patient was one of three in the group who had spasticity, though this was not tested formally. The torque indices can be seen in Table 5-13. The mean torque index showed a greater difference between impaired and unimpaired that almost reached statistical significance (*p*=0.057) and less overlap of values between the groups than the torque angle index.

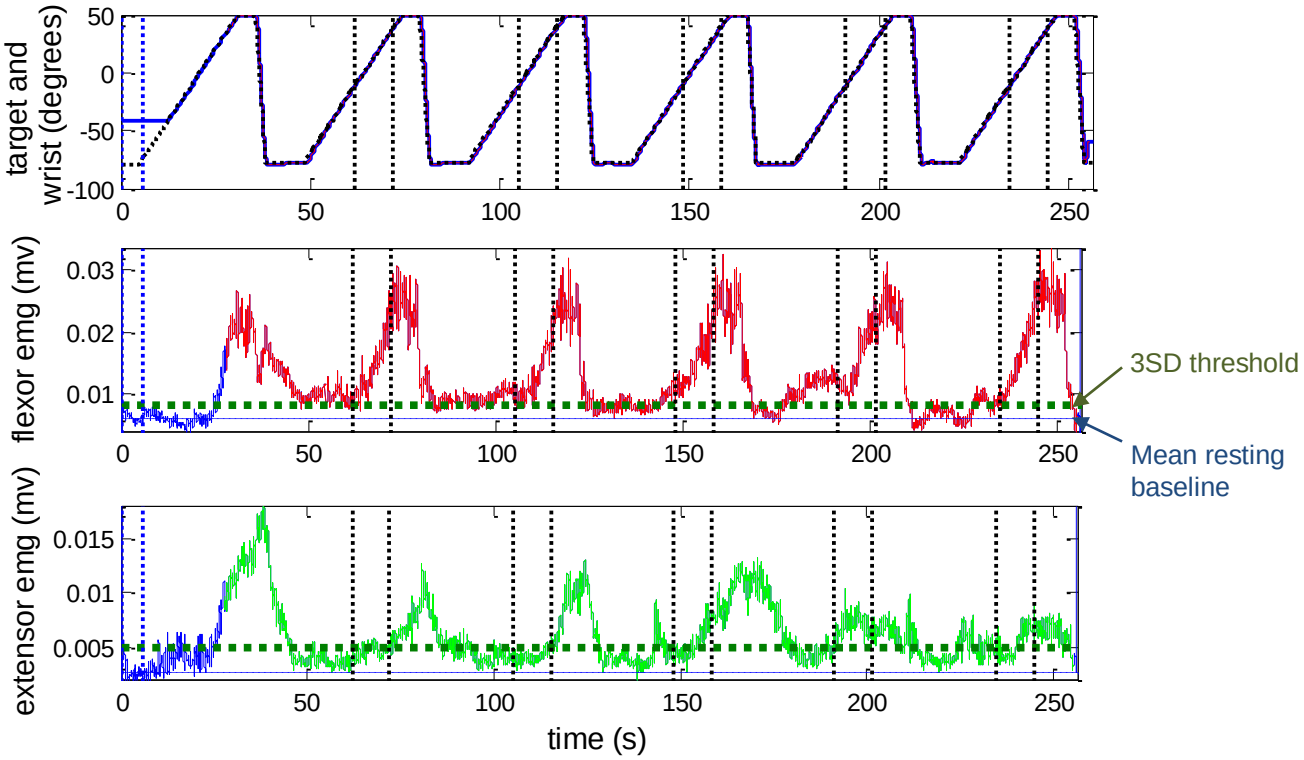


Figure 5-26: Data from the torque angle test showing top - target and wrist movement (black and blue), middle – flexor EMG (red), and bottom – extensor EMG (green). The EMG plots show the mean resting baseline (blue dashed) and the 3SD threshold level (green dotted). The data analysed for this test is between the two vertical lines (black dotted) at each movement cycle. In this impaired participant, increasing flexor EMG activity can be seen in phase with the passive extension that is above the 3SD threshold. This participant was excluded from the non-neural torque analysis because of this evident neural activity.

5.4.4.3. Differences between hand positions

In terms of participant preference, twelve participants (5 stroke and 7 unimpaired) thought the handle was more comfortable and they felt more in control during the tracking tasks, whereas five participants (3 stroke and 2 unimpaired) thought the air splint was more supportive and effective, especially for the extensor MVC test. A deciding factor was that one participant was unable to perform any of the tasks using the handle because it was not supportive enough, even with extra straps around the fingers. This participant had spasticity with contractures that made positioning his arm in the mid-prone position difficult, which is a common problem for those patients with higher levels of spasticity. The air splint with the forearm supports and straps were supportive enough to maintain his arm in this position so that he could isolate some movement at the wrist.

Means and standard deviations of a select number of measurement indices for each of the hand positions and a comparison between impaired and unimpaired groups are shown in

Table 5-14 and Table 5-15. The repeated measures ANOVA showed statistical significance for extensor isometric force for hand position as a factor (p=0.028) and for the step tracking correlation index when both hand position and group factors were considered (p=0.026). A post hoc paired sample t-test showed that in the impaired group there was statistically significant greater extension force using the air splint than the handle (p=0.023). A post hoc independent samples t-test comparing the impaired and unimpaired group step coactivation index using the handle and air splint showed a statistically significant difference between the groups only for the air splint (p=0.030). There was more coactivation in the impaired group and more reciprocal activation/inhibition in the unimpaired group using the air splint.

Table 5-14 Differences in impairment indices from the active tests for the two hand positions and between the impaired and unimpaired groups

Active Tests		Impaired group N=6			Unimpaired group N=9			Between group difference	
Test	Indices	Handle Mean (SD)	Air Splint Mean (SD)	Mean Difference	Handle Mean (SD)	Air Splint Mean (SD)	Mean Difference	Handle	Air splint
Sine	Tracking Index$_{(CC)}$ (degrees^2)	143.65 (86.56)	124.78 (76.09)	18.88	221.57 (12.34)	216.19 (15.59)	5.38	-77.91	-108.22
	Coactivation Index (correlation increase ext EMG)	-0.02 (0.49)	0.07 (0.46)	-0.09	-0.47 (0.21)	-0.49 (0.17)	0.01	0.46	0.60
Step	Tracking Index$_{(totalMAE)}$ (degrees)	5.63 (2.25)	5.21 (2.16)	0.42	3.45 (0.51)	3.71 (0.51)	-0.26	2.18	1.82
	Tracking Index$_{(PL)}$ (degrees/sample)	0.014 (0.005)	0.015 (0.004)	-0.001	0.009 (0.001)	0.010 (0.004)	-0.001	0.005	0.005
	Coactivation Index (correlation increase ext EMG)	0.09 (0.49)	0.26 (0.47)	-0.16	-0.02 (0.18)	-0.18 (0.16)	0.16	0.12	0.42*
	Extensor onset time (seconds)	0.41 (0.14)	0.35 (0.16)	0.06	0.25 (0.10)	0.25 (0.04)	-0.001	0.16	0.15
MVC	IF Extension (Nm)	1.98 (1.58)	2.94 (2.25)	-0.96*	3.55 (1.19)	4.50 (2.51)	-0.95*	-1.57	-1.98

*statistically significant difference between groups (p=0.030)

Table 5-15 Differences in impairment indices values from the passive tests for the two hand positions and between the impaired and unimpaired groups

Passive Tests	Impaired group N=6			Unimpaired group N=9			Between group difference	
Test Indices	Handle Mean (SD)	Air Splint Mean (SD)	Mean Difference	Handle Mean (SD)	Air Splint Mean (SD)	Mean Difference	Handle	Air splint
Stretch Index$_{(area-BL)}$ (mV·s)	0.52 (0.92)	0.32 (0.48)	192	0.02 (0.09)	0.05 (0.12)	-0.03	0.49	0.27
Mean Torque Index (Nm)	0.65 (0.14)	0.71 (0.25)	-0.06	0.30 (0.13)	0.42 (0.10)	-0.12	0.35	0.33

5.4.5. Discussion

5.4.5.1. Defining the tests

In this research both sine and step tracking were chosen as ways in which motor control could be assessed. Although sine tracking is potentially more reliable, because it generates multiple cycles of data that can be averaged, random step tracking, which involves complex acceleration and deceleration, demands cognitive control for which higher-level planning areas of the cortex are recruited (Schaal et al. 2004). This is probably more related to the requirements of day-to-day functional activities involving the wrist than repetitive movements. The step tracking test has also provided additional insights into tracking accuracy (path length at the end-point target position) and muscle activation patterns (extensor muscle onset timing). The step tracking test was carefully designed to be random in terms of timing and displacement of step changes, but also to have graduated amount of displacement so that most patients, even with only small amounts of wrist movement, could complete some of the test. The parameters for timing and displacement that were defined in Pilot Study 2 with unimpaired participants were then tested for the first time with patients in this Pilot Study. These have worked well with this sample of impaired participants with a wide range of movement abilities.

The stretch test was problematic because the 1.5Hz speed at which the test was undertaken was not fast enough over 40º ROM to exclude voluntary flexor activation by some unimpaired participants. These test parameters were used because we had used similar parameters (±30º at 1.5Hz) in a previous study (Turk et al. 2008b) without any issues with voluntary flexor activation by unimpaired participants. The displacement was reduced to ±20º for this study so it was the same as the active sinusoidal test and therefore could more easily be

compared. On re-reviewing the literature on this issue, it was found that others have tested sinusoidal passive displacements using a smaller range of 10 º displacements and found that speeds of at least 3 Hz needed to be used to prevent voluntary tracking activity (Ada et al. 2006; Neilson 1972; O'Dwyer et al. 1996). It was therefore decided that a re-evaluation of the stretch test with varying velocities and range of displacement was needed and this was carried out in Pilot Study 4 (Section 5.5).

The torque angle test was not entirely acceptable because one of the seven impaired participants and two of the nine unimpaired participants had neural activity during the test and therefore could not be included in the torque index analysis, as it aims to measure non-neural stiffness. The unimpaired participants had voluntary extensor activity which may further reduce the torque around the wrist joint. The impaired participant had increasing flexor activity in phase with passive extension (Figure 5-26), which may have increased the flexor torque around the wrist joint. Others who measured non-neural wrist stiffness during 50˚ passive extension displacements in a torque motor controlled rig using constant velocity movements at 10˚/second (Pisano et al. 2000), also found that 29 of the 48 impaired subjects could not be included in the analysis as they also exhibited flexor EMG activity during the test. With the current study the test was purposely undertaken at a slower speed 5˚/second, which may have reduced the presence of flexor reflex activity, but not fully. An alternative method that claims to separate neural from non-neural stiffness measures very small perturbations at joints together with a complex mathematical model, described as a parallel-cascade non-linear system (Kearney et al. 1997; Mirbagheri et al. 2001; Mirbagheri et al. 2007). However, because if its complexity, the model described by Kearney and Mirbagheri was not considered practical for this study which aims to use measures that could be applied easily in a clinical setting. Therefore, although the method tested in this Pilot Study is not ideal it was decided to further evaluate it with a larger group of participants in the main study. Furthermore, as the impaired participant who was excluded from the analysis also had spasticity, it was decided to test spasticity formally with the participants in the main study using a standardised clinical test, the modified Tardieu scale (Boyd and Ada 2001; Morris 2002) (see Methodology Chapter 4, Section 4.6.2).

5.4.5.2. Derivation of Indices

A number of different methods of deriving indices to quantify various motor impairments have been evaluated in this Pilot Study. It was important to exclude indices that were not useful in order to limit the number of measurement variables used in the statistical analysis of the final main study. These indices, with reasons for exclusion, are detailed in Table 5-16

.

Table 5-16: Indices excluded from the main study analysis and reasons for their exclusion

Indices excluded from the main study	Reason
Step tracking index (target MAE)	Similar to Step tracking index (total MAE) but is not as good at distinguishing impaired from unimpaired. This only measures the ability to attain the target; its poor performance suggests that delay in movement may also be an important feature of the impairment
Step tracking index – standard deviation (SD)	Similar to path length but path length is sensitive to smoothness of fluctuations whereas standard deviation is only sensitive to overall range of dispersion of wrist position during the target phase.
Coactivation indices based on • Extension movement • Peak extensor EMG	These methods generated smaller differences between abnormal and normal coactivation. Visual analysis of EMG plots suggested that these approaches included more sections of the data where there is 'normal' coactivation such as antagonist activation occurring towards the end of the movement phase and simultaneous relaxation of both agonist and antagonist muscles at the end of the extension (see Figure 5-22 and Figure 5-23). This would contribute to a positive correlation coefficient between extensor and flexor activity, but does not necessarily reflect 'abnormal' coactivation.
Stretch Index (area-BL)	This measure has a disadvantage in that it needs to be normalised so that comparisons can be made across participants. The global resting baseline within participants was found to be variable which was likely to affect the accuracy and repeatability of the stretch response measure
Torque angle index	This measure is sensitive to the change of resistance with increasing extension angle, rather than resistance itself and is less able to distinguish abnormal stiffness than the mean torque calculation.

- The indices that characterise motor impairments and best distinguish between impaired and unimpaired participants are summarised in a table at the end of this Chapter (Table 5-19, Section 5.6), and are discussed further here:

Accuracy of movement tracking: The indices that characterise motor control in both step and sine tracking clearly distinguish between impaired and unimpaired, confirming what was evident from visual analysis of the wrist movement plots. This extends results seen previously in sine tracking (Notley et al. 2007; Turk et al. 2008b), now showing differences in performance during step-tracking, especially for total tracking accuracy using MAE and accuracy at target end point using path length.

Coactivation: A novel method to quantify coactivation has been employed using a correlation analysis of the agonist (extensor) and antagonist (flexor) EMG calculated only over the time-periods where the agonist EMG is increasing, in accordance with the definition of coactivation (simultaneous activation of both muscles (Sheean 2002)). This coactivation index method was first tested in Pilot Study 1 using sinusoidal tracking data of impaired and unimpaired participants from a previous wrist rig study (Turk et al. 2008b) and showed that it better distinguished abnormal coactivation from that used normally to stabilise a joint and ensure end-point movement accuracy than other methods based on extension movement or peak extensor EMG. Visual analysis of the traces of both sinusoidal and step tracking in Pilot Study 3 suggested that, again, this approach was able to exclude more sections of the data where there is 'normal' coactivation, which provides a major improvement over indices previously used in terms of improved compliance with the usual definition of co-activation.

The wide and rather similar distribution of values for coactivation found in both groups in this study highlights the variety of muscle activation strategies used by both impaired and unimpaired participants, which was evident from visual inspection of the flexor and extensor EMG on the tracking plots. Even in the unimpaired groups whose tracking performance was excellent there were a variety of strategies used. Some appeared to use reciprocal inhibition/activation as described by Sherrington (Sherrington 1906). For others there was overlapping activity of AG1, ANT1 and AG2 in triphasic activity, often with additional bursts of AG and ANT activity as described by others (Brown and Cooke 1990). One unimpaired participant in the sine tracking task used coactivation and achieved good tracking performance. One consideration is that this individual found the task challenging and coactivation has been shown to increase with task difficulty and reduce with learning (Osu et al. 2002). This was not likely to be the case in this study as all participants were allowed to practice the test before data was recorded. If further changes in coactivation might have occurred with longer training is unclear, however, such a requirement is unrealistic for routine clinical use. Although the majority of impaired participants did not have coactivation at levels beyond the normal range during sine and step tracking movements, there are clearly some

individuals who did coactivate. Further investigation of the relationship of coactivation and other impairments with level of tracking performance and functional activity was carried out with more participants in the main study to explore if coactivation affects motor performance.

Extensor muscle onset timing: A method using a local baseline threshold, which best compared with visual analysis of the rectified raw extensor EMG activation pattern, was evaluated in this study. The results using this method showed a trend towards a delay in extensor muscle onset in the impaired group is similar to findings in previous studies (Chae et al. 2002a; Hughes et al. 2010a; Wagner et al. 2007). This did not reach significance possibly due to the small sample size in this Pilot Study, and further investigation of this measure was carried out in the main study.

Stiffness: Despite the fact that not all participants data could be used in the analysis due to presence of neural activity (see Section 5.4.4.1) the mean torque index showed a greater difference between impaired and unimpaired that almost reached statistical significance (p=0.057) than the torque angle index. The mean torque index simply represents the mean non-neural resistance or stiffness around the wrist joint during slow passive wrist extension, and unlike the torque angle index is not sensitive to change over the range of angles tested. From these preliminary findings it can be cautiously suggested that patients with stroke, compared to unimpaired participants, may have more problems with increased stiffness through range rather than stiffness increasing with extension angle.

5.4.5.3. Hand position

Although participant preferences were mainly for the handle, described as having ‘better control’ during the tracking tasks, there were no statistically significant differences in tracking performance between the groups. The air splint was thought to be supportive and one impaired participant with spasticity and contractures could only use the air splint for this reason. Some found the air splint easier to use during the extensor MVC test and evidence for this was seen as the isometric extension force with the air splint was significantly greater for the impaired group than with the handle. Furthermore when comparing the impaired and unimpaired step coactivation index using the handle and air splint, a statistically significant difference between the groups was shown only for the air splint (p=0.030) (Table 5-14), due to more coactivation in the impaired group and more reciprocal activation/inhibition in the unimpaired group. With the handle there was more coactivation in the unimpaired group and less in the impaired group, compared to the air splint. This partially supports our hypothesis that when using the handle, participants (unimpaired in particular) may use ‘normal’ coactivation because of the flexed gripping position of the fingers around the handle.

5.4.6. Conclusions

1. The air splint was more appropriate for use in the main study as it provided support for the upper limb across all the range of impairments, and was better able to distinguish between impaired and unimpaired coactivation than the handle.
2. The sine and step tracking test parameters worked well and the indices derived from them distinguished between impaired and unimpaired performance. Of the four derived step tracking indices evaluated in this Pilot Study, two best differentiate between impaired and unimpaired and were chosen for the main study analysis – total tracking accuracy using MAE and accuracy at target end point using path length.
3. For the step and sine tracking tests, the method of correlation of extensor and flexor EMG when extensor EMG is increasing was better at distinguishing between impaired from unimpaired coactivation than correlation methods based on extension movement or peak extensor EMG.
4. The torque angle test was able to distinguish between neural and non-neural stiffness for most but not all participants. Other methods cited in the literature were considered to be too complex for this clinically-focussed study. It was therefore decided to include this test and its derived index in the main study to further evaluate it with a larger group of participants.
5. Before the main study was undertaken, the stretch test and derivation of the stretch index needed further evaluation with more impaired and unimpaired participants using a range of tests with different velocities and range of displacements – this was the focus of Pilot Study 4.

5.5. Pilot Study 4

5.5.1. Objectives

In Pilot Study 3 the stretch test was problematic because of the presence of voluntary flexor activity in the unimpaired group that was related to the speed of the test. The objectives of this study were firstly to define a fast passive stretch test for the main study which enables calculation of the flexor stretch reflex response (when spasticity is present) but prevents voluntary tracking activity. Secondly, it aimed to derive a stretch index that is not necessarily dependent on a global resting baseline and best distinguishes impaired from unimpaired stretch response. Thirdly, the stretch test at 0.5 Hz ±20˚ was to be evaluated in order to investigate the presence of a stretch response at the same frequency used for the active tracking task, so that the relationship between spasticity measured during passive movement and coactivation during activation could be assessed.

5.5.2. Participants

Five participants with hemiplegia in the chronic phase post-stroke who were recruited from the Faculty of Health Sciences participant database were included in this study. Five older unimpaired adults (age 65 and over) were recruited from a local church community and five unimpaired staff members (under age 65) were recruited from the Faculty of Health Sciences ARM research programme. The selection criteria remained the same as those detailed in the Methodology Chapter Section 4.4. Participant characteristics can be seen in Table 5-17.

Table 5-17: Demographic characteristics for Pilot Study 4 participants

		Impaired (N=5)	Older unimpaired (N=5)	Younger unimpaired (N=5)
Age (years)	Mean (SD)	64.2 (6.6)	69 (4.5)	34.4 (6.0)
	Min - max	56 – 74	65 – 76	30 - 41
Gender	Male	5	3	2
	Female	0	2	3
Time from stroke (months)	Mean (SD)	67.4 (18.3)	N/A	N/A
	Min - max	48 – 91		
Side assessed	Right	2	4	4
	Left	3	1	1

5.5.3. Data collection

To compare stretch tests with different velocities and ranges of displacement, participants were set up in the rig (see Methodology Chapter Section 4.7) with their hand positioned in the air splint (Figure 5-8d). Four 40 second passive tests were carried out: 1.5Hz and 0.5 Hz with ±20˚ displacement around the active midpoint (as used in Pilot Study 3), and 3Hz and 3.5Hz with ±5˚ displacement as used in previous studies (Ada et al. 2006; Neilson 1972; O'Dwyer et al. 1996) without voluntary tracking activity. Higher speeds than 3.5Hz were considered but it was found that passive manual tracking was impossible to carry out. The order of testing was randomised using a Latin square.

5.5.4. Derivation of indices

The signals from each file were plotted and visually checked for any abnormalities. For each of the tests, 40 seconds of data were analysed. As in Pilot Study 3 the data were edited to ensure that the data used for analysis were those where the passive tracking was most accurate to the set target (see Section 5.4.3.6.a). For the 1.5Hz and 0.5Hz tests extension cycles were excluded where the error in tracking was more than ±5˚ off the target extension peak and/or more than ±10˚ off the target flexion peak - as also used in Pilot Study 3. For the 3Hz and 3.5Hz tests, extension cycles were excluded where the displacement was ±2˚off the target flexion and/or extension peak.

5.5.4.1. Methods of analysis

Two methods of analysis were compared:

a) The stretch index was calculated as in Pilot Study 3. This was taken as the mean of the area under the flexor EMG curve normalised by the length of the extension phase (i.e. the average amplitude) for each cycle minus a global resting baseline EMG:

$$\mathbf{SI(area-BL)} = \frac{1}{M}\sum_i\left(\boldsymbol{EMG_{fe}}(i) - \overline{\boldsymbol{EMG_{fe}}}(\boldsymbol{baseline})\right) \quad \text{(Equation 6)}$$

For the 1.5Hz and 0.5Hz tests the resting baseline EMG was calculated by applying a moving average filter with one second window from zero to five seconds of data (the period of rest before the start of the passive tracking). For the 3Hz and 3.5Hz tests a moving average filter was applied with a five second window from zero to 15 seconds into the recording. The baseline flexor EMG level was taken as the minimum value from all of the moving average windows. The method, however, proved not to be satisfactory, firstly because there is no normalisation and although it can be evaluated within participants within one session when the electrodes are not removed, cannot be evaluated within participants over time or across participants. Secondly the global baseline was often found to be variable and because this method was dependant on the baseline, this variability was likely to affect the accuracy and repeatability of the stretch response measure.

b) A second method was evaluated that used a local baseline rather than the global resting baseline, thus the baseline values vary within the recording but are related to each of the cycles which may improve the accuracy of the algorithm (Khalil & Duchene 2000). This was taken as the median of a ratio of the stretch response area normalised by the length of the extension movement (as in (a)) to the local baseline for each cycle (Figure 5-27):

$$\mathbf{SI(area:LBL)} = median\left(\boldsymbol{postEMG}_{fe}(m)/\boldsymbol{preEMG}_{fe}(m)\right) \quad \text{(Equation 7)}$$

Where $preEMG_{fe}(m)$ is the mean EMG area of the flexor over an interval of 0.1s prior to extension on the mth cycle (i.e. the local baseline), and $postEMG_{fe}(m)$ is the equivalent during that extension.

The advantage of this method is that it is normalized, and thus the value of the index can easily be interpreted – which is more difficult for $SI_{(area\text{-}BL)}$ in units of mV.s. Thus if the ratio is 1.0, the stretch response average amplitude is the same as the local baseline, and if the ratio is higher than 1.0, the stretch response average amplitude is greater than the local baseline.

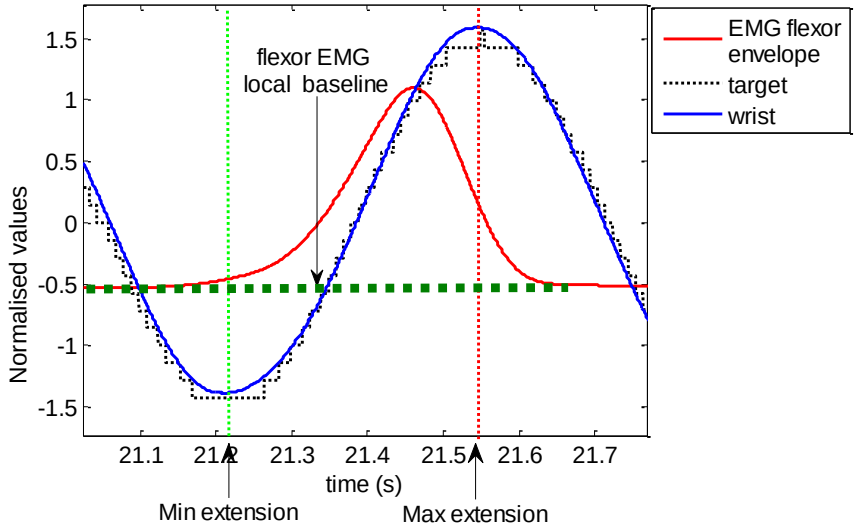


Figure 5-27 Plot to illustrate the second method used to calculate stretch response: the median of a ratio of the stretch response area normalised by the length of the extension phase to the local baseline for each cycle.

5.5.5. Results

A summary of the stretch index data comparing the two stretch index methods and different test parameters for both impaired and unimpaired groups are shown in Table 5-18. Between group mean differences, 95% confidence intervals and *P* values are presented. Although none were statistically significant between impaired and unimpaired, the 3.5Hz, ±5˚ test data with the ratio of stretch response to local baseline index was clearly the nearest to reaching statistical significance (p=0.058). Dot plots (Figure 5-28) with all the impaired and unimpaired values for the 3.5 Hz test using the two different methods show for the global baseline method one impaired participant lies outside the normal (unimpaired) range, and for the local baseline method there are three.

To evaluate the two stretch index methods with the 0.5 Hz with ±20˚ displacement test, data were pooled from Pilot Study 3 and Pilot Study 4. Dot plots showing the impaired and unimpaired values for the two different stretch index methods are shown in Figure 5-29. Using the global baseline method one participant (#13) has a stretch response outside the normal range. It is interesting to note that for this participant in the 0.5Hz ±20˚ displacement test the stretch index is almost ten times as big as in the 3.5Hz, ±5˚ test. With the slower 0.5Hz test both methods show unimpaired outliers with greater flexor activity.

Table 5-18 Differences in values for two stretch index methods using different test parameters in the impaired (N=5) and unimpaired (N=10) groups

Stretch response Test	Indices	Impaired N=5 Mean (SD)	Unimpaired N=10 Mean (SD)	Mean Difference [95% CI]	*P*
1.5Hz, ±20˚	SI $_{(area - GBL)}$ (mV.S)	0.66 (1.08)	0.001 (0.24)	0.66 [-0.66, 1.99]	0.243
	SI $_{(ratio\ area : LBL)}$	1.46 (0.55)	1.02 (0.06)	0.44 [-0.24, 1.12]	0.152
3Hz, ±5˚	SI $_{(area - GBL)}$ (mV.S)	0.37 (0.46)	0.04 (0.07)	0.33 [-0.80, 1.45]	0.343
	SI $_{(ratio\ area : LBL)}$	1.18 (0.27)	1.05 (0.16)	0.13 [-0.14, 0.41]	0.307
3.5Hz, ±5˚	SI $_{(area - GBL)}$ (mV.S)	0.10 (0.17)	0.04 (0.08)	0.06 [-0.15, 0.27]	0.362
	SI $_{(ratio\ area : LBL)}$	1.25 (0.21)	1.00 (0.09)	0.24 [-0.01, 0.50]	0.058

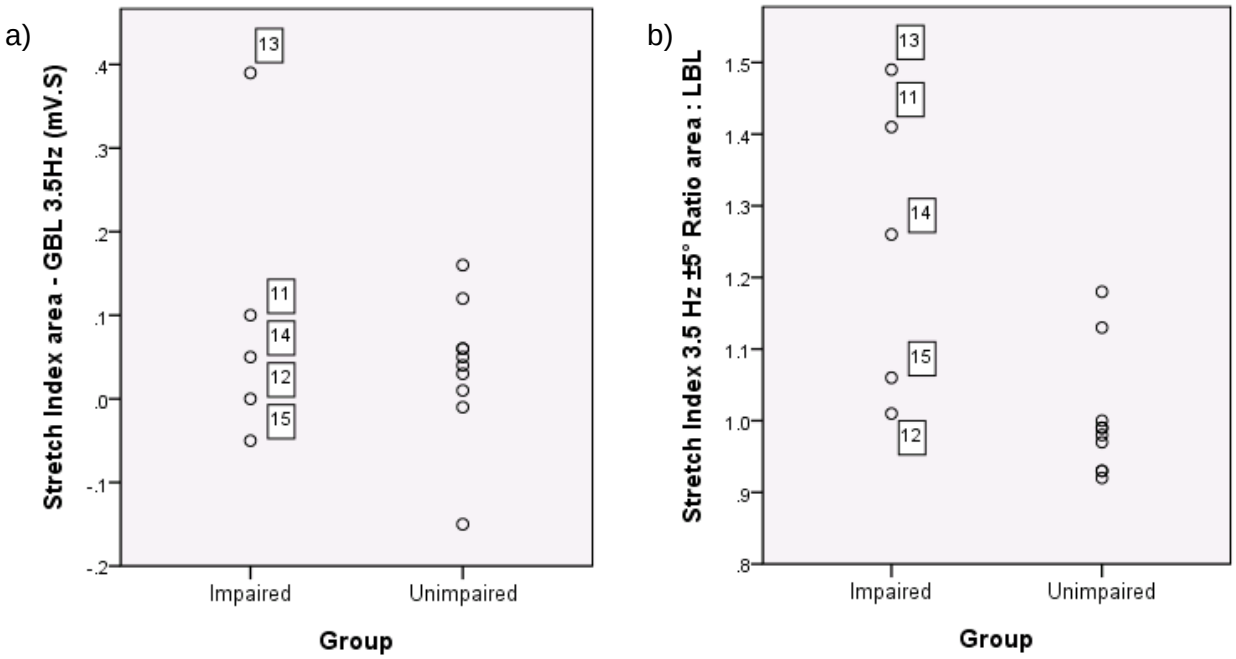


Figure 5-28 Impaired and unimpaired values from the 3.5Hz stretch response test for a) mean areas minus global baseline (GBL) and b) ratio of area to local baseline (LBL). This shows that using method a) only one participant (#13) had a stretch response outside the normal range, whereas using method b) three participants lie outside the normal range.

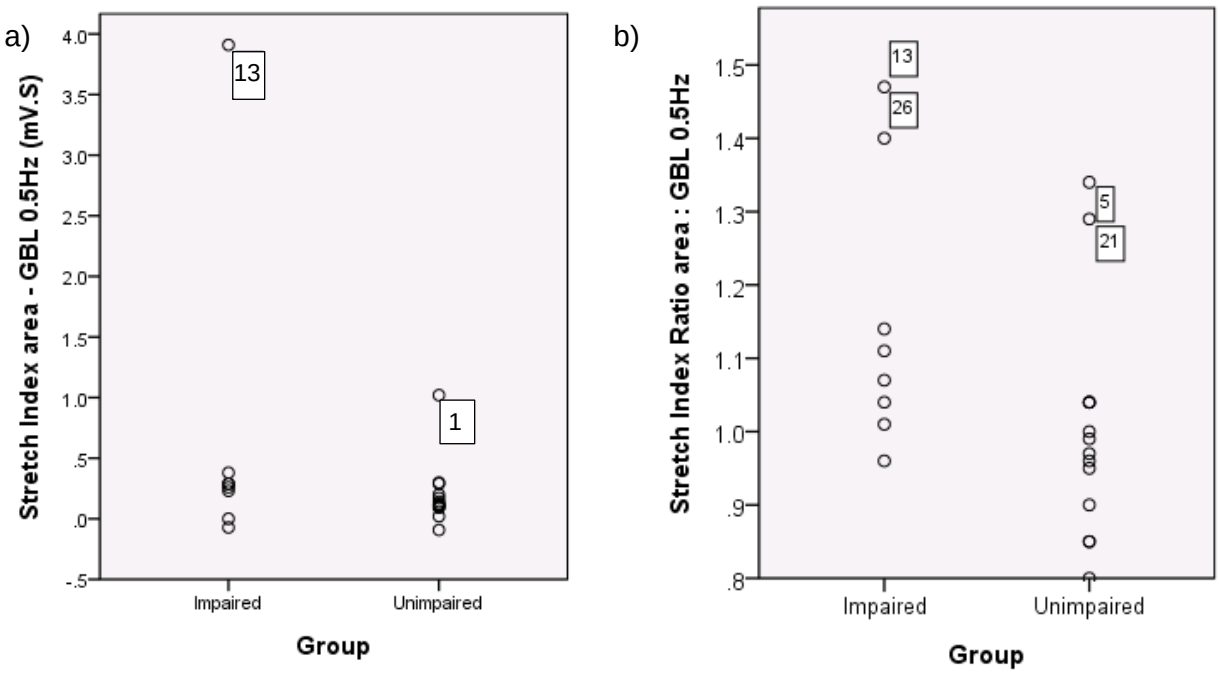


Figure 5-29 Impaired and unimpaired values from the 0.5Hz stretch response test for all participants in Pilot Study 3 & Pilot Study 4 showing a) mean areas minus global baseline (GBL) and b) ratio of area to local baseline (LBL). In a) one impaired participant (#13 who is the same as in Figure 5-28) and b) two impaired participants lie outside the normative range.

5.5.6. Discussion and conclusions

The results have shown that the stretch index method using a ratio of the mean area to local baseline and with data from the 3.5Hz ±5˚ test distinguishes best between impaired and unimpaired. The advantage of using a ratio is that there is no need for normalisation, plus it provides meaningful values (values above 1 indicate a stretch response) rather than units of mV.S. The dot plots of stretch index values from the 3.5Hz test (Figure 5-28) illustrate that using the local baseline method two more participants have stretch indices outside the normative range than with the global baseline method. A reason for this, confirmed by visual analysis of the passive tracking and EMG traces, was that their local baselines during the test were lower in amplitude than the initial 'resting' global baseline. This may be because of initial activation in the muscle created by anticipation of the test, but may also be the effect of the passive extension stretches reducing flexor activity in the flexed position at which point the local baseline is calculated.

The dot plots in Figure 5-29 with the values for the two methods for the 0.5Hz ±20˚ displacement test show a similar pattern with a greater number of impaired participants identified to have a stretch response using the local baseline than the global baseline

method. There were also a number of unimpaired outliers with higher flexor activity; it is hypothesized that with the slower tracking speed participants are not able to prevent voluntary activity. Case #13 has the highest stretch response values throughout all the tests and methods used, with values much higher than other impaired participants in tests with larger displacements – i.e. 0.5 Hz and 1.5Hz with ±20˚ displacement. This suggests that his stretch reflex response has a considerable length dependant component which may be explained by group II afferents as well as velocity dependence (see Chapter 2, Section 2.6.2, the physiology of stretch reflexes).

To conclude, one fast passive tracking test needed to be chosen for the main study, and the 3.5Hz ±5˚ test was better than the 1.5 Hz ±20˚ test at distinguishing between impaired and unimpaired because there was less voluntary tracking activity by unimpaired participants. The 0.5Hz ±20˚ test was also included as a comparison to the active tracking test at the same frequency and displacement, and to give information on the behaviour of the stretch response over a larger angle of displacement. Lastly, the ratio method of stretch response area to local baseline was chosen for used in the main study as it was more accurate in determining the presence of a stretch response than using a global baseline.

5.6. Summary of objectives achieved in the Pilot Studies:

1. Define the testing protocol for the main study:
    - The wrist rig tests and their parameters have been defined (Table 5-19)
    - Resistance during active tracking was set at 10% of each participant's MVC.
    - The stretch response test will be conducted at 3.5Hz ±5˚
    - The torque angle test will be performed at 5º/second
    - More detailed instructions and scoring guidance for the modified Wolf Motor Function Test protocol has enabled better agreement between two assessors.
2. Optimise usability and comfort of the rig from the participants' perspective:
    - With some minor modifications to the usability of the LED tracking display, the rig has been made ready for use with participants in the main study.
3. Derive impairment indices
    - Methods of analysis have been identified to generate indices that characterise motor impairments following stroke and best differentiate between stroke impaired and neurologically intact participants (Table 5-19).
4. Determine the optimal hand positioning in the rig
    - The air splint will be used in the main study as it provides the best support for most participants, and differentiates better between abnormal and normal coactivation.

Table 5-19: The measurement indices that were found to characterise motor impairments following stroke and best differentiate between impaired and unimpaired that are included in the main study analysis

Wrist rig tests and their parameters chosen for the main study	**Indices included in the main study analysis (measurement unit) (Section where method is detailed)**	**Motor impairment**
Active range of movement (AROM)	Extensor AROM (degrees) (Section 5.4.3.1)	Active ROM into extension
Passive range of movement (PROM)	Extensor PROM (degrees) (Section 5.4.3.1)	Passive ROM into extension
Maximal voluntary contraction (MVC)	Extensor IF (Nm) (Section 5.4.3.2)	Extensor muscle weakness
Active sinusoidal tracking – 0.5 Hz ±20º displacement around the midpoint of active ROM. Tracking is first unresisted and then resisted at 10% of extensor IF.	Sine tracking index (cross correlation) (degrees^2) (Section 5.4.3.3 b)	Total motor control accuracy during rhythmic movements
	Sine coactivation index (correlation when extensor EMG increases) (correlation coefficient) (Section 5.4.3.4)	Coactivation of extensors (agonist) and flexors (antagonist) during rhythmic movements
Active step tracking - steps of increasing displacement of the target from 5˚ to 40˚ in 15 second blocks for a total of 90 seconds with random 2-4 second rest intervals between movements of the target. Tracking is first unresisted and then at 10% of extensor IF.	Step tracking index (total Mean Absolute Error) (degrees) (Section 5.4.3.3a)	Total motor control accuracy during discrete movements, specifically including timing of movement, attainment of target and control at target end point.
	Step tracking index (path length) (degrees/sample) (Section 5.4.3.3a)	Motor control accuracy at the target end point, specifically amount of corrective sub-movements
	Step coactivation index (correlation when extensor EMG increases) (correlation coefficient) (Section 5.4.3.4)	Coactivation of extensors (agonist) and flexors (antagonist) during discrete movements
Stretch response test - Fast passive sinusoidal tracking at 3.5Hz, ±5˚ displacement around the midpoint of active ROM, and 0.5Hz, ±20˚ displacement	Stretch index (area of flexor stretch response: local baseline flexor EMG (Section 5.5.4.1)	Spasticity (stretch response) in flexors
Torque/angle test - Slow passive ramp and hold tracking at 5º/second over full passive range of movement	Mean torque index (Nm) (Section 5.4.3.7)	Non-neural stiffness around the wrist

6. Main Study

6.1. Introduction

This Chapter describes the main study. The primary aim was to evaluate the inter-relationships between wrist motor impairments and their association with motor control and functional activity early and late post-stroke. Secondary aims were to confirm the validity of the impairment indices to distinguish between impaired and unimpaired and to undertake a preliminary evaluation of their repeatability. Figure 6-1 shows a flowchart of the main study.

Specific objectives:

1. Evaluate differences in motor impairments between impaired (acute and chronic), and unimpaired groups
2. Evaluate between-days test-retest reliability (active tests) and within-test repeatability (sinusoidal tests)
3. Evaluate associations between motor impairments and motor control accuracy
4. Evaluate inter-relationships between negative, positive and secondary motor impairments
5. Evaluate relationships between motor impairments and functional activity (modified Wolf Motor Function Test (mWMFT)).

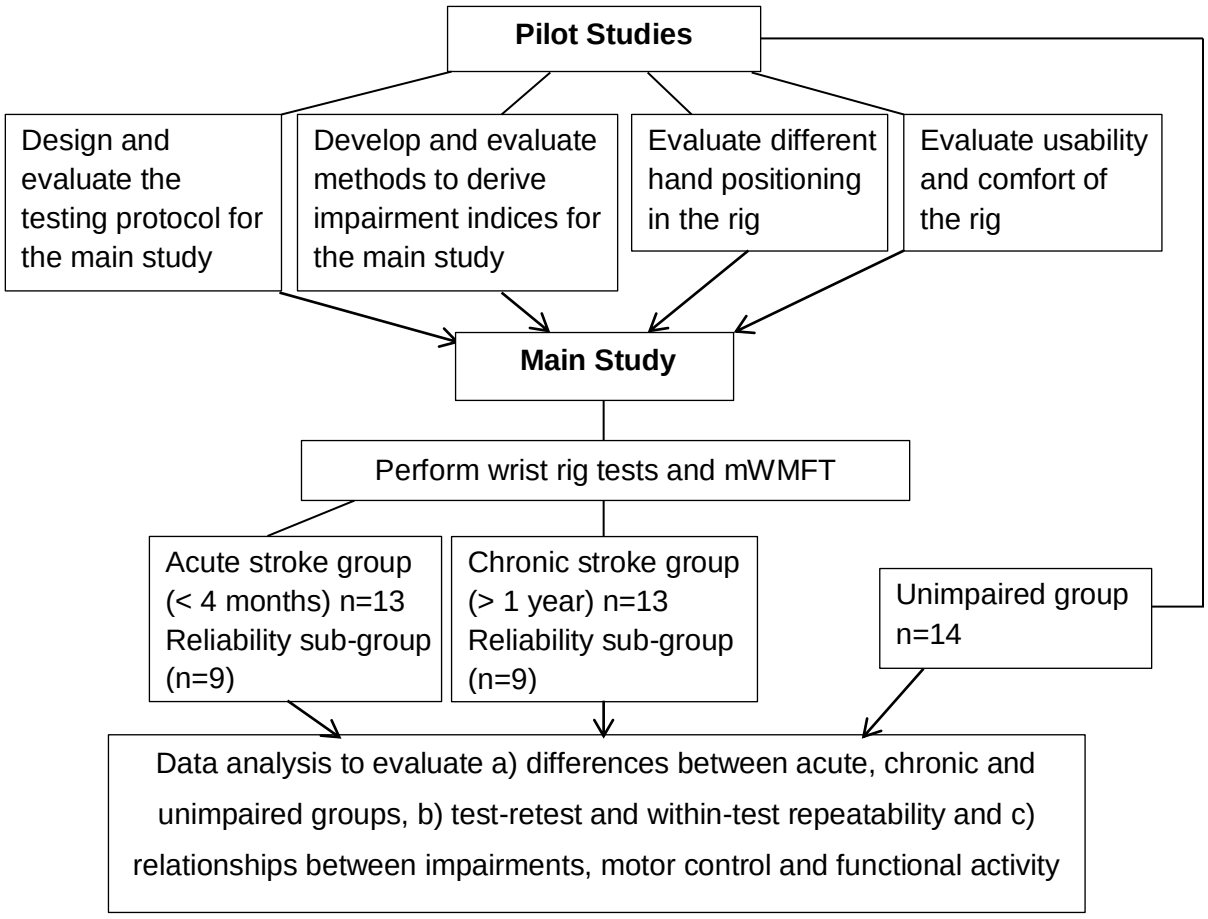


Figure 6-1 Flowchart showing the main study following on and interrelating with the pilot studies

6.2. Methods

6.2.1. Recruitment of Participants

Patients for the acute and chronic groups were identified and selected for participation if they satisfied the inclusion and exclusion criteria as follows:

Inclusion criteria

1. Diagnosis (MRI/CT scan) of first stroke
2. Between 2 and 17 weeks (four months) post-stroke (acute group) or over one year post-stroke (chronic group)
3. Aged 60 or over
4. Upper limb movement deficit: at least, some perceivable activity in the wrist (at least 5˚ flexion/extension movement in the rig), at most, some remaining gross movement deficit i.e. those with only hand dexterity problems were excluded
5. Able to transfer to a chair with the assistance of one therapist; and
6. Informed written consent.

Exclusion criteria

1. Upper limb movement deficits attributable to non-stroke pathology;
2. Unilateral visuo-spatial neglect (star cancellation test score less than 51 (Wilson et al. 1987)) or other, non-corrected, visual deficits likely to compromise ability to attend to the tracking target;
3. Skin allergy to alcohol wipes and sticky tape;
4. Medical, psychological, language or cognitive impairment that, in the opinion of the treating therapist and/or researcher would compromise ability to undertake the testing protocol.

For the acute group, a consecutive sample of older adults with hemiplegia following stroke who were receiving rehabilitation from stroke services based at the three hospital sites in Southampton and South-west Surrey (see Methodology Chapter, Section 4.4.2 for details) were identified by therapy staff as being suitable for the study. Potential participants were invited by their therapist to take part and given a participation information sheet (see Appendix I). For the chronic group, older adults with hemiplegia who had received rehabilitation from the stroke services as above and were identified by therapy staff through their patient records and were sent an invitation and information sheet by letter from the lead therapist of the stroke service. Those who expressed an interest in participating to their therapist or the researcher were recruited following an interview with the researcher (either in person or over the phone) with an explanation of the study and the opportunity to ask questions. If patients had a history of unilateral neglect, a screening test, the star

cancellation test (Appendix E), was performed to ensure that this would not be a confounding factor in the results. Informed consent was obtained and documented (Appendix J) for each recruit.

The data collected from the participants with stroke was compared with the data collected from a convenience sample of older (aged 60 or over) unimpaired participants recruited for the Pilot Studies from a local church and University of the Third Age (U3A) group. The characteristics of all participants are shown in the Results Section 6.3.1, Table 6-1.

6.2.2. The Testing Procedure

Assessment of participants involved performance of the wrist rig tests and the modified WMFT. Prior to data collection in the rig, participants were assessed using clinical scales of spasticity: Tardieu scale (Morris 2002); and wrist joint proprioception: proprioception test in the Nottingham Sensory Assessment (Stolk-Hornsveld et al. 2006) as described in the Methodology Chapter Section 4.6.3, Appendix E. Participants were set up in the rig as described in the Methodology Chapter Section 4.7 and with their hand positioned in the air splint (Figure 6-2). The dominant arm of unimpaired participants and the hemiplegic arm of impaired participants were tested. The wrist rig tests and the order they are undertaken were as described in the Methodology Chapter Section 4.8, and Appendix C) and are summarised here:

- Active range of movement (AROM)
- Passive range of movement (PROM)
- Maximal voluntary flexion and extension isometric contractions (MVC) at the 0˚ and 20˚ flexion positions.
- Torque/angle test - six repetitions of passive ramp and hold at 5˚/s through full passive ROM.
- Stretch response tests with displacement around the active mid-point:
  - 3.5 Hz ±5˚ to calculate the stretch response at a high velocity
  - 0.5 Hz ±20˚, to compare passive stretch response with the active sine tracking task
- Active tracking tasks, first non-resisted then with resistance set at 10% extensor MVC:
  - Sinusoidal tracking test at 0.5Hz, ± 20˚, for 60 seconds
  - Random step tracking task with increasing displacement of the target from 5˚ to 40˚ for 90 seconds and random 2-4 second rest intervals between movements of the target.

Most participants were tested over two days either at their hospital site or at the University laboratory by the researcher (RT). This was considered necessary for most participants

because the testing process, including learning the tests, was quite lengthy and fatigue is a common problem especially early after a stroke. The first session was therefore primarily a practice session and allowed participants to learn and perform the active rig tests and the mWMFT. On the second day participants completed the full protocol of wrist rig tests (passive and active) and performed the mWMFT. For some participants, however, fatigue was not a problem; they quickly learnt the active tasks and were able to complete the full-testing protocol in one day session. For the convenience of these participants, testing was therefore only conducted on one day. Seventeen participants who completed two day sessions of testing and successfully performed the active tests on both days (nine acute and eight chronic participants) were allocated to a reliability sub-group for analysis.

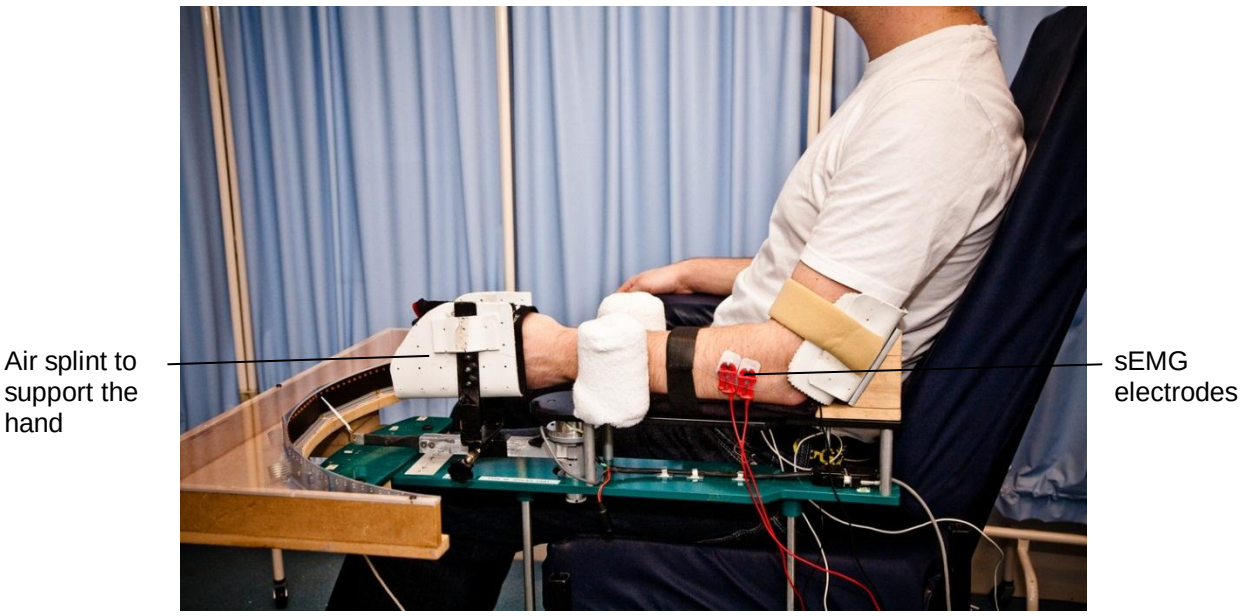


Figure 6-2 Participant set-up in the wrist rig

6.2.3. Data Processing

The processing of signal data was as described in the Methodology Chapter 4, Section 4.9.

6.2.4. Derivation of indices

The impairment indices that were used for the main study and their method of calculation were as described at the end of the Pilot Study Chapter 5, Table 5-19. One change was made to the process of deriving muscle onset timing. Visual analysis of the main study participant data showed that in a few individuals with very poor movement, extensor EMG activation could often not be detected. It was therefore decided that if muscle onset was detected less than four times out of the total of 11 target jumps, the participant would be excluded from the analysis. Additionally, the maximum torque applied during the extension

PROM test was calculated and recorded, so that the amount of force applied by the assessor to gain end of passive range could be verified across the three groups.

6.2.5. Statistical analysis

The statistical tests used in this study analysis are those that were described and justified in the Methodology Chapter, Section 4.11, and are summarized here. Because some of the impairment indices were not normally distributed (see Appendix G), non-parametric tests have been used with all the impairment variables.

6.2.5.1. Validity and repeatability of impairment indices

The results for validity (defined here as ability to distinguish between impaired and unimpaired) and repeatability are presented in three groups of impairment indices according to the negative, positive and secondary features of the upper motor neurone syndrome.

a) Validity (ability to distinguish between impaired and unimpaired)

Differences between the impaired and unimpaired groups were determined using the two independent samples Mann Whitney U test.

b) Between-days test-retest reliability (active tests)

To measure between-days level of agreement of the active test indices Bland Altman methods have been used (Bland & Altman 1986). The Bland and Altman plot of the differences between the day 1 and day 2 readings against the mean value for each participant were examined. The 95% limits of agreement were examined with respect to the within and between-group range of values for each index. A repeatability coefficient (Bland & Altman 1986) for each of the indices was also calculated, and gives a 95% range about a true change that might be expected from measurement error alone. Changes larger than the value of the repeatability coefficient can be considered to be due to a real change in underlying values, rather than random variations.

c) Within-test repeatability (active and passive sinusoidal tests)

Data from each of the tests were divided into three sections of equal number of target cycles. Mean tracking index, coactivation index and stretch index for each section was calculated. Changes were examined between sections one and two, and two and three, and tested for statistical significance ($p<0.05$) using the two related samples Wilcoxon test.

d) Differences between acute impaired, chronic impaired, and unimpaired groups

Differences between the three groups were determined using a Kruskal Wallis Test. Mann Whitney U test was used to determine the chronic vs. unimpaired and acute vs. unimpaired

differences for each impairment variable. Data for each participant across the three groups are presented as dot plots which were used to visually examine differences.

6.2.5.2. Association between impairment indices and motor control accuracy

Preliminary observation of individual step tracking data showed that stroke participants fell into distinct low motor control accuracy (MCA) and high MCA groups (see step tracking values in Results, Section 6.3.2). To compare differences between the low MCA group, the high MCA group and the unimpaired group for all the impairment indices, analysis was undertaken using a Kruskal Wallis test and Mann Whitney *U* tests.

6.2.5.3. Inter-relationships between negative, positive and secondary motor impairments

Relationships between all the impairment indices are presented separately for the acute and chronic groups using Spearman's correlation coefficients and *p* values. A Bonferroni correction was added, after which the statistical significance level was P≤0.004. Strength of relationship/ associations between variables were based on recommended values (Pett 1997); these being: 0.00 to 0.25 no association to weak association, 0.26 to 0.50 a low degree of association, 0.51 to 0.75 moderate to strong degree of association and 0.76 to 1.00 very strong association.

6.2.5.4. Relationships between motor impairments and functional activity (mWMFT)

To examine the importance of impairment indices in explaining performance of the functional activity measure (mWMFT), separately for the acute and chronic groups, a multiple linear regression was calculated using SPSS (PASW statistics v18). A non-parametric quantile regression was also run to compare and verify the results.

The impairments were grouped into negative, positive and secondary features in each patient group, and a series of two regression analyses were performed to determine the most important (statistically significant) contribution of an individual predictor of mWMFT in each feature group and each patient group.

6.3. Results

The results of the main study are presented in three sections. Firstly the characteristics of participants are presented, and missing data explained. The second section relates to the validity (here defined as the ability to distinguish between impaired and unimpaired) and repeatability (between-days test-retest and within-test) of the impairment measurement

indices, and lastly the differences between the acute impaired, chronic impaired and unimpaired groups, showing differences in individuals in each group. In the third section, relationships between impairment indices, motor control accuracy and functional activity are examined.

6.3.1. Participants

Time for recruitment to the Main Study was limited due to prior unforeseen problems with the development of the wrist rig and the detail of analysis required to derive impairment indices from the Pilot Study data. Additionally recruitment was affected at times by the Southampton Stroke Unit being closed for infection control. The final number recruited for the Main Study was 26 impaired participants (13 each in the acute and chronic groups), whose data was compared with fourteen unimpaired participants. Participant characteristics can be seen in Table 6-1.

Table 6-1: Characteristics of study participants

		Impaired			Unimpaired
		Acute (N=13)	Chronic (N=13)	Total (N=26)	(N=14)
Age (years)	Mean (SD) Min – max	74.6 (10.4) 60 – 94	65.6 (5.3) 60 – 74	70.1 (9.3) 60 – 94	73.4 (5.0) 65 – 81
Gender	M : F	5:8	10:3	15:11	4:10
Side assessed	R : L	7:6	6:7	13:13	13:1
Hand dominance	R : L	12:1	13:0	25:1	14:1
Time from stroke (months)	Mean (SD) Min – max	2.2 (1.0) 0.7 – 4	40.6 (27.2) 12 – 91	21.3 (27.2) 0.7 – 91	N/A
Spasticity[a] (0–4)	Mean (SD) Min – max	0.6 (1.0) 0 – 3	1.6 (1.2) 0 – 3	1.1 (1.2) 0 – 3	N/A
Spasticity medication[b]	No : Yes	13:0	9:4	22:4	N/A
Propriception[c] (0-3)	Mean (SD) Min - max	1.2 (1.1) 0 - 3	1.7 (0.6) 0 - 3	1.5 (0.9) 0 - 3	N/A
UL activity[d] (0 – 92)	Mean (SD) Min - max	29 (17) 2 - 64	43 (27) 2 - 75	36 (23) 2 - 75	92

[a] Tardieu scale fast movement score (Morris 2002): 0 - No resistance; 1- Slight resistance, no clear catch; 2- Clear catch at an angle and release; 3- Fatigable clonus (<10 seconds) at a precise angle; 4- Infatigable clonus (>10 seconds) at a precise angle; [b] Anti-spasticity medication – Baclofen or Tizanidine; [c] Wrist proprioception, Nottingham Sensory Assessment (Stolk-Hornsveld et al. 2006) : 2– normal, 1– impaired, 0– absent; [d] modified Wolf Motor Function Test, total function score (Whitall et al. 2006).

All 26 impaired participants completed all the tests except one acute stroke participant who withdrew from the study after the first day practice session as she found the testing process

too tiring. This participant consented for her session one data (the active rig tests and modified WMFT) to be included in the data analysis, but passive test data (stretch index and mean torque) was missing for this participant. Stretch index data is missing for one participant (chronic group) for technical reasons related to data quality. For the mean torque index, data were excluded from the analysis because of flexor EMG activity for two impaired participants (one acute and one chronic) and extensor EMG activity for one impaired (acute) and two unimpaired participants. Data for the analysis of step tracking coactivation from one participant (chronic) and for extensor onset timing from two participants (chronic) could not be included due to either very poor tracking or very low EMG signals. Of the 17 participants allocated to the reliability sub-group, data for one participant (acute) for the sine tracking index, four (one chronic and three acute) for the sine and step coactivation indices, and three (1 chronic and 2 acute) for extensor onset timing was missing from the day 1 session for technical reasons related primarily to data quality.

6.3.2. Validity and repeatability of impairment indices

In this section the validity (here defined as the ability to distinguish between impaired and unimpaired), the test-retest and within-test repeatability, and differences between the acute impaired, chronic impaired and unimpaired are presented. The results are presented in three groups of impairment indices according to the negative, positive and secondary features of the upper motor neurone syndrome. Important results are presented in tables in this Chapter, with the full tables of data analysis in Appendix G.

6.3.2.1. Negative impairments: Sine and step tracking indices, Extension active range of movement, Extensor isometric force and Extensor onset timing

All the negative impairments showed a statistically significantly difference between impaired and unimpaired participants at a *P* level of <0.001 or for extensor onset timing *P*=0.006 (Table 6-2). For between-days test-retest reliability, the Bland and Altman between-days limits of agreement and repeatability coefficients for each of these impairments, expressed in the same units as the impairment measure itself, are reported in Table 6-3. The Bland and Altman Plots (see Appendix G) showed no evidence for a trend in the difference between assessments other than a greater extension active range of movement mean value for the second day recording that was statistically significant (see mean difference and confidence intervals in Table 6-3). However, the mean difference was four degrees, which is small compared to the range of values (-52.3º to 51.2º).

Table 6-2: Median (Interquartile range) and *P* values for negative impairment indices comparing the impaired and unimpaired groups. Statistical significance was tested using the non-parametric Mann Whitney *U* test. Statistically significant between group differences (p<0.05) are in bold.

	Impairment Indices	Group median (IQR)		*P* values
		Impaired (N=26)	Unimpaired (N=14)	Unimpaired - Impaired
Negative Impairments	Sine tracking index (degrees^2)	118.2 (31.7, 193.5)	222.3 (213.8, 236)	**<0.001**
	Step tracking index (degrees)	6.36 (5.57, 11.28)	3.97 (3.52, 4.23)	**<0.001**
	Path length (degrees/sample)	0.022 (0.016, 0.025)	0.009 (0.007, 0.010)	**<0.001**
	Active ROM extension (degrees)	22.1 (-15, 36)	57.8 (53, 65)	**<0.001**
	Extensor IF (Nm)	1.18 (0.2, 2.6)	4.95 (3.1, 6.8)	**<0.001**
	Extensor onset [a] (seconds)	0.41 (0.31, 0.56)	0.29 (0.26, 0.34)	**0.006**

ROM – Range of movement; IF – isometric force; [a] Impaired group n=24;

Table 6-3: Between-days repeatability for the negative impairment indices for 17 impaired participants* (9 acute, 8 chronic) showing the range of values for this group, mean day 2 – day 1 difference and 95% confidence intervals, Bland and Altman limits of agreement and coefficient of repeatability.

	Impairment Indices	Range of values (min – max)	Between-days repeatability		
			Mean difference (day 2 – day 1)	Limits of agreement	Coefficient of repeatability
Negative Impairments	Sine tracking index [a] (degrees^2)	2.0 - 229.6	3.13 [-6.6, 12.9]	(-33.5, 39.8)	±35.32
	Step tracking index (degrees)	4 - 16.42	-0.21 [-0.7, 0.29]	(-2.14, 1.72)	±1.88
	Path length (degrees/sample)	0.012 - 0.050	-0.002 [-0.006, 0.002]	(-0.016, 0.013)	±0.014
	Extension AROM (degrees)	-52.3 - 51.2	4.4 [1.4, 7.4]	(-7.3, 16.1)	±14.1
	Extensor IF (Nm)	0 - 4.8	0.1 [-0.1, 0.4]	(-0.9, 1.2)	±1.1
	Extensor onset [b] (seconds)	0.22 - 1.28	-0.008 [-0.12, 0.11]	(-0.39, 0.38)	±0.37

*Unless stated otherwise; [a] N=16; [b] N = 13; Data was missing due to technical reasons on one day assessment.
AROM – active range of movement; IF – isometric force;

Within-test repeatability for the sine tracking index for the impaired (acute and chronic) and unimpaired groups is illustrated graphically in Figure 6-3. A statistically significant difference

was found in the acute group between the first and second, and second and third sections, which might reflect fatigue or loss of concentration.

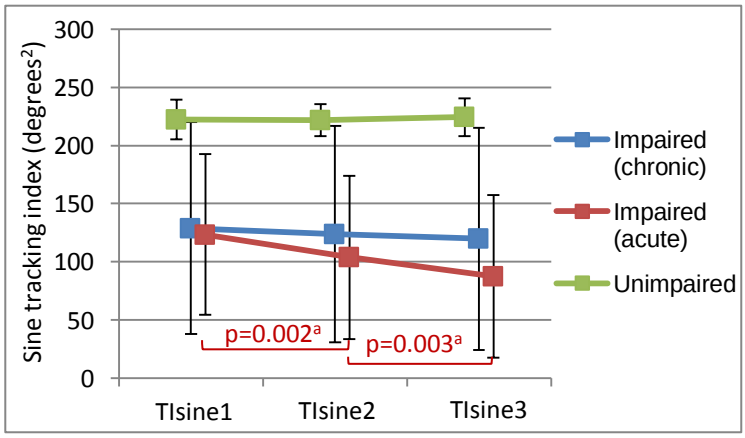


Figure 6-3: Line chart showing the mean and SD (vertical error bars) values for a) sine tracking index in TIsine 1 (beginning section), TIsine 2 (middle section) and TIsine 3 (end section), comparing the impaired (acute and chronic) and unimpaired groups.

[a] Statistically significant difference between sections ($p<0.05$).

Differences between the three participant groups are presented as median and interquartile ranges (IQR) and *P* values in Table 6-4, and individual differences illustrated graphically in Figure 6-4. There were statistically significant differences between the unimpaired and both the acute and chronic groups for all the negative impairments.

Table 6-4: Median (Interquartile range) and P values for negative impairment indices comparing the acute and chronic groups with the unimpaired group. Statistical significance was tested using a Mann Whitney U test. Statistically significant between group differences ($p<0.05$) are in bold. (AROM – active range of movement; IF – isometric force; [a] Chronic group n=11)

Negative Impairment Indices	Group median (IQR)			Kruskal Wallis Test	Mann Whitney *U* test values		*P*
	Acute (N=13)	Chronic (N=13)	Unimpaired (N=14)	*P* values	Unimpaired - Acute	Unimpaired - Chronic	
Sine tracking index (degrees²)	107.8 (41.3, 174.7)	178.8 (6.8, 201.1)	222.3 (213.8, 236)	**<0.001**	**<0.001**	**<0.001**	
Step tracking index (degrees)	6.51 (6, 10.8)	5.90 (4.8, 12.0)	3.97 (3.52, 4.23)	**<0.001**	**<0.001**	**<0.001**	
Path length (degrees/sample)	0.024 (0.022, 0.029)	0.017 (0.015, 0.022)	0.009 (0.007, 0.010)	**<0.001**	**<0.001**	**<0.001**	
Extension AROM (degrees)	19.5 (0.6, 34)	28.8 (-41, 37)	57.8 (53, 65)	**<0.001**	**<0.001**	**<0.001**	
Extensor IF (Nm)	0.51 (0.23, 1.38)	1.98 (0.17, 3.71)	4.95 (3.1, 6.78)	**<0.001**	**<0.001**	**0.002**	
Extensor onset [a] (seconds)	0.5 (0.32, 0.64)	0.4 (0.30, 0.50)	0.29 (0.26, 0.34)	**0.018**	**0.008**	**0.043**	

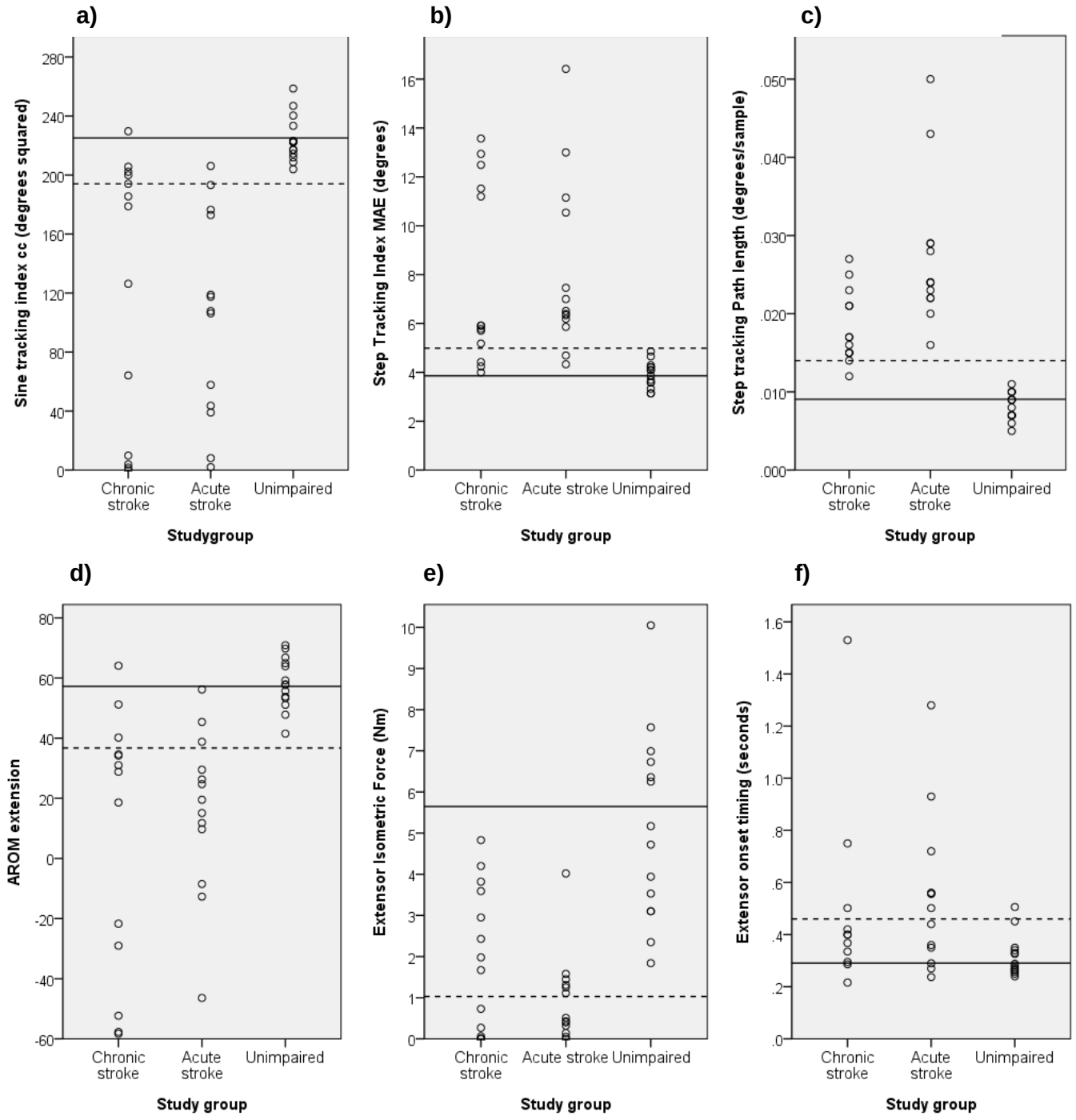


Figure 6-4 (a-f): Dot plots for the negative impairment indices illustrating differences between participants in the chronic and acute impaired and unimpaired groups. The dashed line is 2SD from the mean (solid line) of the unimpaired group. Values above the 2SD line (below for sine tracking index and extensor isometric force) are considered to be 'impaired'.

For most indices there was a greater variability (IQR) across the impaired group compared with the unimpaired group, except for extensor isometric force. In this index the unimpaired group had greater variability, illustrated as the spread of individual values in Figure 6-4 f).

This spread of values can be partly explained by gender differences in unimpaired strength, as is illustrated in Figure 6-5 a) and b). Taking +/- 2SD from the unimpaired mean as a normal range, a clear difference between impaired and unimpaired participants can be seen in all three tracking indices and extensor AROM (Figure 6-4 a – d). For extensor onset timing there is greater overlap between all three groups (Figure 6-4 f), and an overlap between the unimpaired and chronic group for extensor isometric force can be seen (Figure 6-4 e). For the extensor isometric force, however, when the groups are divided into male and female, the overlap between the chronic and unimpaired groups is removed except for one case of each gender (Figure 6-5 a and b).

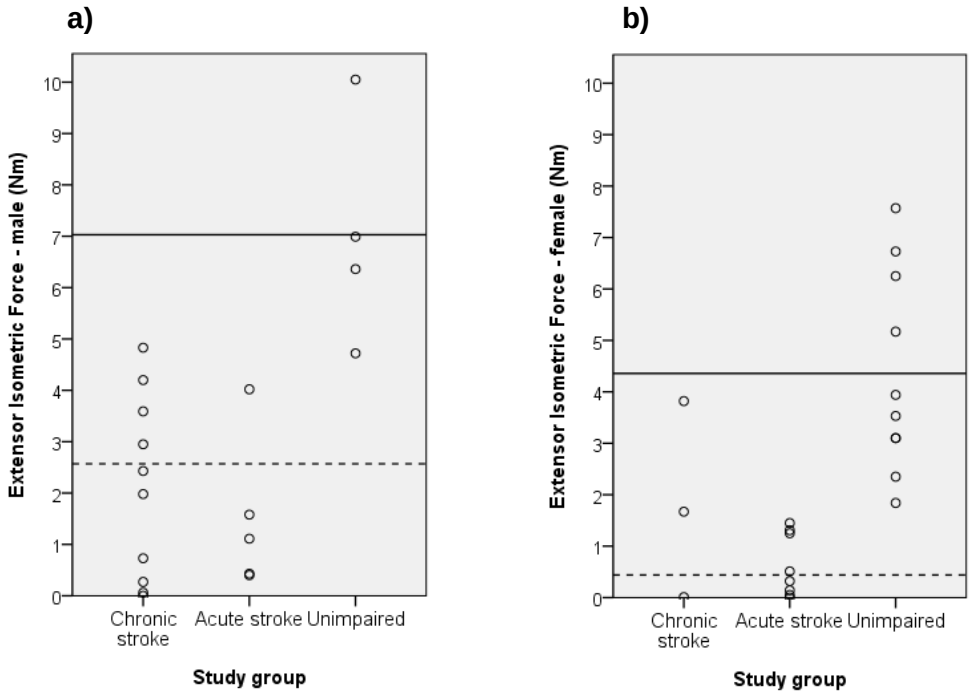


Figure 6-5 a) and b): Dot plots of extensor isometric force for a) male and b) female participants, indicating some gender differences in strength in the unimpaired group which partly contributes to the variability across the unimpaired group strength**.**

6.3.2.2. Positive Impairments: Stretch Index (spasticity) and Coactivation Indices (sine and step tracking)

The sine tracking coactivation index and stretch index at 3.5 Hz were able to statistically significantly distinguish between impaired and unimpaired participants (P=0.024 and P<0.001 respectively) (see Table 6-5). The step tracking coactivation index did not show a statistically significant difference (P=0.558).

Table 6-5: Median (Interquartile range) and *P* values for positive impairment indices comparing the impaired and unimpaired groups. Statistically significant between group differences (p<0.05 in bold) were tested using the non-parametric Mann Whitney *U* test.

	Impairment Indices	Group median (IQR)		*P* values
		Impaired (N=26)	Unimpaired (N=14)	Unimpaired - Impaired
Positive impairments	Coactivation (sine tracking) (correlation coefficient)	0.11 (-0.30, 0.30)	-0.34 (-0.45, -0.20)	**0.024**
	Coactivation (step tracking) [a] (correlation coefficient)	-0.05 (-0.27, 0.17)	-0.12 (-0.28, 0.05)	0.558
	Stretch index [b] (3.5Hz) (ratio SR area: LBL	1.24 (1.05, 1.76)	1.00 0.98, 1.02	**<0.001**

SR – stretch response; LBL – local baseline; [a] Impaired group n=25; [b] Impaired group n=24

Between-days reliability is not presented for the stretch index as it was derived from a passive tracking test which was only assessed during one day session. For the sine tracking coactivation index, there is no trace of a trend in the mean between-days difference, however the step tracking coactivation index showed a statistically significant trend towards less coactivation on day 2 (Table 6-6). For both the coactivation indices the limits of agreement and repeatability coefficients are wide compared to the range of values, especially for the sine tracking coactivation index. Observation of the Bland Altman plot for this index (Appendix G) showed an outlier who went from -0.68 (strong reciprocal inhibition) on day 1 to 0.14 (weak coactivation) on day 2. Despite this change in activation pattern (confirmed by visual inspection of the traces), his good tracking performance (within the unimpaired range) did not change from day 1 to day 2, and underlines the large within subject variability that presents one of the main challenges in the field.

Table 6-6: Between-days repeatability for the coactivation indices from the sine and step tracking tests for 13 participants from the impaired group showing the range of values for this group, mean day 2 – day 1 difference and 95% confidence intervals, Bland and Altman limits of agreement and coefficient of repeatability

Impairment Indices	Range of values (min – max)	Between-days repeatability		
		Mean difference [95% CI]	Limits of agreement	Coefficient of repeatability
Coactivation (sine tracking) (correlation coefficient)	-0.54 - 0.73	0.05 [-0.15, 0.24]	(-0.60, 0.69)	±0.61
Coactivation (step tracking) (correlation coefficient)	-0.50 - 0.71	-0.10 [-0.19, -0.01]	(-0.40, 0.21)	±0.34

Within-test repeatability for the stretch index and the sine tracking coactivation index is illustrated in Figure 6-6. No statistically significant differences between sections 1, 2 and 3 were found. The sine tracking coactivation index shows a trend to reduce in the middle section in all groups, and mostly in the acute group.

a) Stretch index (0.35Hz) b) Sine Coactivation Index

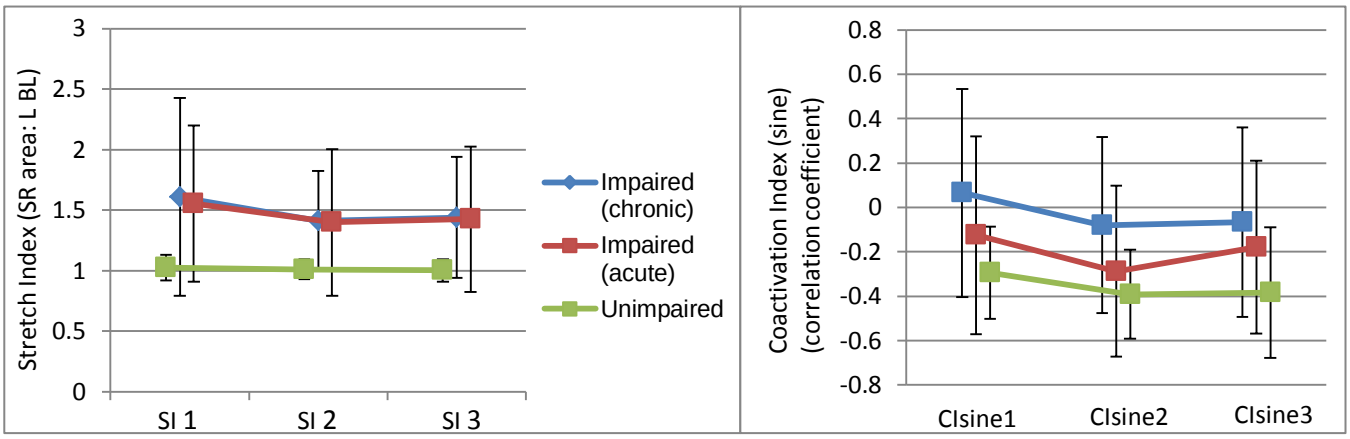


Figure 6-6 a) and b): Line charts showing the mean and SD (vertical error bars) values for a) stretch index in SI 1 (beginning section), SI 2 (middle section) and SI 3 (end section), and b) the equivalent sections for the sine tracking coactivation index (CIsine1, CIsine2, CIsine3), comparing the impaired (acute and chronic) and unimpaired groups.

Differences between the acute, chronic and unimpaired groups are shown in Table 6-7 and individual differences are illustrated in the dot plots in Figure 6-7. Statistically significant differences are seen for the stretch index between both the acute and chronic groups and the unimpaired group, and between the chronic and unimpaired groups for the sine tracking index. There was a greater difference for the step tracking coactivation index between the chronic and unimpaired groups but not statistically significant.

Table 6-7: Median (Interquartile range) and *P* values for positive impairment indices comparing the acute and chronic groups with the unimpaired group. Statistically significant group differences (Mann Whitney U test, p<0.05) are in bold.

Positive Impairment Indices	Group median (IQR)			Kruskal Wallis Test *P* values	*P* values	
	Acute (N=13)	Chronic (N=13)	Unimpaired (N=14)		Unimpaired - Acute	Unimpaired - Chronic
Coactivation (sine tracking) (correlation coefficient)	-0.2 (-0.45, 0.07)	0.14 (-0.19, 0.42)	-0.34 (-0.45, -0.20)	**0.014**	0.356	**0.003**
Coactivation (step tracking) [a] (correlation coefficient)	-0.09 (-0.33, 0.12)	0.04 (-0.20, 0.31)	-0.12 (-0.28, 0.05)	0.459	0.884	0.237
Stretch index [b] (ratio SR:LBL)	1.15 (1.05, 1.76)	1.34 (1.04, 1.93)	1.00 0.98, 1.02	**<0.001**	**<0.001**	**<0.001**

[a] Chronic group n=12; [b] Acute and chronic group n=12; SR – stretch response; LBL – local baseline

In both coactivation indices there was wide variation across the unimpaired group. Taking +/- 2SD from the unimpaired mean as a normal range, clear differences were seen in the stretch index, whereas in both coactivation indices there was greater overlap between the groups. Six individuals for sine tracking and three for step tracking had coactivation values outside the normal range, more in the chronic group than acute.

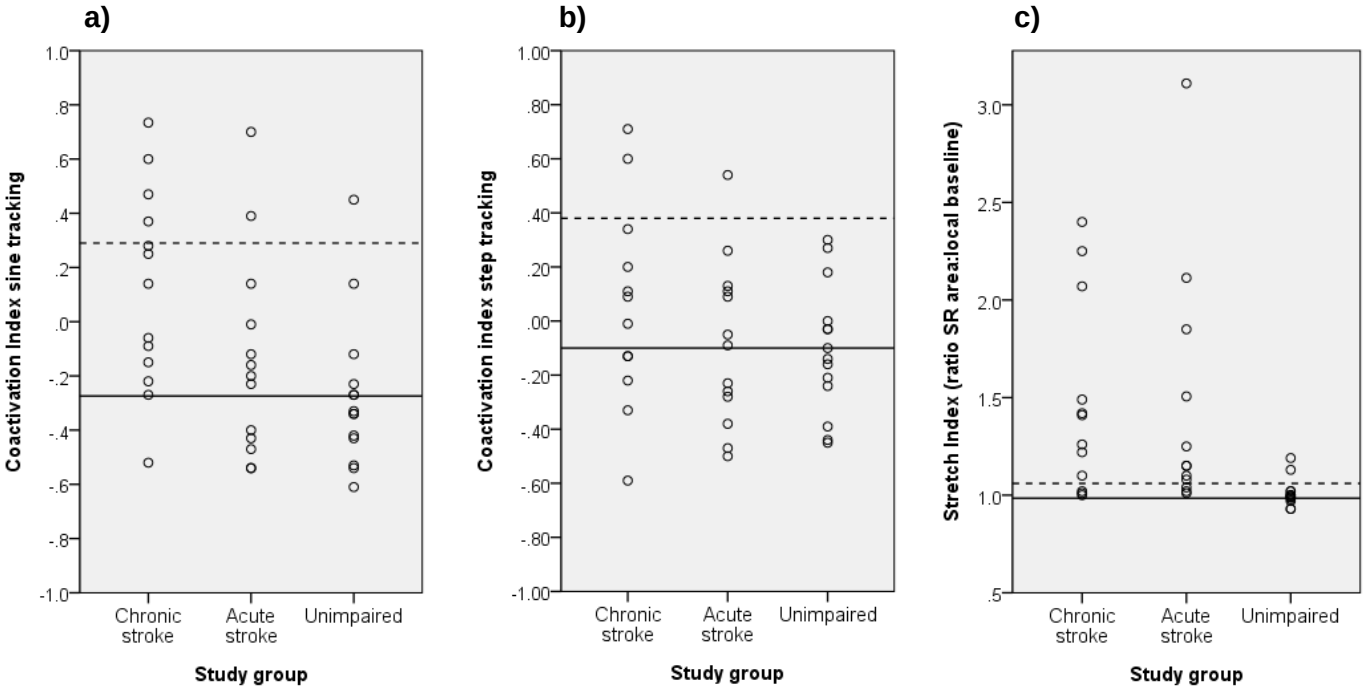


Figure 6-7 a)-c): Dot plots for the positive impairment indices illustrating differences between participants in the three groups. The dashed line is 2SD from the mean (solid line) of the unimpaired group. Values above the 2SD line are considered to be 'impaired'.

6.3.2.3. Secondary impairments: Extension passive range of movement and Mean torque index (non-neural stiffness)

There was a statistically significantly difference between impaired and unimpaired participants for extension passive range of movement (PROM) (P<0.001) but not for mean torque (P= 0.109) (see Table 6-8).

Table 6-8: Median (Interquartile range) and *P* values for secondary impairment indices comparing the impaired and unimpaired groups. Statistically significant between group differences, tested using the non-parametric Mann Whitney *U* test, (p<0.05) are in bold.

	Impairment Indices	Group median (IQR)		*P* values
		Impaired (N=26)	Unimpaired (N=14)	Unimpaired - Impaired
Secondary impairments	Passive ROM extension (degrees)	60.1 (42.4, 65.7)	70.09 (65.5, 73.9)	**<0.001**
	Mean torque [a] (Nm)	0.49 (0.33, 0.87)	0.45 (0.39, 0.65)	0.109

[a] Impaired group n=22, unimpaired n=11

Between-days reliability is not presented for mean torque as it was derived from a passive tracking test which was only assessed during one day session. The between-days reliability data for extension PROM can be seen in Table 6-9. There was no trend in the mean between-days difference. The limits of agreement and coefficient of repeatability values are similar to the extension AROM values, though the extension PROM range is smaller. Observation of the Bland Altman plot showed that there was an outlier with a between-days difference of 18º, whereas most other between-days values were grouped between ±10º (Appendix G).

Table 6-9: Between-days repeatability for extension passive range of movement for 13 participants from the impaired group showing the range of values for this group, mean day 2 – day 1 difference and 95% confidence intervals, Bland and Altman limits of agreement and coefficient of repeatability

Secondary Impairment	Range of values (min – max)	Between-days repeatability		
		Mean difference [95% CI]	Limits of agreement	Coefficient of repeatability
Extension PROM (degrees)	21 - 69.8	2.3 [-1.1, 5.7]	(-10.9, 15.5)	±13.4

Differences between the acute, chronic and unimpaired groups are shown in Table 6-10 and individual differences are illustrated in Figure 6-8. Extension PROM was statistically significantly lower in the acute and chronic groups compared to the unimpaired group, and the differences can be clearly seen in the dot plot (Figure 6-8a). To verify that the force applied by the assessor to gain end of passive range of movement was comparable across the different groups, a Kruskal Wallis test comparing the maximum torque applied during the PROM test across the three groups was used. The results showed that there was no significant difference between the groups (p=0.874). The acute group had statistically significantly lower mean torque compared to the unimpaired group, whereas there was no statistically significant difference between the chronic and unimpaired groups.

Table 6-10: Median (Interquartile range) and *P* values for secondary impairment indices comparing the acute and chronic groups with the unimpaired group. Statistical significance was tested using a Mann Whitney U test. Statistically significant between group differences (*P*<0.05) are in bold.

Impairment Indices	Group median (IQR)			Kruskal Wallis Test *P* values	*P* values	
	Acute (N=13)	Chronic (N=13)	Unimpaired (N=14)		Unimpaired - Acute	Unimpaired - Chronic
Ext PROM (degrees)	48.9 (31.2, 55.8)	60.1 (42.4, 65.7)	70.09 (65.5, 73.9)	**<0.001**	**<0.001**	**0.007**
Mean torque [a] (Nm)	0.18 (0.07, 0.27)	0.49 (0.33, 0.87)	0.45 (0.39, 0.65)	**0.002**	**0.002**	0.853

PROM – passive range of movement; [a] Acute group n=10, chronic n=12, unimpaired n=11

Figure 6-8b) shows the overlap of values between all the groups for mean torque. Like active ROM, gender was found to have an effect on non-neural stiffness. Male unimpaired participants had higher mean torque than female, and when the groups were divided by gender, the overlap of values between the groups reduced (Figure 6-8 c and d). These dot plots showed that in the chronic group some participants had lower mean torque values than the normal range, but two outliers (one male, one female) had much higher torque values.

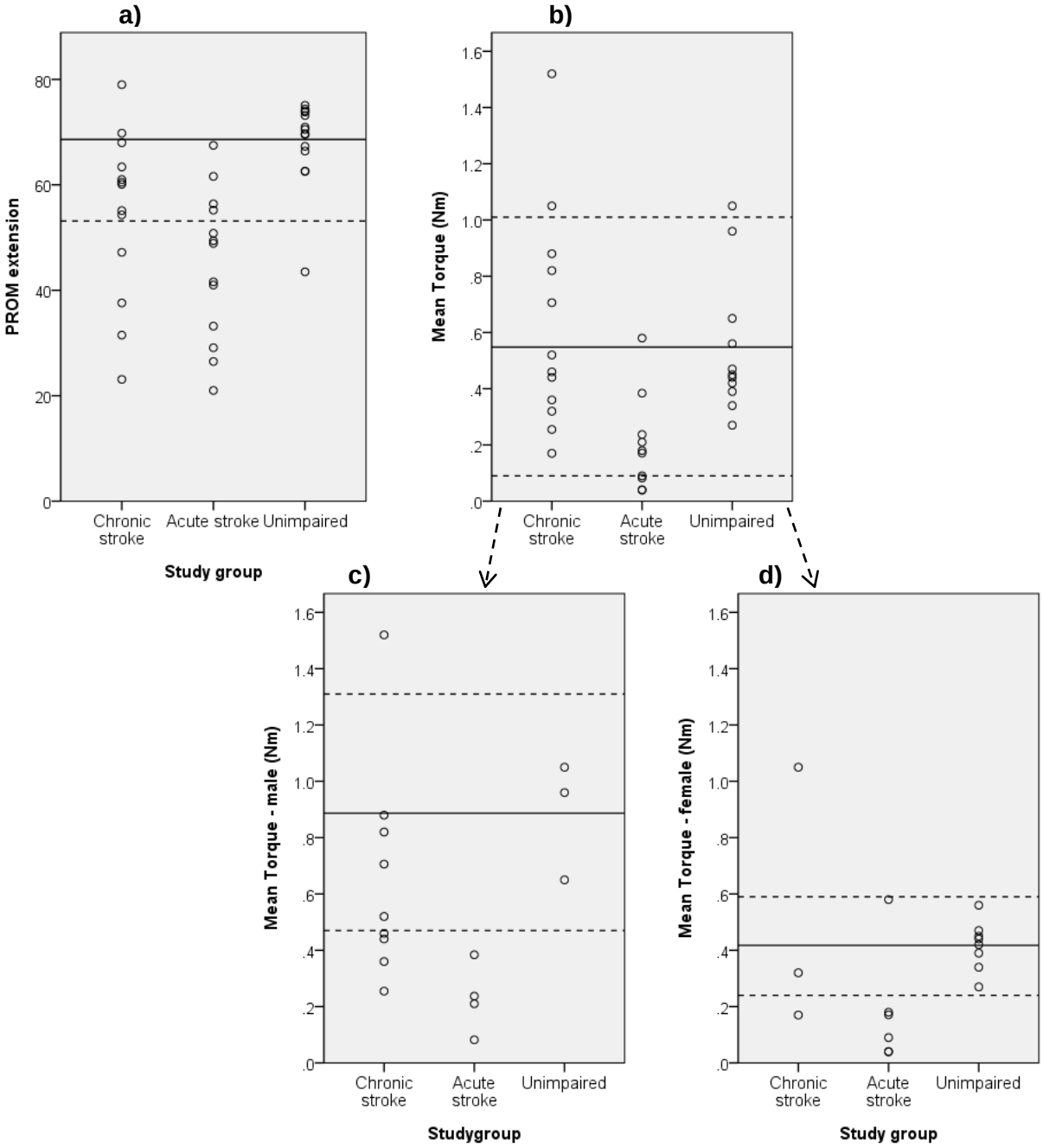


Figure 6-8 a) - d): Dot plots for the secondary impairment indices **(a)** and **(b)** illustrating differences between participants in the chronic, acute and unimpaired groups. Values for the mean torque index have been divided to show differences between male **(c)** and female **(d)**. The dashed line is 2SD from the mean (solid line) of the unimpaired group. Values above (or below) the 2SD line are considered to be 'impaired'.

6.3.3. Association between impairment indices and motor control accuracy (MCA)

When the individual step tracking data was plotted on dot plots, it could be seen that the impaired stroke participants were separated into two clear groupings, those with an error up to 7.5º (high MCA), and those with an error of between 10.5º and 16.5º (low MCA) (see step tracking values in Section 6.3.2 Figure 6-4 b).

The values for all impairment indices in the low and high motor control accuracy (MCA) groups and unimpaired group are shown in Appendix G, Table G-6. The Kruskal Wallis Test showed that most impairments indices were statistically significant across the three groups, except for the mean torque index. The impairments that showed statistically significant difference between low and high MCA (Mann Whitney *U* tests) were extension AROM (p=<0.001), extensor isometric force (p=0.001), extensor onset time (p=0.022), coactivation sine tracking (p=0.001) and step tracking (p=0.003), and extension passive range of movement (p=0.022). No statistically significant difference was seen for stretch index and mean torque index.

The low MCA group was statistically significantly different from the unimpaired group in all impairment indices except mean torque index. The high MCA group was statistically significantly different from the unimpaired group in extension AROM (*p*=<0.001), extensor isometric force (*p*=0.001), stretch index (*p*=<0.001), extension PROM (*p*=0.002) and mean torque index (*p*=0.021). Most impairment measures in both the low and high MCA groups had either lower or higher values than the unimpaired group. However, the mean torque was lower in the high MCA group than unimpaired and non-significantly higher in the low MCA group.

When observing the dot plot of step tracking performance, in particular the individuals who had low MCA and high MCA, and comparing their values in other impairment dot plots, some clear patterns have emerged (Figure 6-9). Patients with low MCA in the acute group were also those with the weakest wrist extensors, and those with low MCA in the chronic group had the most coactivation and weakest wrist extensors. Patients with higher MCA also were those with nearest normal wrist extensor strength.

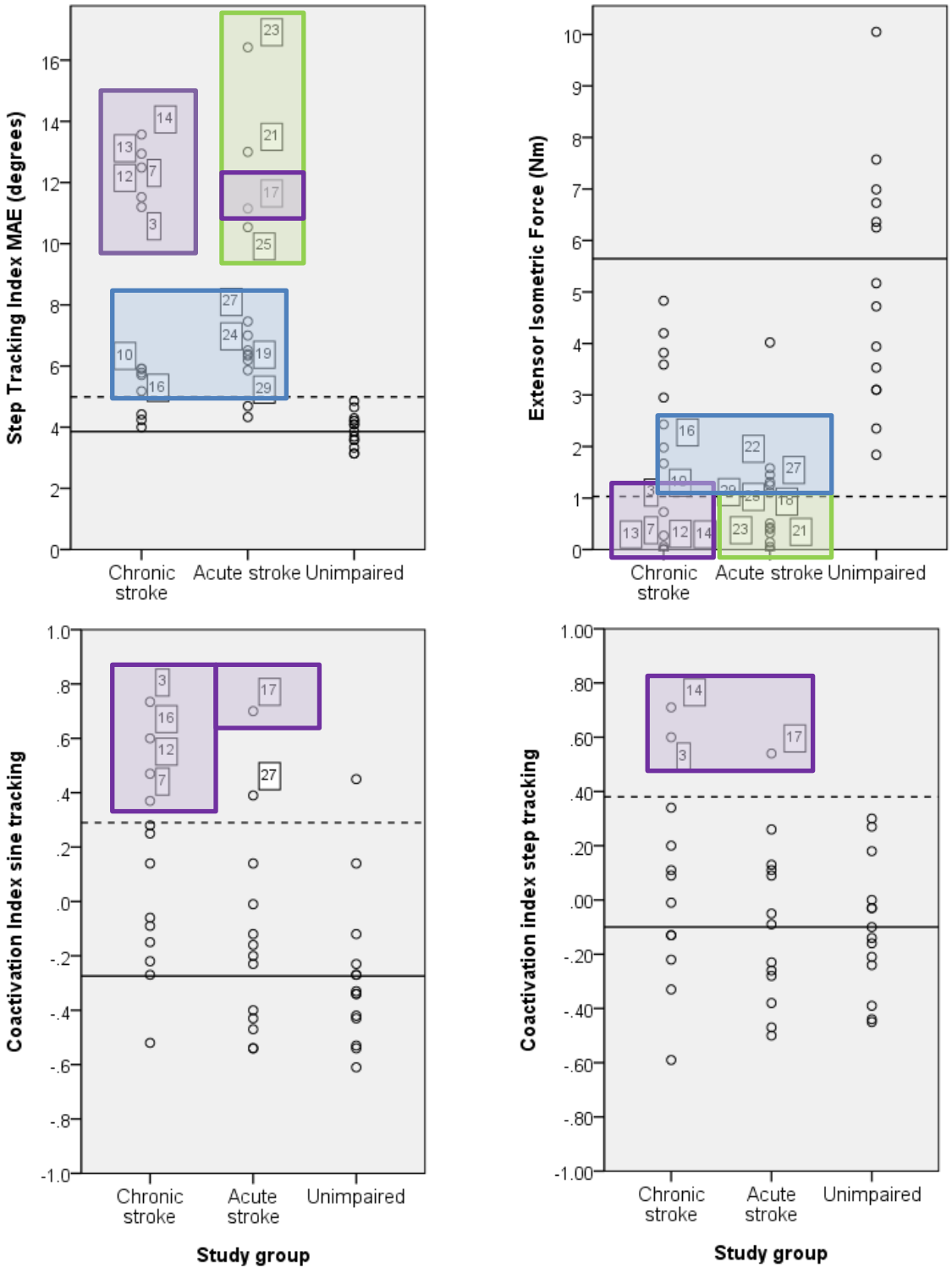


Figure 6-9: Dot plots with sub-groups showing impaired participants with low motor control accuracy (MCA) who also had weakness (acute group), or had both coactivation and weakness (chronic group), and those with higher MCA also had moderate weakness (both groups). The numbers next to the dots refer to individuals.

6.3.4. Inter-relationships between negative, positive and secondary motor impairments

Acute and Chronic group correlation coefficients (Spearman's) for all the impairments are presented in Appendix G, Table G-7 and Table G-8. For the negative impairments , in the acute group the tracking indices statistically significantly correlated with each other and extensor onset timing, and extensor isometric force correlated with extensor active range of movement. In the chronic group, all the negative impairment inter-relationships were significant with the exception of extension AROM with extensor onset time, and path length which showed no to weak correlation with all other impairment variables.

Table 6-11: Statistically significant (p<0.05) Spearman's correlation coefficients between negative impairments for acute group (N=13) and chronic group (N=13). Shaded cells are statistically significant values following Bonferroni correction (p<0.004)

Group	Impairment indices	Correlation	Group	Impairment indices	Correlation
Acute	Sine TI with Step TI	-0.912 (*P*<0.001)	Chronic	Sine TI with Step TI	-0.863 (*P*<0.001)
	Sine TI with Ext onset	-0.619 (*P*=0.024)		Sine TI with Ext onset	-0.661 (*P*=0.027)
	Step TI with Ext onset	-0.619 (*P*=0.024)		Step TI with Ext onset	0.638 (*P*=0.035)
	IF ext with AROM ext	0.775 (*P*=0.002)		IF ext with AROM ext	0.725 (*P*=0.005)
				Sine TI with AROM ext	0.681 (*P*=0.010)
				Step TI with AROM ext	-0.676 (*P*=0.011)
				Sine TI with IF ext	0.846 (*P*<0.001)
				Sine TI with IF ext	-0.780 (*P*=0.002)
				IF ext with Ext onset	-0.651 (*P*=0.030)

TI: Tracking Index; Ext: extension; IF: Isometric force; AROM: active range of movement

For the positive impairments (Table 6-12), the coactivation indices significantly correlated with each other in both patient groups. In the acute group there was a moderate correlation of the step tracking coactivation index with the stretch index at 0.5Hz that approached significance (r=0.573, p=0.051). In the chronic group there was a moderate non-significant correlation of stretch index at 3.5Hz with sine tracking coactivation (r=0.531, p=0.075). The sine tracking coactivation index significantly correlated with the tracking indices in both groups and with extensor onset in the acute group, and extension AROM in the chronic group. The step tracking coactivation index significantly correlated with the sine tracking index. The stretch index at 3.5Hz was only weakly correlated with all other impairments in the

acute group, and weak to moderately correlated in the chronic group; none of these reached statistical significance.

Table 6-12: Statistically significant (*p*=0.05) Spearman's correlation coefficients between positive and negative impairments for acute group (N=13) and chronic group (N=13). Shaded cells are statistically significant values following Bonferroni correction (*p*<0.004)

Group	Impairment indices	Correlation	Group	Impairment indices	Correlation
Acute	CI Sine with CI Step	0.748 (*P*=0.003)	Chronic	CI Sine with CI Step	0.592 (*P*=0.043)
	CI Sine with Sine TI	-0.878 (*P*<0.001)		CI Sine with Sine TI	-0.725 (*P*=0.005)
	CI Sine with Step TI	0.880 (*P*<0.001)		CI Sine with Step TI	0.615 (*P*=0.025)
	CI Sine with Ext onset	0.763 (*P*=0.002)		CI Sine with AROM ext	-0.692 (*P*=0.009)
	CI Step with Sine TI	-0.571 (*P*=0.041)		CI Sine with IF ext	-0.698 (*P*=0.008)
	CI Step with SI (0.5Hz)	0.573 (*P*=0.051)		CI Step with Sine TI	-0.669 (*P*=0.017)
				CI Step with Step TI	0.795 (*P*=0.002)
				CI Step with IF ext	-0.834 (*P*=0.001)
				SI (3.5Hz) with SI (.5Hz)	0.776 (*P*=0.003)

CI: coactivation index; TI: Tracking Index; Ext: extension; SI: stretch index; IF: Isometric force

For the secondary impairments (Table 6-13), extension PROM significantly correlated with extension AROM and extensor isometric force in both groups. The mean torque index was not significantly correlated with any impairment in either group.

Table 6-13: Statistically significant (*p*=0.05) Spearman's correlation coefficients between secondary and negative impairments for acute group (N=13) and chronic group (N=13). Shaded cells are statistically significant values following Bonferroni correction (*p*<0.004)

Group	Impairment indices	Correlation	Group	Impairment indices	Correlation
Acute	PROM ext with AROM ext	0.758 (P=0.003)	Chronic	PROM ext with AROM ext	0.720 (P=0.006)
	PROM ext with IF ext	0.555 (P=0.049)		PROM ext with IF ext	0.566 (P=0.044)

6.3.5. Relationships between motor impairments and functional activity (mWMFT)

Correlation coefficients (Spearman's) for all the impairments and functional activity measure (mWMFT total function score) are presented in Appendix G, Table G-7 and Table G-8 and

indicate differences in impairment and activity relationships in the acute and chronic groups. Statistically significant correlation coefficients are presented in Table 6-14. In the acute group, very strong and strong (Pett 1997) statistically significant associations were found between mWMFT and two negative impairments: extension AROM and extensor isometric force and a moderate association with one secondary impairment: extension PROM. The correlation coefficient of one other negative impairment indicated a moderate degree of association which approached statistical significance: sine tracking (r=0.539, p=0.057). In the chronic group, more statistically significant relationships were found. Strong to very strong associations were found between mWMFT and negative impairments: sine and step tracking, extension AROM, extensor isometric force, extensor onset timing; and positive: sine tracking coactivation index, step tracking coactivation index; and stretch index. MWMFT was not significantly correlated to path length or mean torque index in either groups, and the correlation coefficients indicated a weak to low degree of association (Pett 1997).

Table 6-14 Statistically significant (p=0.05) Spearman's correlation coefficients between impairments and functional activity (mWMFT) for acute group (N=13) and chronic group (N=13). Shaded cells are statistically significant values following Bonferroni correction (p<0.004)

Group	Impairment indices	Correlation with mWMFT	Group	Impairment indices	Correlation with mWMFT
Acute	AROM ext	0.787 (P=0.001)	Chronic	Sine TI	0.863 (p<0.001)
	IF ext	0.707 (P=0.007)		Step TI	-0.835 (p<0.001)
	PROM ext	0.624 (P=0.023)		Ext onset	-0.647 (P=0.031)
				AROM	0.791 (P=0.001)
				IF ext	0.758 (P<0.003)
				CI (sine)	-0.786 (P=0.001)
				CI (Step)	-0.697 (P=0.012)
				SI (3.5Hz)	-0.720 (P=0.008)

Linear regression was used to examine the importance of the impairment measures in explaining performance of the functional activity measure (mWMFT) and the results verified using quantile regression. In stage one of this process, each impairment was entered separately into a linear regression and a quantile regression analysis with mWMFT, to examine which were statistically significant predictors in each of the negative, positive and secondary feature groups (Appendix G Table G-9). The impairment variables which uniformly

failed to reach significance in both patient groups using both forms of analysis, were path length (negative feature), stretch index (positive feature), and mean torque index (secondary feature), and were removed from further regression analysis. Other variables remained in the analysis because in one or other group, or in one or other form of analysis, they reached, or at least approached, statistical significance.

Because there were two or more remaining impairment variables in the negative and positive feature groups, in the second stage of regression analysis, these impairments were entered into a forward stepwise regression with mWMFT to determine the most important one. In the acute group, for the negative impairments, there was no significant effect of sine tracking index (p=0.498), step tracking index (p=0.450), extensor AROM (p=0.162) and extensor onset timing (p=0.068) whereas extensor isometric force was significant (p<0.001) (quantile regression: p=0.003). For the positive impairments neither coactivation indices were statistically significant (sine p=0.795, step p=0.116). This left extensor isometric force (negative) and extension PROM (secondary) as the most important predictors of mWMFT for this patient group (Table 6-15). In the chronic group, for the negative impairments there was no significant effect of extensor isometric force (p=0.905), step tracking index (p=0.621), extensor AROM (p=0.327) and extensor onset timing (p=0.810) whereas the sine tracking index was significant (p<0.001) (quantile regression: p=0.001). For the positive impairments, there was no significant effect of step tracking coactivation index (p=0.063) whereas sine tracking coactivation index was significant (p=0.001) (quantile regression: 0.050). Thus the sine tracking index (negative), sine tracking coactivation index (positive), and extension PROM (secondary), were the most important predictors of mWMFT for this patient group (Table 6-15).

Table 6-15: Linear regression of mWMFT on negative, positive and secondary impairments

Acute Group	**Impairment variable**	**R^2**	**95 %CI**	***P* value**
Negative	Isometric Force	68.9%	7.1, 18.5	<0.001
Secondary	Extension PROM	37.1%	0.10, 1.32	0.027
Chronic Group	**Impairment variable**	**R^2**	**95 %CI**	***P* value**
Negative	Tracking Index $_{(sine)}$	88.5%	0.21, 0.36	<0.001
Positive	Coactivation Index $_{(sine)}$	66.4%	-79.1, -26.3	0.001
Secondary	Extension PROM	37.7%	0.15, 1.92	0.026

6.4. Summary of findings

Presented here is a summary of the main findings in this Chapter. Discussion of these points, and how they relate to previous research findings and to clinical practice, follows in Chapter 7.

6.4.1. Validity and repeatability of indices:

1. With all the impairment participants grouped together, all the negative impairments (sine and step tracking indices, extension AROM, extensor isometric force and extensor onset timing), the sine tracking coactivation index and stretch index (positive), and extension PROM (secondary) distinguished between impaired and unimpaired. The step tracking coactivation index (positive) and mean torque index (secondary) did not.
2. For between-days test-retest repeatability in the active tests, the impairment indices derived from EMG signals – extensor onset timing and coactivation indices – showed wide 95% limits of agreement and coefficients of repeatability.
3. Within-test repeatability of indices showed a statistically significant deterioration of the sine tracking index was seen, only in the acute impaired group. Other indexes tested (isometric force, sine tracking coactivation index and stretch index) did not show this,
4. With the impaired participants in acute and chronic subgroups, all the negative impairments, the stretch index and extension PROM were statistically significantly different compared to the unimpaired group. In the acute group, both the coactivation indices did not significantly differ from unimpaired. In the chronic group the sine tracking coactivation index was statistically significantly different, whereas the step tracking coactivation index was not.
5. For most indices a greater interquartile range was observed for impaired participants than for unimpaired. However for some impairment measures (extensor isometric force, mean torque index and the coactivation indices) the unimpaired range was almost as wide, if not wider (in extensor isometric force), than the impaired groups. Gender differences were found to contribute to the variability in the unimpaired group in extensor isometric force and mean torque index. The variability in coactivation indices indicates the breadth of muscle activation strategies used in normal movement.

6.4.2. Association between impairment indices and motor control accuracy (MCA)

6. The factors that distinguished low MCA from high MCA were smaller extension AROM and PROM, reduced extensor isometric force, delayed extensor onset timing and coactivation (sine and step tracking). There was no statistically significant difference for spasticity (stretch index) and non-neural stiffness (mean torque index).

7. Sub-groups of impaired participants were identified which related to the level of MCA. Those patients with low MCA in the acute group were also those with the most extensor weakness, and those with low MCA in the chronic group also had the most coactivation and extensor weakness. Those patients with higher MCA also were those with extensor strength nearer the normal range.

6.4.3. Inter-relationships between impairment indices

8. There were more statistically significant inter-relationships in the chronic than acute group.
9. Most of the negative impairments in the chronic group were significantly correlated, except for path length which did not correlate with any other impairment measure. In the acute group the tracking indices and extensor onset timing were significantly correlated, as well as extension AROM with extensor weakness.
10. Within the positive group there was a moderate correlation between coactivation (step tracking at 0.5 Hz) and spasticity (stretch index at 0.5Hz) in the acute group that almost reached statistical significance (p=0.051).
11. None of the positive impairments (coactivation and spasticity) statistically significantly correlated with the secondary impairments - non-neural stiffness (MTI) and contracture (extension PROM). MTI did not significantly correlate with any other impairment measure.
12. Extension PROM significantly correlated with extension AROM and extensor weakness.

6.4.4. Relationships of impairment indices with functional activity

13. Using Spearman's correlation, the impairments that were related to functional activity (mWFMT) in the acute group were extensor weakness, extension AROM and PROM.
14. In the chronic group, there were many more impairments that were associated with functional activity. As well as weakness and loss of AROM, other negative impairments included sine and step tracking accuracy and delayed extensor muscle onset. The positive impairments also had a strong influence, as the stretch index and both coactivation indices were significantly correlated with the mWFMT. The secondary impairments were only weakly correlated.
15. Regression analysis showed that the most important negative impairment contributor to functional activity in the acute group was extensor weakness, and in the chronic group was the sine tracking index. The most important positive impairment contributor, in the chronic group only, was sine tracking coactivation. Extension PROM was the most important secondary impairment contributor in both groups.

7. Discussion

The aim of this thesis was to advance understanding of the neuromechanical mechanisms associated with normal and impaired functional activity and recovery and the relationship between motor impairments and loss of activity in the upper limb of older adults, early and late post-stroke. This has clinical importance, because currently there is a lack of objective impairment measures and therefore the choice of treatments are not well informed. This study has used a comprehensive approach to the evaluation of motor impairments. A previous study at the metacarpophalangeal joints (Kamper et al. 2006b), and our preliminary research at the wrist (Burridge JH et al. 2005; Turk et al. 2008b), have also evaluated a wide range of motor impairments and assessed their relationship with functional activity, but this is the first study to compare impairments at the acute and chronic phases post-stroke. Furthermore novel methods have been developed and evaluated to quantify motor control accuracy during discrete movements, coactivation, muscle onset timing and spasticity and stiffness.

A neuromechanical tool (the wrist rig) and tests to measure a wide range of motor impairments have been developed. In Pilot Studies (Chapter 5) the testing protocol was optimised and physiologically and clinically relevant motor impairment indices were derived from the neuromechanical signals, and then evaluated. In the Main Study (Chapter 6) the wrist rig tests and a test of upper limb functional activity were applied to a sample of older impaired participants in the acute and chronic stages post-stroke, and the results were compared with a sample of unimpaired participants. A preliminary analysis quantified test-retest and within test repeatability of the impairment indices. Relationships between impairments and between impairments and functional activity have been quantified. In this Chapter, the most clinically important and novel findings from Chapters 5 and 6 are examined and discussed in the context of previous published research. The implications for clinical practice and the limitations of the study are discussed, and plans for future research presented.

In the Sections that follow, the results are discussed in the context of the negative, positive and secondary impairment features of the upper motor neurone syndrome.

7.1. Negative Impairments

Previous research has repeatedly identified that the negative impairments associated with the UMN syndrome are critical to function and our findings support this (Ada et al. 2006;

Bohannon et al. 1991; Burridge et al. 2008; Canning et al. 2004; Chae et al. 2002b; Kamper et al. 2006b; Mercier and Bourbonnais 2004; Wagner et al. 2006; Zackowski et al. 2004). Most importantly we have identified valid and reliable tests to quantify a range of negative impairments that have the potential to be adapted for clinical use to inform choice of treatment and monitor progress. We have also identified the relationships between negative impairments and function and how they differ between sub-acute and chronic populations. The negative impairments discussed below are: accuracy of motor control, measured in the tracking tasks; wrist extensor weakness; reduced range of active movement and wrist extensor muscle onset time.

7.1.1. Motor control accuracy - Sinusoidal and Step tracking

Finding suitable parameters to assess motor control presents methodological challenges. There are multiple ways in which movement control can be assessed. In this work the analysis has been restricted to measures from movement tracking tasks at the wrist, which are of interest for stroke rehabilitation, based on published research, seminal literature on motor control and pathophysiology.

Using our chosen methods of measuring motor control from movement tracking tasks, we were able to statistically significantly distinguish between the unimpaired and impaired group, both when the acute and chronic groups were analysed together and separately, confirming what was evident from visual analysis of the wrist movement plots.

Tracking ability or skill is complex and can be measured in a variety of different ways (Ada et al. 1996; Dietz et al. 1991; Feys et al. 2006; Halaney & Carey 1989). In this study a sinusoidal tracking test (Turk et al. 2008b) was used to represent rhythmic movements of the wrist, and a novel step tracking test was developed to represent discrete movements. Although sine tracking is potentially more reliable, because it generates multiple cycles of data that can be averaged, random step tracking, which involves complex acceleration and deceleration, demands cognitive control for which higher-level planning areas of the cortex are recruited (Schaal et al. 2004). This is probably closer to the requirements of day-to-day activities involving the wrist than repetitive movements and therefore possibly more related to function. The step tracking test has also provided additional insights into tracking accuracy (path length at the end-point target position) and muscle activation patterns (extensor onset timing).

The sine tracking index using cross-correlation has been used previously to characterise overall tracking accuracy during the sinusoidal tracking task (Notley et al. 2007) and has been shown as a valid method to distinguish unimpaired motor control accuracy from

impaired in the chronic phase post-stroke (Turk et al. 2008b). The step tracking measurement methods chosen for the Main Study assessed accuracy during the total task using mean absolute error (MAE), and path length at the end-point target position. This was chosen because in Pilot Study 3, with a small number of impaired participants in the chronic phase, these methods distinguished best between impaired and unimpaired compared to two other similar measurement methods (MAE and standard deviation at the end-point target position). The results of both these studies were corroborated in the Main Study of this research with a larger sample.

Repeatability between day 1 and day 2 assessments was evaluated using Bland Altman statistics – the mean difference, 95% levels of agreement and the repeatability coefficient. The mean difference between repeated measurements was evaluated for any statistically significant systematic trend, which was not present for the sine and step tracking and path length indices. The 95% levels of agreement are more difficult to interpret; the decision as to what level of discrepancy between assessments is indicative of lack of agreement needs to be made on clinical rather than purely statistical grounds. This is difficult to decide at this stage because these measurements are new, and have not been used during rehabilitation studies. It may be useful to compare the 95% levels of agreement to the range of values for impairment indices, and it can be said that for both tracking indices they were relatively narrow, but for path length were relatively wide (-0.016, 0.013 deg/sample) compared to the range of values (0.012 - 0.050 deg/sample). The repeatability coefficients obtained in this study are benchmark values that can be used in future studies in which the wrist rig tests are used to measure change in an individual's stroke condition following an intervention. The sine tracking index has previously been assessed for test-retest repeatability within one session (Turk et al. 2008b) and the repeatability coefficient was ±58 degrees^2, whereas in this study evaluating between-days repeatability, the repeatability coefficient was smaller at ±35 degrees^2. The difference between these repeatability coefficient values is likely to be due to the studies having different patient samples, but may also be due to having a different target display for the sinusoidal tracking task. The first study used a moving target on a screen at eye-level, whereas for this study the target was an LED display placed close to the hand being tested. Thus the target and wrist movement can be viewed simultaneously, which may reduce the visuo-perceptual demands of the task, improving the repeatability of results.

Evaluation of sine tracking within-test repeatability showed that the performance in both impaired groups tended to deteriorate during the test, and in the acute group this was statistically significant. Considering the nature of this task which is to maintain repeated flexion and extension movements of 40º for one minute, it is probable that the cause of the

reduction of tracking performance is neuromuscular fatigue. This is a clinically recognised problem for those with stroke especially during the acute and sub-acute phases, and has been identified in research during MVC tasks (Knorr et al. 2011; Riley and Bilodeau 2002), but has not previously been identified in research involving tracking tasks.

Relationships of tracking performance with other impairments and with function will be discussed in Sections 7.4 and 7.5.

7.1.2. Extensor weakness (isometric force) and active extension range of movement

Extensor weakness and limited active extension range of movement are important negative impairments that are commonly measured during the assessment of a stroke patient, though often not objectively. Weakness and active range of movement are simple to measure, requiring no signal processing of multiple signals.

The findings from both the Pilot and Main Studies confirm the important presence of both these impairments in the impaired group. Similar observations have been made by numerous others (Bohannon et al. 1991; Bourbonnais & Vanden 1989; Meskers et al. 2009). The acute group had statistically significantly more weakness and loss of range of movement, than the chronic group and unimpaired group, and the chronic group also was statistically significant different to the unimpaired group.

The repeatability analysis revealed that for the isometric force measurement there was no evidence of a trend in between-days measurement, and the repeatability coefficient was small (±1 Nm) compared to the range of values (0 to 5 Nm), which confirms the findings of other studies using strength testing equipment more suited to clinical use (Bertrand et al. 2007; Riddle et al. 1989). For extension active range of movement a greater mean value for the second day recording (4º) that was statistically significant, however, this is small compared to the range of values (-52.3º to 51.2º). Test-retest reliability of the assessment active range of movement in stroke patients using simple clinical equipment such as a goniometer has not been published up to now, though a scale such as the Fugl Myer which contains a range of movement testing within it, has been shown to have excellent reliability (Platz et al. 2005).

There is a clear clinical perception that extensor weakness is closely related to loss of extensor ROM, and Spearman correlations in this present research study show a very strong and statistically significant association between these impairments in both the acute and chronic groups, thus corroborating that perception. Correlation between weakness and range

of movement at the finger has been shown previously (Cruz et al. 2005). However, strong to very strong relationships were also found between the coactivation indices and both weakness and AROM, which will be explored further in Section 7.2.1 on coactivation.

7.1.3. Extensor onset timing

This study has used a new method of calculating muscle onset timing that may directly relate to reduced motor drive and explain a reduction in isometric force. The method involved a simple comparison of the EMG envelope with a threshold based on the envelope during a baseline period (Hodges & Bui 1996), but unlike previous research, used a local (i.e. immediately prior to the muscle activation) rather than global (i.e. before the start of the task) baseline. Consistent with previous studies (Chae et al. 2002a; Hammond et al. 1988b; Hughes et al. 2010b; Wagner et al. 2007) a statistically significant delayed onset of the extensor muscles was found during discrete movements (step tracking) in the impaired group compared to the unimpaired controls. The delay was statistically significant in both impaired groups compared to unimpaired, but more so in the acute than the chronic group. These findings corroborate previous studies where delayed muscle onset has been found in participants with chronic stroke during isometric contractions at the hemiplegic wrist compared to the non-hemiplegic side (Chae et al. 2002a; Hammond et al. 1988b), and during supported reaching movements at the elbow (Hughes et al. 2010b). In a study with an acute group of post-stroke participants, delayed onset of wrist, elbow and shoulder muscles during unsupported reaching improved to within normal limits from the acute to sub-acute phase (Wagner et al. 2007).

The discrete movement task can be broken down into three components: signal detection (visual detection of target LED change in position), signal processing and selection of motor strategy, and task execution (extensor contraction to move to target position), all of which could be impaired by a stroke lesion (Chae et al. 2002a). It is not possible to establish from this study where the cause of delayed muscle activation lies, but it has been suggested that motor processing may cause a large proportion of the delay shown in a previous study (Chae et al. 2002a).

For between-days repeatability of extensor onset timing, the limits of agreement and repeatability coefficient were wide compared to the range of values. It is not possible to establish from this study whether the variability is due to variability inherent in measurement from the random signal that is the surface EMG or due to day-to-day change in muscle activation patterns in participants.

Extensor onset timing was moderate to strongly associated with weakness in the chronic but not acute groups. This finding is similar to a previous study which found that slowness to generate force in the upper limb post-stroke significantly contributes to weakness. It makes clinical sense that patients who are weak, also are slow to activate their muscles and generate force. There was also a very strong association between extensor onset timing and coactivation during sine tracking, which will be explored further in Section 7.2.1.

7.2. Positive Impairments

In general, there is a consensus in recent literature that positive impairments are not as important to functional activity as negative impairments (Ada et al. 2006; Burridge et al. 2008; Canning et al. 2000; Katz et al. 1992). Positive impairments are clinically perceived to be associated with secondary impairments such as contracture, and there is some evidence that corroborates this (Ada et al. 2006). The positive impairments discussed below are co-activation and spasticity measured as a response to rapid passive stretch.

7.2.1. Coactivation during sinusoidal and step tracking

In this study a new method has been developed and tested to quantify coactivation, and in particular to distinguish abnormal coactivation from that used normally to stabilise a joint and ensure end-point movement accuracy. To do this we have measured coactivation during a dynamic movement which we also consider to be much more clinically relevant than the more commonly used (and easier) method of measurement during an isometric contraction. We have used a correlation analysis of the agonist (extensor) and antagonist (flexor) EMG calculated only over the time-periods where the agonist EMG is increasing, in accordance with the usual definition of coactivation (simultaneous activation of both muscles (Sheean 2002)).

This coactivation measurement method provides a major improvement over indices previously used for a number of reasons:

- Other methods have calculated coactivation during isometric contraction (Chae et al. 2002b; Hammond et al. 1988a; Kamper et al. 2006b), whereas our method measures during movement, which is more related to functional activity, and addresses the important question ‘What is the clinical relevance of inappropriate coactivation during activity?’
- Our method includes both the agonist and antagonist EMG in the calculation, and thus complies with the strict definition of coactivation (simultaneous activation of both muscles (Sheean 2002)). Others have focussed their calculation on the flexor EMG by either

comparing with the unimpaired limb or unimpaired controls (Gowland et al. 1992; Kamper & Rymer 2001), or by a ratio of flexor EMG during extension and flexion (Turk et al. 2008b).

- Other methods have calculated the area of agonist and antagonist EMG overlap (Hu et al. 2007) but validity in distinguishing impaired and unimpaired subjects was not demonstrated. This is important as some tasks require more 'normal' coactivation than others, as demonstrated in the differences between the muscle activations patterns seen during sine and step tracking in the unimpaired group in this study. The measurement method used in this study, for the first time in the literature, targets the exclusion of sections of the data where there is 'normal' coactivation, thus focussing more on the sections where abnormal coactivation may occur.
- Previously coactivation has been measured using cross-correlation of the flexor and extensor EMG and the presence of coactivation was said to occur using an arbitrary threshold based on proportion of variance of the antagonist EMG and the phase of the two opposing muscle activation bursts (Canning et al. 2000). Thus coactivation was deemed to be either present or it was not. The coactivation index used in the current research provides a correlation coefficient ranging between +1 and -1 with positive values indicating simultaneous activation (coactivation) and negative values alternating activation (reciprocal inhibition/activation), providing a graded scale which is easily interpreted. Thus the values represent not just the extent to which the opposing muscle groups are activating simultaneously, but also reciprocally, and both of these factors may contribute to the strong association of this measure with motor control accuracy.

In Pilot Study 3, visual analysis of the traces suggested that this approach was able to exclude more sections of the data where there is 'normal' coactivation, compared to other methods based on time-periods during peak extensor EMG or during extension movement. Statistical analysis showed greater differences between unimpaired and impaired coactivation for this method in both sine and step tracking, but none reached statistical significance. In the Main Study with a larger sample, a statistically significant difference was found between the impaired and unimpaired groups for coactivation during sine tracking ($p=0.024$) measured using our method. When the impaired group was separated into chronic and acute, the analysis revealed that it was in the chronic group where the statistically significant difference lay ($p=0.003$); the acute group did not show a statistical significant difference. This contrasts with the findings of our previous study of chronic stroke patients, where the difference between impaired and unimpaired coactivation during the same wrist sine tracking test (with on-screen, rather than LED targets), was measured using a flexor modulation index (ratio of flexor activity as an antagonist and agonist) which showed a non-

significant trend (p=0.07) (Turk et al. 2008b). This result is unlikely to be influenced by sample size as the first study calculation was based on 10 participants in each group compared to 13 chronic impaired and 14 unimpaired in this study.

In contrast to sine tracking, the step tracking coactivation index did not show a statistically significant difference between impaired and unimpaired. The reason for this is not that the mean impaired coactivation index was any less, but that the mean unimpaired group coactivation index was less negative suggesting a tendency towards less reciprocal activation and more coactivation in the step tracking task. This suggests that the triphasic activity during fast discrete movements tends towards more coactivation while rhythmic movements use more reciprocal activation. This confirms the findings from an elbow study of unimpaired fast discrete extension movements which showed that the reciprocal activation of the agonist and then antagonist bursts was always followed by coactivation of both muscles (Yamazaki et al. 1995).

The wide distribution of values for coactivation found in all groups in the Main Study confirmed the initial findings from Pilot Study 3. This highlights the variety of muscle activation strategies used by both the impaired and unimpaired participants, which was evident from visual inspection of the flexor and extensor EMG on the tracking plots. Even in the unimpaired groups whose tracking performance was excellent there were a variety of strategies used. Some appeared to use reciprocal inhibition/activation as described by Sherrington (Sherrington 1906). For others there was overlapping activity of AG1, ANT1 and AG2 in triphasic activity, often with additional bursts of AG and ANT activity as described by others (Brown & Cooke 1990). Although the majority of impaired participants did not have coactivation at levels beyond the normal range during sine and step tracking movements, there are clearly some individuals who did coactivate, and more so in sine than step tracking.

In the main study, a small but statistically significant reduction in step tracking coactivation index from day 1 to day 2 was found, suggesting that patients may coactivate less (or use more reciprocal activation) with repeated day-to-day assessments; such a trend can be expected as a result of ‘training’ which tends to lead to more energy-efficient movement strategies (Osu et al. 2002). The limits of agreement and repeatability coefficients for both coactivation indices were wide, in sine tracking almost as wide as the spread of values in the sample (-0.60 to 0.69 and ± 0.61 respectively compared to minimum to maximum range of -0.54 to 0.73), indicating a large amount of variability between day 1 and day 2. This is partly due to the outlier in the chronic group whose activation patterns changed dramatically from clear reciprocal inhibition on day 1 to slight coactivation on day 2, which was evident from visual analysis of the sine tracking and EMG plot for this participant. With this outlier

removed, the group sine coactivation index limits of agreement and repeatability coefficient are less wide (-0.46 to 0.43 and ±0.42 respectively) and similar to step tracking results. The effect of this outlier is exaggerated because of the small sample size which is a limitation of this study. The other reasons for variability may be that muscle activation patterns do vary from day-to-day in patients, or it may be due to variability inherent in surface EMG measurement. Visual inspection of traces did show a clear change in coactivation between these repeated measurements. Furthermore, in some cases (in both the impaired and unimpaired groups) even within the same recording, clear changes in coactivation were observed, suggesting that the level of coactivation can sometimes be modulated by voluntary or other factors. This within-session variability for the sine coactivation index is evident in Figure 6-3, Chapter 6 Main Study, although was not statistically significant.

Coactivation is associated with the negative features of the UMN syndrome. A statistically significantly correlation was found between the tracking indices (see Section 7.4 for further discussion), extensor onset timing in the acute group, and extensor muscle weakness and AROM in the chronic group. The relationship between delayed extensor onset timing and coactivation have not been evaluated previously in the literature, although a study involving tracking training combined with FES in a two dimensional robot, found that both delayed onset timing and coactivation improved post treatment (Hughes et al. 2010b). The relationship between coactivation, weakness and AROM is a key finding in this study, and relates to the close association with tracking performance (see Section 7.4 for detailed discussion).

A key question that this study was hoping to address was whether there was a relationship between coactivation and spasticity. In the acute group there was a moderate correlation which approached statistical significance (r=0.573, p=0.051) between coactivation measured during the sine tracking test, and spasticity measured during a passive sinusoidal test using the same timing and displacement parameters, but no correlation in the chronic group. Additionally there was a moderate and less statistically significant relationship (r=0.531, p=0.075) between sine coactivation and spasticity measured using the 3.5 Hz test. These findings suggest that the association of coactivation and spasticity is still unresolved.

7.2.2. Spasticity – Stretch index

The stretch indices were calculated from two different tests – a fast test at 3.5Hz with 10º displacement, and a slower test at 0.5 Hz with 40º (± 20 º) displacement. The latter was used to compare the stretch response in passive tracking with coactivation in active tracking

using a test with the same parameters. A new method of calculating the stretch index has been used. In previous studies the area of the flexor EMG activity in response to stretch was calculated as the increase with respect to the mean global resting baseline (Sorinola et al. 2009; Turk et al. 2008b), or the mean plus 3 SD of a global baseline (Pisano et al. 2000). Because the global resting baseline was found to be variable, a local baseline was used instead. The use of a ratio of the SR area to the local baseline meant that the measure was normalised without having to use other methods such as %MVC, and the value of the index can easily be interpreted. Thus if the ratio is 1.0, the stretch response average amplitude is the same as the local baseline, and if the ratio is higher than 1.0, the stretch response average amplitude is greater than the local baseline. The results from Pilot Study 4 confirmed that this method of measuring the index, with the 3.5Hz ± 10^{o} displacement test, showed the greatest difference between impaired and unimpaired, though it did not quite reach statistical significance.

In the Main Study with a larger sample, and consistent with prior studies (Pisano et al. 2000; Turk et al. 2008b), there was a statistically significant difference in the stretch index between impaired and unimpaired (p<0.001), and this was shown in both the acute and chronic groups when analysed separately (p<0.001). Observation of individual data on the dot plots Figure 6-7) confirmed these findings. The unimpaired values were mainly narrowly grouped at 1.0, and although some impaired participants also had stretch index values at or near to 1.0 (more in the acute group than chronic), there were clearly some individuals who have much higher levels of stretch response.

Although spasticity tested at 3.5Hz distinguished impaired from unimpaired, no statistically significant associations were found between spasticity and other impairment variables. Moderate non-significant associations (r=0.531, p=0.075) were found between spasticity and sine tracking performance, AROM and sine coactivation indices only in the chronic group, which, with a larger sample size, may reach statistical significance.

7.3. Secondary impairments

Secondary impairments are biomechanical changes to soft issues and joints that occur as a result of the primary (negative and positive) impairments. The secondary impairments discussed below are contracture or loss of extension passive range of joint movement, and non-neural stiffness of muscles and joints.

7.3.1. Contracture - Extension passive range of movement

Loss of extension passive range of movement (PROM) indicates contracture, a secondary impairment seen after stroke (Ada et al. 2006). Judgement of the end of passive range of movement can be subjective. In this study a clear definition was used to identify end of passive range (the point where resistance from tissues increases either to a block or where further movement is difficult but remains pain-free). Additionally the maximum force applied by the assessor was recorded, and no statistical difference in this value was found across the three participant groups.

In Pilot Study 3, the difference in extension PROM between impaired and unimpaired did not reach statistical significance, whereas in the main study it did, with more difference in the acute group ($p<0.001$) than the chronic group ($p<0.007$).

A key finding in this study is that contracture is strongly associated with extension AROM, and moderately associated with extensor isometric force, but only very weakly associated with positive impairments such as spasticity. The correlations used in these analyses cannot be used to infer causal connections between these variables. A longitudinal study, which evaluated the causal relationship between spasticity and weakness and the development of contracture at the elbow, found that spasticity made a significant contribution to contracture within the first four months post-stroke, and that weakness made a significant contribution to contracture later on at six to nine months post-stroke (Ada et al. 2006).

7.3.2. Non-neural stiffness – mean torque index

The mean torque index was designed to measure non-neural resistance to passive movement (stiffness) towards the end of passive extension range. The index was based on the method used in a previous measurement of spasticity study (Pisano et al. 2000), though slower speed of movement (5º/second compared to 10º/second) was used during the test in an attempt to minimise the presence of neural activity, which in the previous study was present in 39 of the 58 patients. In Pilot Study 3, three participants were unable to entirely avoid any flexor and extensor activation: two unimpaired participants with voluntary extensor activity (in spite of instructions to the contrary) and one impaired participant with increasing flexor activity in phase with passive wrist extension. In the Main Study, flexor EMG activity was present for two impaired participants (one acute and one chronic) and extensor EMG activity for one impaired (acute) and two unimpaired participants. The impaired participant with flexor activity in the Pilot Study was considered to have spasticity, although this was not formally measured using a clinical scale. This raised the possibility that those with higher

levels of spasticity may not be able to be measured using this stiffness index. However, for the two impaired participants with flexor activity in the Main Study, one had moderate spasticity (score 2 on the Tardieu scale), whereas the other had none, and there were three other participants with a score of 3 on the Tardieu scale who did not have flexor activity and therefore were included in this part of the analysis.

In the Pilot Study, the mean torque values in the chronic impaired group were higher and almost reached statistical significance compared to the unimpaired group. Contrary to these findings, in the Main Study, the mean chronic group values were only slightly higher than the unimpaired, and nowhere near statistically significant. In fact, the mean values of the acute group were statistically significantly lower than unimpaired. Observation of the dot plots explained these findings. Most of the acute group values were below the normal stiffness range, which fits with the clinical picture in the acute phase where low muscle tone and weakness predominate. Only two impaired participants in the chronic group were above the normal stiffness range (one male and one female) with most within the normal stiffness range of even below it. Furthermore stiffness did not contribute to poor motor control accuracy, and no relationships were found between this stiffness and any other impairment measure or with the mWMFT. It is clear that of the two secondary impairments, loss of PROM or contracture is a more important measure than stiffness measured using the mean torque index.

7.4. Association between impairment indices and motor control accuracy (MCA)

Participants with poor tracking performance, whether they were in the acute or chronic group, were compared against those with better performance and the unimpaired. This was to evaluate which impairments underlie the inability to perform a) simple flexion / extension movements in the rig and b) accurately track the target. The impairments that distinguished low MCA from high MCA were smaller extension AROM and PROM, reduced extensor isometric force, delayed extensor onset timing and coactivation (sine and step tracking). There was no statistically significant difference for spasticity (stretch index) but both the low and high MCA group were distinguished from the unimpaired group suggesting that spasticity may be present within the impaired group but does not determine the relative level of motor control within the patient group. Coactivation also was statistically significant between the low MCA and unimpaired group and not the high MCA group, suggesting that this is a major contribution to poor motor control.

Further observation of sub-groups revealed that it was the chronic patients with coactivation who had the low MCA. They also were the sub-group with the most weakness, though it is not possible to know whether their weakness was due to poor activation of the extensors, or coactivation where the flexors counteract the effect of the extensors. Further evidence for this relationship is that coactivation was shown to be strongly correlated with weakness and AROM in the chronic group. In the acute group, those with low MCA were also the sub-group with the most weakness, though there was one participant (#17) who also had coactivation. The finding that those participants with moderate weakness problems and no coactivation were those in the high MCA group, further strengthens the argument that weakness and coactivation strongly relate to motor control. Further evidence for this was found in the correlation between the sine and step tracking indices, isometric force and coactivation indices. There was a moderate to very strong association between the coactivation indices and tracking indices in both the acute and chronic groups. Weakness was very strongly associated to tracking performance in the chronic group, but had only a low association in the acute group, where extensor onset timing was the impairment that was most strongly associated (Section 7.1.3).

7.5. Relationships between impairment indices and functional activity

Relationship between impairments and functional activity (mWMFT) was evaluated in this study using correlation to assess individual associations without taking into account other impairments, and multiple regression analysis to evaluate best prediction of mWMFT among the negative, positive and secondary impairment groups. In the acute group the Spearman's correlation showed that extensor weakness, AROM and contracture were related to functional activity, and similarly the regression analysis showed that the most important negative impairment contributor to functional activity was extensor weakness (R^2=70%), and extension PROM was the most important secondary impairment contributor (R^2=37%). In the chronic group all the negative impairments were strongly or very strongly associated with functional activity except for path length. This may be because this measure relates more to delicate precision tasks, which the mWMFT does not address. The most important negative impairment contributor to functional activity was sine tracking accuracy (R^2=89%), the most important positive impairment contributor was sine tracking coactivation, and again, extension PROM was the most important secondary impairment contributor (R^2=37%).

Thus, consistent with the findings of other studies (Ada et al. 2006; Bohannon et al. 1991; Burridge et al. 2008; Canning et al. 2004; Chae et al. 2002b; Kamper et al. 2006b; Mercier & Bourbonnais 2004; Wagner et al. 2006; Zackowski et al. 2004), negative impairments, in

particular weakness, AROM and motor control accuracy, have been found to most relate to functional activity post-stroke. This study is the first to evaluate both the acute and chronic phases, and determine that weakness is most important in the acute phase, and motor control accuracy is the most important in the chronic phase. Another study found weakness to be more important than motor control accuracy (termed dexterity), but they evaluated stroke patients in a longitudinal study only in the acute to sub-acute phase (up to 27 weeks). In our previous study with patients in the chronic phase (> 1 year post-stroke) sine tracking was found to be the impairment that contributed the most (R^2 = 56%) to the variance in the Action Research Arm test (ARAT) score, whereas extensor isometric force showed less contribution (R^2 = 33%).

It is important to point out that, unlike sine tracking, step tracking did not show a statistically significant association to function in the regression analysis, and although in the correlation analysis it was very strongly associated with functional activity in the chronic group, showed only a low non-significant association in the acute group. One hypothesis of this study was that step tracking would be more related to functional activity because of the nature of discrete movements being closer to day-to-day activities of the upper limb than rhythmic movements. However these findings suggest that sine tracking is more related to functional activity. One possible reason for this is that while step tracking involved discrete movements and rest periods, sine tracking involves constant movement over a one minute period. It is likely that impaired participants found this tiring, as shown in the statistically significant reduction in sine tracking performance over the test period. This cannot be assessed with the step tracking test as the task becomes more difficult over time. Fatigue, a common symptom seen clinically following stroke, can also limit patients' ability to carry out functional activities. In the mWMFT, the first tasks involved simple single movements from one position to another. However, the later more functional tasks, such as turning over three cards, or stacking three chequers, involved a series of complex movements, which are likely to induce fatigue. Another difference between step and sine tracking is at the cortical level it involves. Rhythmic movements at the wrist were found to involve the cerebrum on the contralateral side of the moving limb, whereas discrete movements involved widespread areas of the ipsilateral cerebrum, and specific areas in the contralateral cerebrum (Schaal et al. 2004). Considering a stroke lesion damages the contralateral cerebrum, it is possible that those with hemiplegia may find rhythmic movements more challenging, whereas discrete movements such as step tracking, which use the intact side of the brain as well as the side of the lesion, may be easier to undertake.

Unlike the findings of some studies of isotonic contractions (Canning et al. 2000; Gowland et al. 1992; Kamper et al. 2006b; Wagner et al. 2007) and similar to others using isometric contractions (Chae et al. 2002b), the positive impairment coactivation (measured during sine coactivation) also seems important to functional activity but more in the later stages post-stroke. It is possible that the more careful method of measuring coactivation used in this study may contribute to this finding. This method is different to any used previously, evaluates the correlation between the antagonist and agonist curves excluding some time-periods when 'normal' coactivation occurs, and measures the extent of reciprocal activation as well as coactivation.

Contracture has also been found to be important contributor in both the acute and chronic phases, though lower than that of the negative impairment weakness in the acute and chronic group and positive impairment coactivation in the chronic group. Contracture has previously been found to be an important impairment after stroke (O'Dwyer et al. 1996; Pandyan et al. 2003a; Vattanasilp et al. 2000). The previously mentioned longitudinal study (Ada et al. 2006) however, found that contracture never made a major contribution to functional activity loss up to a year post-stroke, and only statistically significantly contributed at the six week period post-stroke.

7.6. Summary of acceptance of the hypotheses

The five null (H_0) and alternative (H_1) hypotheses were listed in Chapter 2, Section 2.15. Here the hypotheses are discussed in relation to whether they have been found to be accepted by the findings of the study:

1. *The alternative hypothesis is accepted: Negative impairments will relate more to loss of functional activity than positive and secondary impairments, especially in acute participants.*

In general, the negative impairments have been found to relate more to functional activity than the positive and secondary impairments, in particular extensor weakness and active range of movement in the acute group, and loss of motor control accuracy in the chronic group. However, coactivation (positive impairment) was also found to relate to functional activity in the chronic group, and contracture (secondary impairment) related to functional activity in both groups.

2. *The alternative hypothesis is accepted: Positive and secondary impairments will relate to loss of functional activity in some individuals, especially in the chronic group.*

Abnormal coactivation was found to be present in some individuals, more in the chronic group, and those tended to have the worst functional activity, and motor control accuracy

scores. As has been indicated above, coactivation (chronic group) and contracture (acute and chronic groups) were found to relate to functional activity. Spasticity was present in the impaired group (shown by the statistically significant difference between impaired and unimpaired), but did not relate to functional activity. Stiffness was lower in the acute group, and also did not relate to functional activity.

3. *The null hypothesis is accepted: Motor control accuracy and coactivation measures from step tracking (discrete movements) will not relate more to upper limb functional activity than the same measures from sinusoidal (rhythmic) tracking.*

The findings show that sine tracking accuracy and coactivation during sine tracking are more related to functional activity than the step tracking measures. This was discussed further in Section 7.5 above.

4. *The alternative hypothesis is accepted: Negative impairments will relate more with each other rather than with positive and secondary impairments*

In general, the negative impairments did strongly relate with each other, particularly the sine and step tracking indices, extensor weakness, extension AROM and extensor onset timing. The step tracking path length measure did not relate to any other impairments.

5. *The null hypothesis is accepted: Positive impairments will not relate more with each other and with secondary impairments*

Coactivation (positive impairment) was found to strongly relate more to the negative impairments – sine and step tracking indices, extensor onset timing in the acute group, and extensor muscle weakness and AROM in the chronic group. Only a moderate non-significant relationship was found between coactivation and spasticity in the acute group. Spasticity was not found to relate to secondary or negative impairments. Contracture (secondary impairment) was found to strongly relate to the negative impairments extensor muscle weakness and AROM. Stiffness did not relate to any other impairments.

7.7. Implications for clinical practice

- In the acute group, the impairments that were found to be important to functional activity were extension ROM and extensor isometric force, therefore therapy should be focussed on techniques to increase muscle activity, range of movement and strength.
- Contracture (loss of PROM) was found important to functional activity in both the acute and chronic phase, but was found to be more related to weakness and loss of active range of movement than the positive impairments of coactivation or spasticity. This suggests that techniques which encourage activity and strengthening as well as stretching joints at the same time would be beneficial. These include technologies such as FES or active splinting e.g. SaeboFlex (Saebo, Inc.).

- When present (more likely in the chronic phase) positive impairments such as coactivation and spasticity should be addressed. Specific treatment for the problem of coactivation is not clear; however, a recent study of botulinum toxin therapy suggested a reduction in coactivation measured using EMG (Gracies et al. 2009). Other studies have shown a reduction in coactivation using less direct techniques such as FES and robot training (Burridge & McLellan 2000; Hu et al. 2007).
- A fundamental message arising from this research is the need to measure impairments more objectively in clinical practice so that treatment could be better targeted. Some impairments that have been found to be very important to functional activity such as strength and active range of movement are relatively simple and easy to measure using off-the shelf devices. Other impairments such as tracking performance, coactivation and spasticity are also important but are more complex to measure. Clinically relevant devices need to be developed and the problem of variability in EMG measurement remains a challenge.

7.8. Limitations of the study

The results from this study need to be interpreted whilst acknowledging the limitations of the study. Limitations in the methodology have been minimised where possible, or where this was not possible are addressed here, and identified to be addressed in future research.

7.8.1. Sample size

The relatively small number of participants recruited for the Main Study was regarded as a convenience sample, and has resulted in limited strength of the statistical findings. A power calculation was performed earlier in the research project based on pilot data from 10 participants with chronic stroke. The data consisted of 9 impairment variables; wrist flexor and extensor strength, active range of movement, 2 motor control indices (sinusoidal and step tracking performance), 2 coactivation indices (from sinusoidal and step tracking EMG), spasticity index, and stiffness index – and a measure of arm activity, the Wolf Motor Function Test (WMFT). The calculation was based on regression analysis i.e. the effect sizes were based on R-squared values - the percentage of variation in the arm activity score that is explained by the predictor (impairment) variable(s). A regression analysis using the existing data showed that the first eight variables (all except the stiffness index) were individually strongly associated with the WMFT - all produced a large R^2 and therefore a large effect size. However a regression based on the final variable (stiffness index) had a lower R^2 - a medium rather than large effect. The calculation at 80% power found that the joint predictive value of the 8 best-predicting variables could be adequately described with 54 cases but, with the final variable included, more cases are needed to have the same level of confidence. A sample size of 70 (35 in each impairment group) was therefore proposed. This calculation

was limited by using data from only a small number of participants, and would need to be repeated using the full data set for a subsequent suitably-powered trial, however, it gives an indication of how this study is under-powered.

7.8.1. Number of impairment variables

The purpose of this research was to evaluate a considerable number of impairment variables so that the heterogeneity of stroke participants could be assessed. The disadvantage of this, however, is that it reduces the strength of the statistical findings. In this study multiple comparison procedures have been performed, and to control the type I error a Bonferroni correction has been used. However, this is a conservative test so that the probability of rejecting an effect that does actually exist is increased (type II error).

7.8.2. Impairments only been measured at the wrist

Impairments have only been measured using simple flexion-extension movements at the wrist, whereas functional activity involves multi-joint, multi-directional movements. Despite this, some strong correlations have been found. Further research to determine impairments and their relationship with functional activity at other joints is warranted.

7.8.3. Acute and chronic group participants

Comparisons have been made between acute and chronic impaired participants, but these are not the same individuals, therefore the question of how impairments and functional activity change over time has not been fully addressed. A future follow-up study is planned where the acute group in this study will be reassessed when they are in the chronic phase (see Future research, Section7.9).

7.8.4. Analysis of test-retest reliability

Preliminary test-retest reliability analysis was carried out in this study. This only included the active tests, as on a practical level it was not feasible to conduct the passive tests at both day1 and day 2 sessions. Also not all participants were included in the reliability sub-group. Some participants who were able to complete the full testing protocol on day 1 were not included. Generally they were those who had travelled from further away, they had less problems with fatigue and tended to be the more physically able. The smaller numbers in the reliability sub-group reduced the power of the statistical results.

7.8.5. Hand dominance

For practical reasons and to identify ‘best performance’ the unimpaired participants were all tested using their dominant arms. It seems likely that in unimpaired tracking performance, the dominant side performs better than the non-dominant, however this is not known warrants

further investigation. However, the impaired participants were tested using their hemiplegic arm, which for 14 of them was their dominant arm, and for 12 was their non-dominant arm. Thus any effect of hand dominance has not been controlled for in this study. However, the relevance of dominance is questionable as when a person has a stroke, their non-hemiplegic side immediately becomes their dominant side which tends to over-ride any pre-morbid hand dominance.

7.8.6. Gender matching

For practical reasons it was difficult to match the impaired and unimpaired groups in terms of gender. This was because the unimpaired group were recruited first, and because of the larger older female population compared to male, there were more female volunteers for the study. Gender has been shown to have an effect on some impairments, especially muscle strength and stiffness, and the fact that gender was not controlled for may have reduced the strength of the statistical results.

7.9. Recommendations for future research

The following studies are proposed for future research, the first two of which are already in the planning stages, one with MSc students, and one other involving a team of researchers working across multiple sites in the UK.

- A follow-up study of the acute participants sample from the Main Study, who will be re-tested when they are over a year post-stroke i.e. in the chronic phase, using the same testing protocol. The purpose of this is to evaluate changes in motor impairments and functional activity from the acute to the chronic phase to enhance understanding of natural recovery and the changing relationship between impairments and functional activity.
- To use the wrist rig neuromechanical impairment measures, along-side biomechanical assessment of upper limb movements (motion analysis), and measures of cortical activity (e.g. TMS), in a longitudinal trial to understand underlying mechanisms and determine the nature of the course of upper limb recovery post-stroke.
- To use the neuromechanical impairment measures derived from this study as impairment level outcome measures in a clinical trial to evaluate the underlying mechanisms of therapy-induced recovery e.g. functional strength training or botulinum toxin therapy.
- To apply the wrist measurement and analysis methods to another joint such as the elbow, to compare differences between the wrist and elbow motor impairments and their relationship with functional activity.

- To evaluate test-retest reliability with all the wrist rig measures with a larger sample population as this study has only provided a preliminary test-retest reliability analysis.
- To evaluate impairment problems in sub-acute patients undergoing rehabilitation using the wrist rig measures and compare decision making regarding treatment based on the neuromechanical measures, with those based on current therapists' clinical assessment. This would be to identify the differences between a therapy plan based on quantitative neuromechanical assessment compared to that based on a subjective clinical assessment.
- To develop more clinically suitable assessments tools, especially for the measurement of spasticity and coactivation, or evaluate current off-the-shelf tools to use in clinical assessment. The lab-based wrist rig measures would be used in the validation of these tools.
- Further evaluation of the relationship between coactivation, weakness and active range of movement, to identify whether coactivation or reduced muscle activation is the cause of weakness and loss of active movement.

7.10. Summary

This Chapter has discussed the findings of this study which provide answers to the original study objectives and questions. Differences between impaired and unimpaired groups have confirmed the validity of the impairment indices derived from the wrist rig tests, and preliminary evaluation of repeatability highlighted the challenge of repeated assessment using EMG. Important relationships between impairments, motor control accuracy and functional activity have been discussed in reference to the literature and the relevance to clinical practice. Limitations of the study have been discussed, and plans for future research presented. The following Chapter of this thesis summarises the main conclusions from this research.

8. Conclusions

This study has been the first to provide a comprehensive evaluation of motor impairments measured at the wrist, using neuromechanical methods, with a sample of participants with hemiplegia in both the acute and chronic stages post-stroke and with unimpaired controls. Previously developed indices have been used to describe motor control during a rhythmic, extensor muscle weakness, and active and passive extension range of movement. Novel methods have been developed and evaluated to quantify motor control accuracy during discrete movements, coactivation, muscle onset timing and spasticity and stiffness. Results from the study confirmed the validity of most impairments to distinguish between impaired and unimpaired except coactivation (step tracking) and stiffness. Most impairments distinguished between acute, chronic and unimpaired groups except both coactivation indices in the acute group, and step tracking coactivation and stiffness in the chronic group. Repeatability coefficients for the active test indices have been presented as benchmark values for use in future trials. The muscle activation indices showed lower repeatability and therefore their use to measure change over time is limited. It is not clear how much the between-days variability is due to genuine variability within patients or the random nature of EMG measurements.

The impairments that distinguished between poor and good motor control accuracy were reduced extensor weakness, delayed extensor onset timing, coactivation and smaller extension AROM and PROM, suggesting that these are important impairments to consider in deciding upon intervention and to measure progress. Somewhat surprisingly, coactivation was more strongly associated with motor control accuracy than with spasticity or stiffness.

The main contributor to functional activity in the acute phase was extensor weakness as well as loss of active and passive range of movement. In the chronic phase, there were many more impairments that were associated with functional activity. In general the negative impairments, especially motor control accuracy (sine tracking) were found to have more influence on functional activity than the positive impairments. However, unlike the findings of previous studies (Burridge et al. 2008; Canning et al. 2000) in this study coactivation (sine tracking) showed a strong and statistically significant relationship with functional activity. Contracture also significantly contributed to functional activity in both phases, though was strongly associated with the negative impairments weakness and loss of active range of movement rather than spasticity or stiffness.

The findings in general support the notion that rehabilitation strategies should focus on increasing muscle strength and prevention of contracture. However, assessment of more

complex impairments like motor control accuracy and coactivation may be crucial to better target therapy, especially in the later phases post-stroke.

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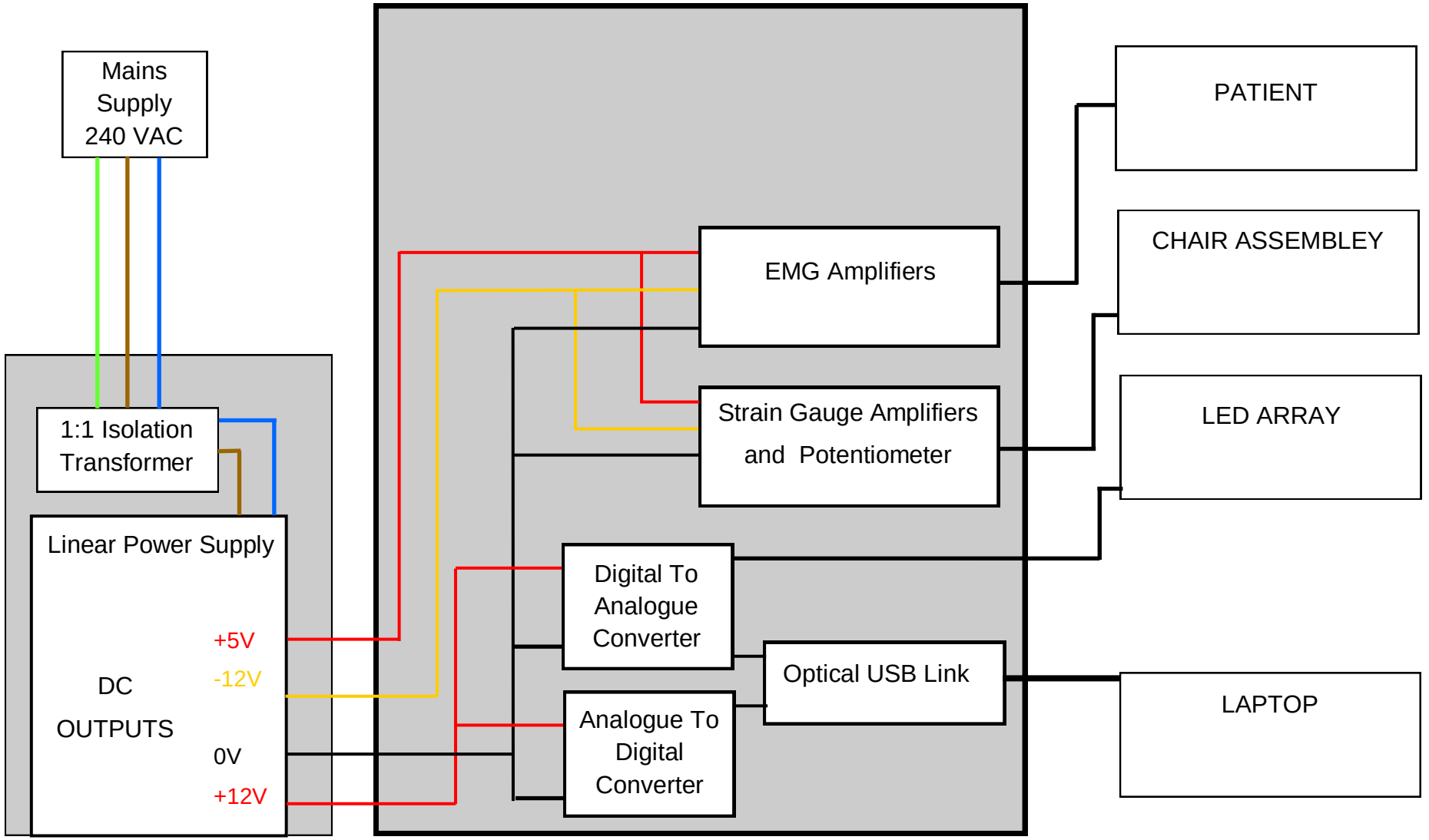
Appendix A - Wrist Rig Block Diagram



Appendix B - Bench testing and Calibration

In order to test the system and its outputs and calibrate the measurements, bench tests on the rig components were carried out by the researcher and Dr Simpson with the assistance of ISVR technicians. This process involved iterative testing, (modification and retesting) to ensure that the rig system and output data were valid and reliable. The following section details the bench testing and calibration processes undertaken following the rebuild of the wrist rig. The calibration coefficients for each output (angle, torque, EMG) were calculated and inserted into a customised Excel spread sheet (Table B-1). This Excel spread sheet was read by the specially designed Matlab® wrist rig software when processing signals and representing signals on graphs in appropriate units of measurement (degrees; Nm; mV).

Potentiometer (angle)

The resistance of the potentiometer is converted to a voltage in the appropriate electronic circuits, which needs scaling so the angle of the wrist joint can be calculated. The potentiometer output was tested initially to investigate noise levels and adequate resolution (< 1 degree). Calibration of angles was undertaken by making marks on the LED display board which represented actual angle values. The zero degrees point (where the wrist is in line with the forearm) was already determined on the wrist rig, and angles to the left were positive angles, and to the right were negative angles. The lever arm was moved to different angles (in steps of 10 degrees) according to the marks on the LED display and voltage values from the potentiometer were recorded (see Table B-1). Linear regression was performed between the known angles and measured voltages and the gradient and offset values calculated. The resultant calibration coefficients were entered into the Excel spread sheet (Table B-1).

LEDs on the target tracking display

Each LED is activated over a distinct, narrow range of voltages, and in order to light each LED individually, which is important for the tracking task, knowledge of the correct voltage for each was needed. Testing was therefore undertaken to find the voltage relating to each LED that related to an angle every 2º between -79º to 79º. These voltages (showing approximately linear spacing) were recorded in a lookup table (see Table B-1), and used to determine the output voltage driving the LEDs at each instant in time.

Pivot strain gauge

The initial plan was to use the pivot strain gauge (mounted in the shaft between the slip-clutch and the wrist) to measure the torque when resistance was applied at the slip clutch; however it was found that the pivot strain gauge measurements showed a slow drift over time and zero torque did not give a constant voltage over all angles. This we thought was due to the position of the axle in the pivot joint being slightly off vertical, and possibly due to the material (Perspex) used, which may display 'creep'. As the resistance applied by the slip clutch could be measured by the lever arm strain gauge (with the subject's wrist removed), it was decided not to use the pivot strain gauge.

Lever arm strain gauge

Initial testing was undertaken to investigate noise levels, gain and drift of the lever arm strain gauge. The gain on the amplifier was modified so that it was sufficient to measure both resistance to passive movement (very low levels of torque) and maximum voluntary contraction (higher levels of torque). The signals were found to remain stable, with no drift over time in gain and offset, so it was decided to use the lever arm strain gauge to measure both passive resistance to movement of the limb, and the resistance set in the rig at the slip clutch.

Calibration of lever arm strain gauge was undertaken as follows. Weights between 0-150g at 20g or 50g intervals were hung freely from the end of the lever arm on a string over a freely running pulley system, with a 90˚ angle (perpendicular) to the lever arm and the weights pulling both to the left (+ve direction) and to the right (-ve direction). Measurements were carried out with the lever arm set at 0˚ (in line with the arm support) and at a 30˚ angle. An example of true and measured torque (after calibration) is shown in Figure B-1, where all measured points lie very close to the desired line of equality. The calibration coefficients are shown in Table B-1.

To further check the lever torque calibration, 0 – 2Kg weights were hung at a point 15 cm from the centre of the pivot joint and at 11 cm position from the pivot joint. Later in the study, during the use of the system and on repeated recalibration and further assessment of the lever torque, an offset was seen in the range of 0.05v-0.1v. The strain gauge wiring was checked and a problem was found causing a short circuit which was thought to be the source of the offset. The system was rewired and further assessment showed stability.

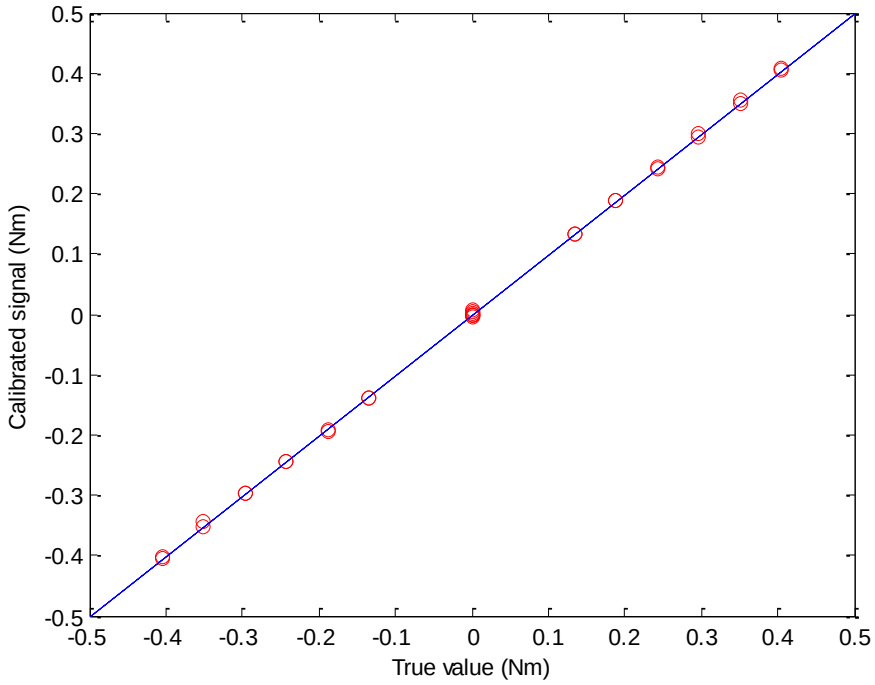


Figure B-1 Results from calibration of lever torque. The horizontal axis shows the true torque (given by the weights and the distance along the lever arm), and the vertical axis shows the measured torque, after applying the calibration coefficients to the voltage output.

However, the lever torque was regularly calibrated, and the calibration coefficients were found to have changed following the pilot study. As these had remained stable through repeated assessments during the bench testing and calibration process, and changes to the pivot joint and electronics were also made following the pilot study, the source of the change was not clear. Because the accuracy of the calibration of this sensor was very important, it was decided to recalibrate before and after each testing session in the main study. As it became clear that the calibration coefficients were remaining stable, recalibration then occurred after every second testing session for the remainder of the data collection.

EMG

Shielded and unshielded EMG leads were tested for signal quality and, on visual analysis, less noise was found in the signal with the shielded leads which were then used throughout the study. Initial testing of EMG showed very large signal to noise ratio so that the output from muscles was not detected. Rewiring of connections and change of the power supply was needed to reduce the noise. Some 50 Hz and harmonics (mains noise) remained but this was successfully removed using a notch filter during processing of the raw signal (see Methodology Chapter 4, Section 4.9). Calibration of both EMG outputs was undertaken using calibrated

voltage levels at the input to the EMG amplifier and linear regression (see calibration coefficients in Table B-1).

Testing the performance of the slip clutch in setting resistance

When the slip clutch was completely turned ‘off’ the lever arm moved freely with very little friction detected, when the slip clutch was gradually tightened (to increase the resistance) the lever arm torque remained approximately constant through all angles of the movement. With increasing resistance, however, a ‘backlash’ was felt at the beginning and end of movement. This feature meant that there was a small angle over which no resistance was exerted and it made it difficult to move and place the lever arm precisely. It was found that this inherent problem of the commercial slip-clutch, caused by ‘play’ in the mounting, has limited the usefulness of applying resistance during movement. Other methods to apply constant resistance with smoother movement were considered but were found to be costly in terms of time and money and thus beyond the scope of this project.

Table B-1: Calibration coefficients for wrist rig outputs, and voltages to drive the LEDs for each angle, from -79 to 79 degrees.

Outputs	**gain**	**added offset**		
Angle	-67.2318	200.9842		
EMG1	0.66667	0.63158		
EMG2	0.70778	1.0348		
Lever torque	1.7415	-1.2771		
Volts for measured angles	**Angles**	**Volts**		
	-79	0.096	1	2.0776
	-77	0.1562	3	2.1275
	-75	0.2063	5	2.1875
	-73	0.2565	7	2.2379
	-71	0.3066	9	2.2881
	-69	0.3567	11	2.3381
	-67	0.4069	13	2.3884
	-65	0.4569	15	2.4381
	-63	0.497	17	2.4883
	-61	0.5569	19	2.5384
	-59	0.5968	21	2.5883
	-57	0.6467	23	2.6385
	-55	0.6969	25	2.6984
	-53	0.7469	27	2.7483
	-51	0.807	29	2.7987
	-49	0.8569	31	2.8487
	-47	0.9069	33	2.8983
	-45	0.9468	35	2.948
	-43	0.987	37	2.9986
	-41	1.0366	39	3.0483
	-39	1.0867	41	3.0885
	-37	1.1467	43	3.1487
	-35	1.1869	45	3.1989
	-33	1.237	47	3.2489
	-31	1.2871	49	3.2988
	-29	1.3374	51	3.349
	-27	1.3871	53	3.3991
	-25	1.4371	55	3.4492
	-23	1.4869	57	3.4992
	-21	1.537	59	3.5491
	-19	1.5871	61	3.599
	-17	1.6371	63	3.6489
	-15	1.6874	65	3.6994
	-13	1.7375	67	3.7393
	-11	1.7775	69	3.7892
	-9	1.8375	71	3.8392
	-7	1.8778	73	3.8892
	-5	1.9275	75	3.9394
	-3	1.9873	77	3.9893
	-1	2.0275	79	4.049

Appendix C – Wrist Rig Testing Protocol

Methods

Signals recorded during each test

EMG – wrist flex/ext

Target angle (set by data file)

Movement angle (potentiometer)

Lever arm force - Passive Movement / Isometric Force (strain gauge on lever arm)

Hinge Force - Isokinetic Movement (force applied on sensor by subjects' activity) / Rig Resistance (resistance to movement applied by the braking mechanism set at each test for individual subject)

General Points

- All signals will be displayed during the tests in real time
- All signals will be displayed on graphs at the end of the recording; a single graph can be displayed by clicking on the graph.
- Files will be saved automatically and default names will be given but can be changed in the spread sheet file.
- Extension angle is upwards on the graph and +ve, flexion angle is downwards and –ve.

1. Initial Set up

- Register subject details: initials/ number / date / side tested / assessor / assessment no.
- Save participant file
- Test outputs

2. Active Range of movement (AROM)

- Start AROM Test
- Ask subject to move wrist to their maximum range of extension and flexion
- Press AROM button to exit
- There is a semi-automatic recording of maximum and minimum values. Peak maximum and minimum default values are selected but values can also be selected manually.

Automatic online calculation

- Mid-range for each subject is calculated as the mid-point between maximum and minimum. This is calculated at the initial assessment only.

3. Passive Range of Movement (PROM)

- Start PROM Test
- Assessor holds the buttons a the end of the lever arm and moves wrist to their maximum range of extension and flexion
- Press PROM button to exit
- There is a semi-automatic recording of maximum and minimum values. Peak maximum and minimum default values are selected but values can also be selected manually.

Automatic online calculation

- Passive mid-range for each subject is calculated as the mid-point between maximum and minimum. This is calculated at the initial assessment only.

4. Isometric Force (IF) / Maximum Voluntary contraction (MVC)

- Immobilise rig at zero˚ for wrist
- Select MVC button and press 'extension' to start test
- Ask the subject to push as hard as possible into extension against the pin for 5 seconds until asked to stop and give standard verbal encouragement throughout. Then rest (for 10 seconds), then repeat the maximal contractions twice more (seconds each with 10 seconds rest).
- The force into extension is recorded; the 3 peak maximum values of force are selected automatically but can be adjusted manually.
- Select 'flexion'.
- Ask the subject to push as hard as possible into flexion against the pin for 5 seconds until asked to stop and give standard verbal encouragement throughout. Then rest (for 10 seconds), then repeat the maximal contractions twice more (seconds each with 10 seconds rest).
- The force into flexion is recorded; the 3 peak maximum values of force are selected manually.

Automatic online calculation

- Flexor / Extensor MVC_{force} is derived from maximum peak force of 3 tests.

5. Active Tracking

a) Sinusoidal tracking

- Ensure no resistance is applied.
- Click tracking tab and select data file of sinusiodal tracking with desired test range through which the test is conducted (e.g. +/- 20˚ about mid-range of subject's active range of movement) and desired target oscillation rate (e.g.0.5 HZ)
- Explain the tracking test to the subject and instruct them to follow the lit LEDs as accurately and smoothly as possible.
- Start the tracking test and LEDs to switch on at mid-point (initial rest period to record a baseline EMG signal with no voluntary activity (15 secs).
- Target starts to move at the set frequency in sinusiodal pattern. Encourage subject in a standard way. Data plots automatically appear on screen on line. Check data represents subject's performance.
- Wait for total set time or press exit to stop
- All signals are recorded and saved automatically

Repeat as necessary

b) Step tracking

- Ensure no resistance is applied.
- Click tracking tab and select data file of square wave pattern with pre-determined frequencies, amplitudes and timing in a random order with the desired range (amplitude) through which the test is conducted (e.g. increasing range from +/- 5˚ to +/- 40˚ about mid-range of subject's active range of movement
- Explain the tracking test to the subject and ask them to move to LED that is switched on as quickly and accurately as possible and to hold the position until another LED lights up.
- Start the tracking test and LEDs to switch on at mid-point (initial rest period to record a baseline EMG signal with no voluntary activity (15 secs).
- Target starts to move at the set square wave pattern. Encourage subject in a standard way. Data plots automatically appear on screen on line. Check data represents subject's performance.
- Wait for total set time or press exit to stop
- All signals are recorded and saved automatically

Repeat as necessary using other selected data files

c) Tracking with resistance

- Set resistance at hinge joint – unstrap subject's arm from the arm support and ask them to lift their arm away from the rig. Twist the slip clutch to increase resistance. Start the 0.5Hz sinusoidal tracking test and push lever arm back and forth holding onto the end stop whilst tracking the target. Read off force levels online and by adjusting the slip clutch set appropriate resistance level – percentage of participants extensor MVC.
- Place and secure subject's arm onto armrest and conduct tracking tests a) and b) as above.

6. Stretch Response Test

- Ensure resistance clutch is fully released
- Click Stretch test tab to select data file of sinusoidal wave pattern with desired range and target oscillation rate
- Explain the tracking test to the subject and ask them to close their eyes, relax their arm and try not to help the movement during the test.
- Start tracking target. For the initial 5 seconds of the test LEDs light up at passive/active mid-range and the rig should remain still so a baseline EMG is recorded.
- LEDs light up in sinusoidal wave. The assessor then starts moving lever arm by holding the end of the rig at the set position so that the lever arm lines up with the lit LEDs
- Wait for total time or press exit to stop
- Data plots automatically appear on screen. Check data.

Repeat using other selected data files

7. Force/angle Test

- Click browse to select data file of triangular wave pattern with desired target speed.
- The subject is asked to relax , close their eyes and encouraged not to help the movement
- Start the test, the LEDs will one by one light up at a constant rate
- The assessor will move the subject's wrist passively following the moving target (lit LEDs) by holding a fixed position at the end of the lever arm and hold the position of last lit LED for 5 secs.
- Lit LED returns to full passive flexion range, assessor returns lever arm to the same position and allows a rest period of 10 seconds.
- The target LEDs light up as before and the movement is repeated six times.
- Wait for total time or press exit to stop.
- Data plots automatically appear on screen. Check EMG data to check for stretch response and any voluntary activity.

Appendix D – Ethical and Research Governance approval forms

UNIVERSITY OF Southampton
School of Health Sciences

Ruth Turk
School of Health Sciences
Building 45

18 December 2008

Dear Ruth

Ethics Submission No: SoHS-ETHICS 08-002

Title: Pilot arm motor impairment measures

I am pleased to confirm **full approval** for your study has now been given. The approval has been granted by the School of Health Sciences Ethics Committee.

You are required to complete a University Insurance and Research Governance Application Form (IRGA) in order to receive insurance clearance before you begin data collection. The blank form can be found via the SUSSED portal under Research Governance Office
http://www.resource1.soton.ac.uk/corporateservices/rgo/regprojs/whatdocs.html .

You need to submit the following documentation in a plastic wallet to Dr Martina Prude in the Research Governance Office (RGO, University of Southampton, Highfield Campus, Bldg. 37, Southampton SO17 1BJ):

Completed IRGA Research Governance form
Copy of your research protocol/School Ethics Form (final and approved version)
Copy of participant information sheet
Copy of SoHS Risk Assessment form, **signed**
Copy of your information sheet and consent form
Copy of this SoHS Ethical approval letter

Continued overleaf

Your project will be registered at the RGO, and then automatically transferred to the Finance Department for insurance cover. **You can not begin recruiting until you have received a letter stating that you have received insurance clearance.**

Please note that you have ethics approval only for the project described in your submission. If you want to change any aspect of your project (e.g. recruitment or data collection) you must request permission from the Ethics Committee and RGO (students should discuss changes with their supervisor before submitting the request to the Ethics Committee).

Yours sincerely

pp 

Professor Sue Latter
Chair, SoHS Ethics Committee

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e: sml@soton.ac.uk
f: +44 (0)23 80 597900

UNIVERSITY OF Southampton

Ms Ruth Turk
School of Health Sciences
Building 45
University of Southampton
University Road
Highfield
Southampton
SO17 1BJ

01 December 2008

RGO Ref: 6173

Dear Ms Turk

Project Title A Pilot Study to Test Quanitive Measurement of Motor Impairments at the Wrist Post Stroke

This is to confirm the University of Southampton is prepared to act as Research Sponsor for this study, and the work detailed in the protocol/study outline will be covered by the University of Southampton insurance programme.

As the sponsor's representative for the University this office is tasked with:

1. Ensuring the researcher has obtained the necessary approvals for the study
2. Monitoring the conduct of the study
3. Registering and resolving any complaints arising from the study

As the researcher you are responsible for the conduct of the study and you are expected to:

1. Ensure the study is conducted as described in the protocol/study outline approved by this office
2. Advise this office of any change to the protocol, methodology, study documents, research team, participant numbers or start/end date of the study
3. Report to this office as soon as possible any concern, complaint or adverse event arising from the study

Failure to do any of the above may invalidate the insurance agreement and/or affect sponsorship of your study i.e. suspension or even withdrawal.

On receipt of this letter you may commence your research but please be aware other approvals may be required by the host organisation if your research takes place outside the University. It is your responsibility to check with the host organisation and obtain the appropriate approvals before recruitment is underway in that location.

May I take this opportunity to wish you every success for your research.

Yours sincerely

Dr Lindy Dalen
Research Governance Manager

Tel: 023 8059 5058
email: rgoinfo@soton.ac.uk

AHMC/STA/hph

27 April 2009

National Research Ethics Service
SOUTHAMPTON & SOUTH WEST HAMPSHIRE
RESEARCH ETHICS COMMITTEE (B)
1ST Floor, Regents Park Surgery
Park Street, Shirley
Southampton
Hampshire
SO16 4RJ

Tel: 023 8036 2466
023 8036 3462
Fax: 023 8036 4110

Email: scsha.SWHRECB@nhs.net

Mrs Ruth Turk
Research Fellow
University of Southampton
School of Health Sciences
Building 45, Highfield
University of Southampton
SO17 1BJ

Dear Mrs Turk

Full title of study: **Quantitative measurement of impairments and how they relate to upper limb function of the older adult in sub-acute and chronic stages post-stroke**

REC reference number: **09/H0504/21**

Thank you for your letter of 15 April 2009, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Acting Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission at NHS sites ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

UNIVERSITY OF Southampton

Ms Ruth Turk
School of Health Sciences
Building 45
University of Southampton
University Road
Highfield
Southampton
SO17 1BJ

23 December 2008

Dear Ms Turk

RGO Ref: 6222

Project Title **Quantative Measurement of Impairment and How They Relate to Upper Limb Function of the Older Adult in Sub-Acute and Chronic Stages Post-Stroke**

I am writing to confirm that the University of Southampton is prepared to act as sponsor for this study under the terms of the Department of Health Research Governance Framework for Health and Social Care (2nd edition 2005).

The University of Southampton fulfils the role of Research Sponsor in ensuring management, monitoring and reporting arrangements for research. I understand that you will be acting as the Principal Investigator responsible for the daily management for this study, and that you will be providing regular reports on the progress of the study to the Research Governance Office on this basis.

I would like to take this opportunity to remind you of your responsibilities under the terms of the Research Governance Framework, and the EU Clinical Trials Directive (Medicines for Human Use Act) if conducting a clinical trial. We encourage you to become fully conversant with the terms of the Research Governance Framework by referring to the Department of Health document which can be accessed at:

http://www.dh.gov.uk/assetRoot/04/12/24/27/041224

In this regard if your project involves NHS patients or resources please send us a copy of your NHS REC and Trust approval letters when available.

Please do not hesitate to contact me should you require any additional information or support. May I also take this opportunity to wish you every success with your research.

Yours sincerely

Dr Martina Prude
Head of Research Governance
Tel: 023 8059 5058
email: rgoinfo@soton.ac.uk

UNIVERSITY OF Southampton

Ms Ruth Turk
School of Health Sciences
Building 45
University of Southampton
University Road
Highfield
Southampton
SO17 1BJ

RGO REF - 6222
School Ethics Ref - SOHS-ETHICS 08-002

23 December 2008

Dear Ms Turk

Professional Indemnity and Clinical Trials Insurance

Project Title **Quantative Measurement of Impairment and How They Relate to Upper Limb Function of the Older Adult in Sub-Acute and Chronic Stages Post-Stroke**

Participant Type:	No Of Participants:	Participant Age Group:	Notes:
Patients	40	Adults	

Thank you for forwarding the completed questionnaire and attached papers.

Having taken note of the information provided, I can confirm that this project will be covered under the terms and conditions of the above policy, subject to written informed consent being obtained from the participating volunteers.

Insurance will only be activated when we have received a copy of the Ethics Committee approval and you must not begin your project prior to this. Please forward a copy of the Ethics Committee approval letter as soon as it is to hand to complete the insurance placement.

If there are any changes to the above details, please advise us as failure to do so may invalidate the insurance.

Yours sincerely

Ruth McFadyen

Mrs Ruth McFadyen
Insurance Services Manager

Tel: 023 8059 2417
email: hrm@soton.ac.uk

cc: File

Appendix E – Clinical Measurement Protocols

The star Cancellation Test

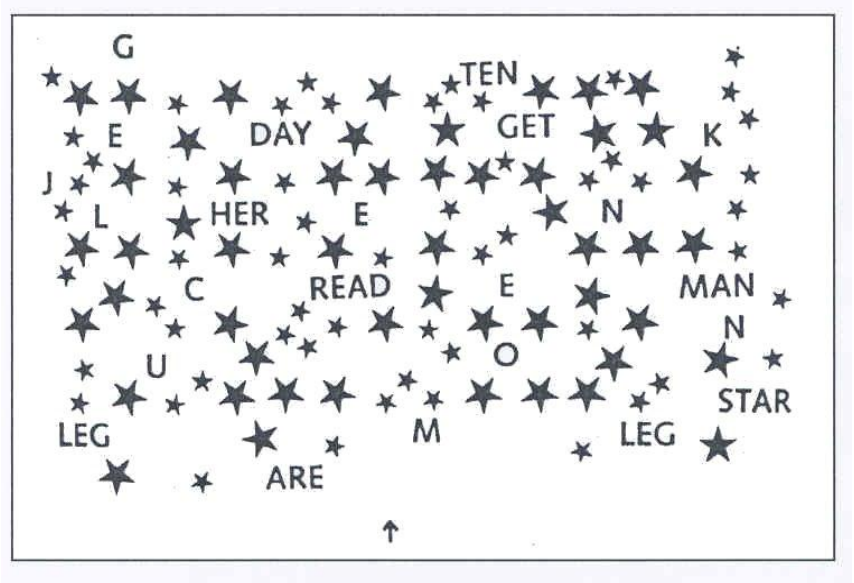


Figure A-1 The star Cancellation Test (SCT) from the Behavioural Inattention Test (Wilson et al. 1987). In the SCT, the patient is required to cross out 54 small stars (two on the midline and are crossed out by the health professional for the purposes of instruction) 27 on the left and 27 on the right. The small stars are randomly distributed among non-verbal and verbal distractors (52 larger stars, 13 letters and 10 short words) (Fig 2). The cut-off score that indicates neglect is recommended as 51.

Table E-1: The Tardieu scale protocol and soring used in this study and based on the protocol by Morris et al (Morris 2002)

Position	Participant in a sitting position, elbow flexed by 90°
Specified velocity of extension stretch movement	V3: As fast as possible (faster that the rate of the natural drop of the limb segment under gravity)
Quality of muscle reaction (X):	0: No resistance throughout the course of the passive movement 1: Slight resistance throughout the course of the passive movement, with no clear catch at a precise angle 2: Clear catch at a precise angle, interrupting the passive movement, followed by release 3: Fatigable clonus (<10 seconds when maintaining pressure) occurring at a precise angle 4: Infatigable clonus (>10 seconds when maintaining pressure) occurring at a precise angle
Angle of muscle reaction (catch) felt during extension stretch (Y):	Measured in degrees flexion or extension relative to the zero position (hand in a straight line with forearm)

Table E-2: Specific starting positions, movements and hand grips for testing proprioception used in this study, based on a revised version of the Nottingham Sensory Assessment (Stolk-Hornsveld et al. 2006).

Starting position	Participant in a sitting position, elbow flexed by 90°
Movement and instruction	Three passive flexion and extension of the wrist throughout the full available range of movement, the patient was asked: 'Is your hand moving upwards or downwards?'
Assessor hand grips	Distal (moving) hand: place the thumb on the lateral aspect and the index finger on the medial aspect of the hand. Proximal (fixing) hand: fix the distal end of the forearm.
Scoring	0 – Absent: Patient does not detect the movement taking place. 1 – Impaired: Patient detects the movement taking place but the direction is not correct on all three occasions. 2 – Normal: Patient correctly detects the direction of the movement taking place on all three occasions.

Appendix F - Wolf Motor Function Test Instruction Manual

Rebecca Stuck (University of East Anglia) and Ruth Turk (University of Southampton)
September 2009

The original version of the WMFT was by Dr. Steven Wolf (1989), Emory University, and later modification of this was based on observations during a visit of three persons from UAB (Edward Taub, Paul Blanton, and Karen McCulloch). A further version of the test was written by David Morris, M.S.P.T, Jean Crago, M.S.P.T and Edward Taub, PhD (2001). Additional modifications were made by Sandy McCombe Waller and Jill Whitall, (University of Maryland Baltimore) to collect data on subjects with mild and moderate hemiparesis (Whitall et al. Arch Phys Med Rehabil, 2006).

This instruction manual for the WMFT is based on the protocol from Morris et al, 2001, but incorporates the scoring scale and additional sub-tasks from Whitall et al (2006) as it is more suitable for both mild and moderate severity of hemiparesis. In this version, however, the standardisation of the table height as well as the chair position to each subject has been included with the aim of accommodating all sizes and heights of subjects. Subjects will be allowed to practice each task first with their nonparetic arm whereas previous guidelines have not included this suggestion. A template has been added for precise positioning of objects as well as a list of required materials and equipment, and the instructions have been changed to UK English. Also in this version (September 2009) task numbers 8 and 14 have been removed as the weighted object tasks will not be required for the current study.

General Instructions

1. The final time score will be median (and/or mean) time required for all timed tasks executed. One hundred twenty seconds is the maximum time allowed for each task attempted. Since medians will be used, all scores above the median (whether, e.g., 62 sec or 120 +) have the same weight. Thus, if the examiner feels that the subject cannot possibly complete the task, they can terminate in order to prevent excessive subject discouragement. The time to be recorded would be 120 +.

2. Functional Ability is scored using a 5-point scale (page 3). Specific guidance is also given for each task in the manual. For the Functional Ability score the total and mean score can be used.

3. In order to assure a standard placement of test objects, a template should be taped to the desk so that its front edge is flush with the front edge of the desk. The outline of each test objects should be traced on the template in the position in which it should be placed.

4. The position and setup of the table and chair are different in this version of the WMFT. The table height is adjusted to reflect the height of the subject and the position of chair is set up to accommodate the subjects arm length as all tasks require some form of reaching. The starting position should be optimal for the task performance (e.g. desk does not block/restrict movement, subject can reach objects). Final chair positioning should be established using the less-affected upper extremity and recorded on the recording form so that the position can be replicated in later tests. The height of the table should also be recorded. If testing both arms the same chair position should be used. For more detailed guidance see Subject Positioning section on page 4.

5. The non-paretic limb is not generally tested, but can be tested in order to compare what is 'normal' when scoring for the paretic limb

6. Subjects wearing long sleeves should roll the sleeve up on the affected arm before beginning the test.

7. Starting point: The point at which timing begins (i.e. when the examiner says, "Go.")

8. For all timed tasks, subjects should be encouraged to perform the tasks as quickly as possible.

9. Timing is carried out using a stopwatch. (It was felt this was adequate since test subjects are primarily subjects with motor deficits who give large performance times.)

10. Verbal encouragement may be given to subjects during the task attempts to maintain motivation or attention. The phrase "good effort, keep going, don't give up" should be repeated in a calm, confident voice. The phrase should be repeated approximately 12 times over the 2 minute period (i.e. once every 10 seconds).

11. Each task should be described and demonstrated two times at the time the instructions are given. Note: subjects may practice the task with their non-paretic arm but not with the paretic arm before being tested.

12. If objects are dropped on the floor during a task attempt, the tester should quickly return the object to the starting position without interrupting the timing process. It may be useful to have back-up items (i.e. extra paper clip, pencil etc.) so that the item can be replaced quickly if dropped. If it takes longer than 5 seconds to replace an item the task should be repeated.

13. The purpose of the examination is not to test cognitive ability. Therefore if a subject appears confused about or misunderstands the task on the first attempt, the task should be repeated. Entire verbal instructions and demonstration can be repeated 1 time per task and subjects may practice the task again with their non-paretic arm. If the subject performs the task incorrectly the second time, a 120+ is assigned for the time score.
14. Some tasks have several subtasks. At each testing point have the subject attempt all subtasks in the specified order and record the time and functional ability score for each subtask.

15. Pre-post comparisons for timing and function score must compare like strategies.

16. Filming is optional but maybe advantageous for non-blinded raters and to prevent other forms of bias

Instructions to the subject: These instructions should be given to each subject as an introduction each time the WMFT is administered:

"*Today I am going to see how well you can use you arm.*

There are 15 tasks that I will ask you to do as quickly as you can.

Before each task I will read you the instructions and demonstrate the task 2 times.

You may practice the tasks with your unaffected arm while I am demonstrating, but not with your affected arm, I can explain again if you do not understand. Please try and do each part of the test even if you do not think that you can do it. The tasks will be timed, you can work on each task for up to two minutes, but if it is obvious that you are unable to carry out a task then we will stop and move on to the next task. Do you have any questions?"

Functional Ability Scoring Scale:

0 = Does not / unable to attempt with the involved arm
1 = Involved arm does not participate functionally and the task is not achieved; however an attempt is made to use the arm
2 = Arm does participate and the task is achieved, but movement is influenced to some degree by compensatory movements and/or abnormal movement patterns or performed slowly and/or with effort
3 = Arm does participate and the task is achieved in one attempt; movement is close to normal but slightly slower; may lack precision, fine co-ordination, or fluidity
4 = Arm does participate; movement appears to be normal, timely (pay attention to expected normal times) and controlled.

Scoring guidance for each specific task is given throughout the manual

Positioning of the Subject

- The subject must be seated in an upright position with their legs in front of the chair, and feet in contact with floor throughout testing. The assessor may provide foam padding to the back of the chair to ensure that an upright position is maintained.(Yozbatiran, 2008)
- The height of testing-table should be approximate to the subject's midabdomen, with the difference in chair-table height of 20-30 cm considered optimal. Shoulders should be in neutral elevation/depression when forearms pronated on the testing-table. Chair to table height should be recorded on baseline and replicated for all reassessments
- Position of the chair will be determined by the length of their upper limb. Use the grid on page 4 to determine position of chair in relation to table. Record the placement of the chair on the Wolf cover sheet.
- Pay careful attention to subject's body and arm position for each task. Make sure effort for tasks is coming from the arm and not from trunk movement. The head is held in a neutral upright position.

Positioning of Subjects – task specific instructions:

In previous versions of the WMFT the chair is placed at 8.5cm away from the table assuming that subjects' average height is 5'8". Where subjects are substantially taller or shorter than 5'8" the chair position is adjusted so that patients can reach the items on the template (Morris, Crago and Taub 2001), though this adjustment is not standardised.

In order to standardise the tasks to the size of each individual, in this version, the assessors determine the distance of the chair from the table by measuring the subjects arm length. This is done using the following procedure and grid:

Measure each subject's non-paretic arm from acromion to tip of thumb when their arm is relaxed down by side in sitting. Use the grid below to determine chair placement in terms of distance from table. Once positioned, ensure the subject can reach the 40cm line with non-paretic thumb; the chair can be moved closer if required as long as it is recorded on the score sheet.

Subject Positioning Table

Length of subject arm from acromion to tip of thumb	Tasks 1-4 Chair facing sideways Distance from table to side of seat	Tasks 5-6 and 9-17 Chair facing forwards Distance from table to front of seat
60cm (or less)	Side of seat next to table	Front of seat next to table
65cm	Approx 4cm	Approx 4cm
70cm	Approx 8cm	Approx 8cm
<70cm	Up to 12cm	Up to 12cm

Filming Instructions

Although a study has suggested that videotaping is not required to generate accurate scores (Whitall, 2006), it may be advantageous to videotape examinations for later rating by a panel of blinded clinicians to the pre-post treatment status of the subject or to other considerations that might bias ratings. Camera height and position should allow a view that included maximal clarity of the task end position on the template.

Guidance for filming positions:

Filming position side: tasks 1-6, 8 17 (gross tasks)
View of the whole body while the subject's side being tested is placed next to desk. The edge of the camera tripod should be placed approx 3 feet to the side of the desk and directly in line with the back edge of the desk. The camera should be facing the subject and the view should include the subject's entire body.

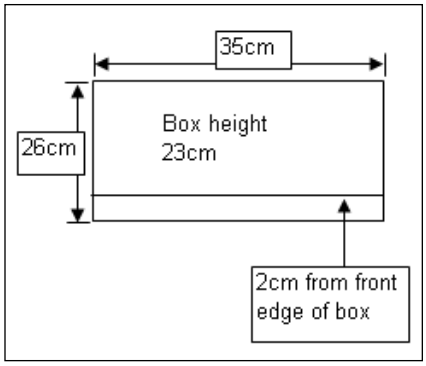
Filming position side-close: tasks 9-13, 15-16 (fine motor tasks)
Profile of Expanded View of Limb being tested: The camera tripod remains in the same position at the side position. The camera view should be zoomed in to focus on the fine motor skills. The view should include the patient's entire upper extremity.

Materials, equipment and template

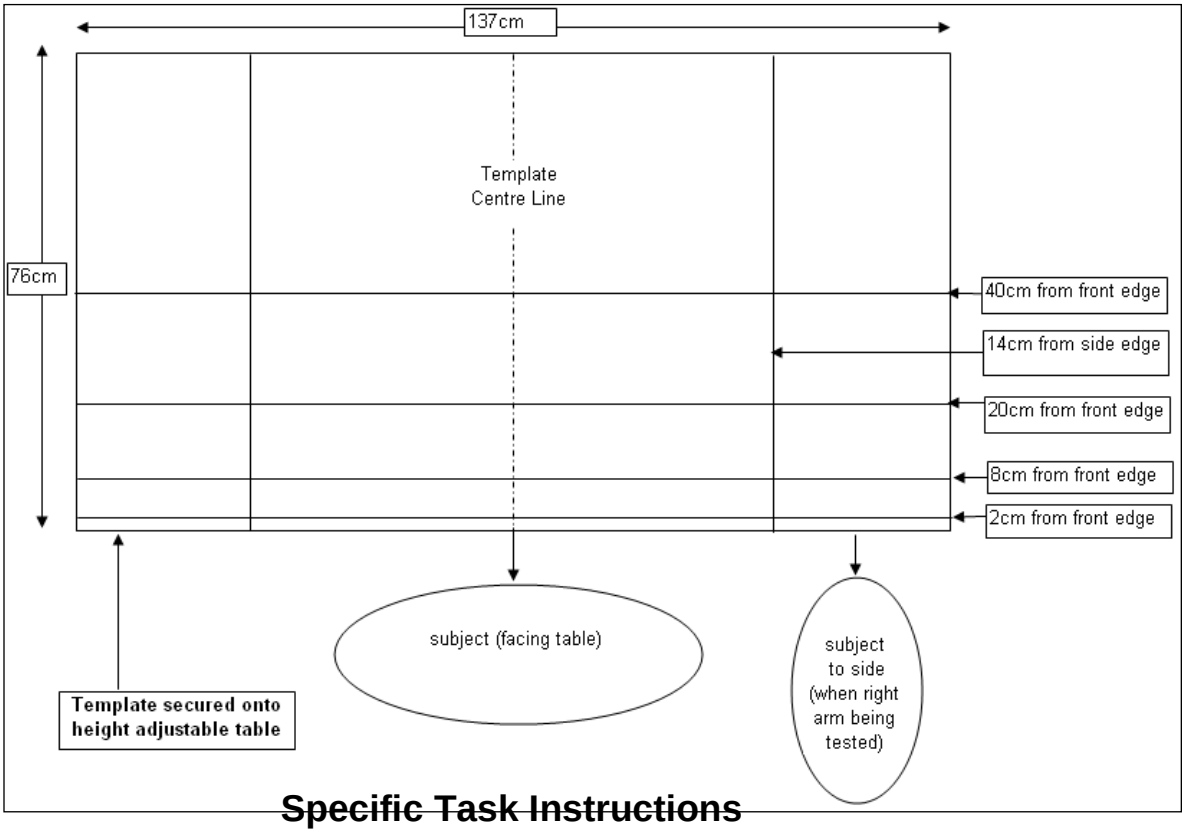
Materials and Equipment

- Height adjustable table to fit template (137 x 76cm)
- A standard upright chair / wheelchair with firm back and without armrests
- A laminated template (with object positioning, placement and target lines)
- Stopwatch
- A box (23cm H / 35 cm L / 26 cm W)
- Weights – 1lb wrist weight with Velcro strap; 3 lb weight
- 12oz unopened soft drink can
- 7 inch pencil
- 2 inch paper clip
- 3X5 inch playing cards
- 3x checkers size:
- Standard Yale Key and lock mounted at 16cm height on a board, tumblers of the lock set to allow 180^0 arc, with 90^0 of that arc on either side of midline
- Small dish towel – approx size: 57cm x 41 cm
- Shopping basket with handle
- Adjustable height, rolling bedside table – set at 15" above testing- table

Box Dimensions



Template dimensions and Lines



Specific Task Instructions

1. Forearm to table (side)

SET UP	TASK	VERBAL INSTRUCTIONS
Starting position: • Position chair according to guidance above and record on scoring sheet • Hips against chair back • Both feet on floor or supported with footplates at 90º • Filming position (side)	Task description: • Subject attempts to place forearm on the table (adjacent and parallel to front edge) by abduction at the shoulder. (Some shoulder flexion will probably also be necessary to get arm past the edge of table.) "Forearm" is defined as the wrist and elbow. The palmar surface of the hand need not be flat. Timing ends when both the forearm and hand touch the table. Timing procedure: • Start on word "Go" and ends when subject's forearm and hand touch the table in the required position. Measure: • The time elapsed from the starting point to the moment the forearm and hand touch the table in the required fashion.	Verbal Instructions: "When I say "Go" Place your forearm on the table as quickly as you can like this (examiner demonstrates). Make sure you place your arm and hand completely on the top of the table Ready, Go."

Task specific scoring guidance

Score 0=

No voluntary movement seen at involved joints.

I.e. if movement seen only in hand and there is no reaching movement then subject scores a 0

Score 1=

Movement seen at involved joints

2. Forearm to box (side)

SET UP	TASK	VERBAL INSTRUCTIONS
Starting position: • Subject seated in chair, as position 1. • Hips against chair back • Hand not being tested placed on thighs • Shoulder of tested arm abducted with forearm pronated and placed flat on the table with radial edge adjacent to front edge of table; elbow at line 14 cm from edge of end of table (with the shoulder joint not flexed or extended). Palmar surface of hand need not be flat. If final position of arm on previous task is not 14 cm from side edge of table, move subject's arm into correct position before beginning this task. • Box is placed at 14cm from the side edge of the table, and at 8cm from the front edge • Box should be stabilised by someone during the trial • Filming position (side).	Task description: • Subject attempts to place forearm (as defined above- from wrist to elbow) on the box by further abduction at the shoulder. (Again some shoulder flexion may be necessary to clear edge of box.) At the end, the forearm should be flat on the box with the hand drooping over side edge of box. The wrist must be beyond the line 2 cm from the front edge of box and the elbow must be beyond the front edge of the box. Timing procedure: • Starts on word "Go" and ends when subject's forearm is flat on box with the hand drooping over the edge of the box. Measure: • The time elapsed from the starting point to the moment the forearm touches the top of the box in the required fashion with the hand drooping over the edge of the box.	Verbal Instructions: "When I say "Go" place your forearm on the box as quickly as you can like this (examiner demonstrates). Place you arm so that your hand is drooping over the edge of the box and your wrist is past the line. Ready, Go."

Task specific scoring guidance

Score 0=

No voluntary movement seen at involved joints.

I.e. if movement seen only in hand and there is no reaching movement then subject

3. Extend elbow (to the side)

SET UP	**TASK**	**VERBAL INSTRUCTION**S
<u>Starting position:</u> • Subject seated in chair as position 1. • Hips against chair back. • Hand not being tested on thighs • Shoulder of tested arm abducted with forearm resting flat on table in a pronated position. Palmar surface of hand need not be flat on table • Forearm being tested adjacent to front edge of table; elbow at line 14 cm from side edge of table (with the shoulder joint not flexed or extended)	<u>Task position:</u> • Subject attempts to reach across the 40 cm line on template (drawn from the front edge of the table) by extending the elbow (to the side). Elbow can be lifted off the table during the task. This may be the only way shorter subjects can reach 40 cm line. Shoulders should be kept level to prevent leaning with the trunk. Some external rotation at the shoulder is necessary to carry out this movement, but the examiner should prevent too much of this movement. <u>Timing procedure:</u> • Starts on the word "Go" and ends when the subject's thumb passes the line. <u>Measure:</u> • The time elapsed from the starting point to the time the thumb crosses the line.	• "When I say "Go" slide your hand across the table by straightening your elbow so that your thumb reaches over this line like this • Your elbow is allowed to rise off the table. • Keep your body as still as you can. Ready, Go." Note: the subject should slide their hand across the table. Repeat the task if they lift their hand off of the table.

Task specific scoring guidance

Score 0= No voluntary movement seen at involved joints.

I.e. if movement seen only in hand and there is no reaching movement then subject scores a 0

Score 1= Movement seen at involved joints but does not achieve task

Score 2= Achieves task but with excessive compensation at the trunk (rotation or leaning)

Score 3= Achieves task with minor trunk compensation and loss of elbow extension

Score 4 = Must demonstrate full range of elbow extension (in comparison to non-paretic arm)**.** Hand must remain in contact with the table

4. Extend elbow (to the side) – with 1 lb weight

SET UP	TASK	VERBAL INSTRUCTIONS
Starting position: • Subject seated in chair as position 1. • Hips against chair back • Hand not being tested on thighs • Shoulder of tested arm abducted with forearm resting flat on table in pronated position exactly as in last task. • Forearm of arm to be tested adjacent to front edge of table; elbow at line 14 cm from side edge of table (with the shoulder joint not flexed or extended); palmar surface of hand need not be flat. • 1 lb weight (sandbag) placed at ulnar edge of wrist; bottom edge of weight aligned with ulnar styloid process. • Filming position (side)	Task description: • Subject attempts to push the sandbag across 40 cm line (drawn from front edge of table) by extending the elbow and to a lesser extent externally rotating the shoulder. Elbow should be kept on the table throughout the task (different from previous task) and shoulders should be kept level to prevent leaning with the trunk. Again, the examiner needs to be aware of subject's trunk leaning and/or excessive external rotation at the shoulder to perform task (especially true for taller men) Timing procedure: • Starts on the word "Go" and ends when the leading edge of sandbag crosses line. Measure: • The time elapsed from the starting point to the time the leading edge of the sandbag initially crosses the line.	Verbal instructions: • "When I say "Go" push the weight across the line by straightening your elbow as quickly as you can like this • This time keep your elbow on the table. • Keep you arm in contact the weight until you have finished • Try to keep your body as still as possible Ready, Go." Note: If the elbow is lifted, allow a 2nd attempt.

Task specific scoring guidance

Score 0= No voluntary movement seen at involved joints.

I.e. if movement seen only in hand and there is no reaching movement then subject scores a 0

Score 1= Movement seen at involved joints

Score 2= Accomplished with excessive compensatory trunk movement and/or very limited elbow extension

Completes task but hand does not remain in contact with the weight

5. Hand to table (front)

SET UP	TASK	VERBAL INSTRUCTION
Starting position: • Position chair facing the table according to guidance above. Record position on scoring sheet) • Both hands on thighs • Hips against chair back • Filming position (side)	Task description: • Subject attempts to place involved hand on the table. The heel of the hand must rest beyond taped line 2 cm from front edge of table. The palmar surface of the hand need not be flat (Place most of the hand in the circle.) Timing procedure: • Starts on the word "Go" and ends when the heel of the hand and fingers touch table beyond the taped 2 cm line. Measure: • The time elapsed from starting point to moment the heel of the hand and fingers touch table beyond the taped 2 cm line	Verbal instructions: • "When I say "Go" place your hand in the circle on the table as quickly as you can like this (examiner demonstrates) Ready, Go."

Task specific scoring guidance

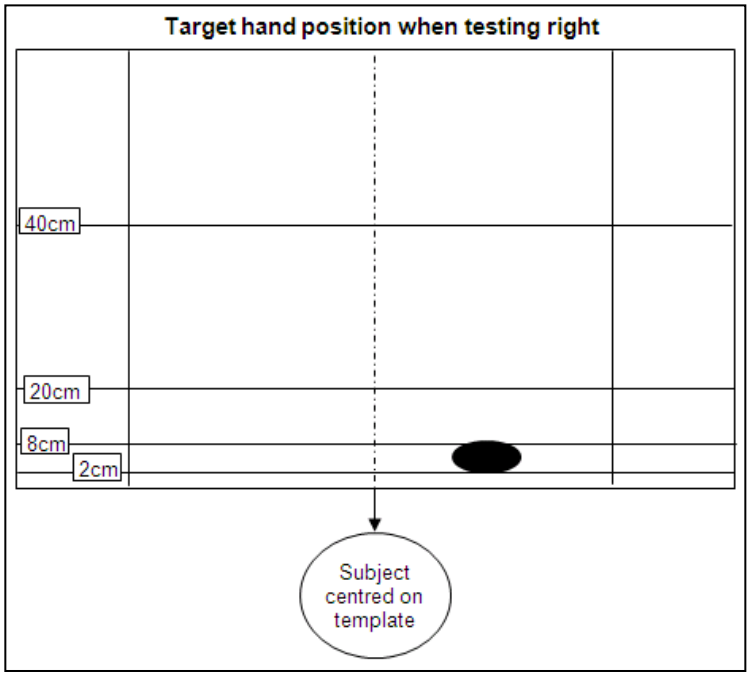
Score 0=

No voluntary movement seen at involved joints. I.e. if movement seen only in hand and there is no reaching movement then subject scores a 0

Score 1=

Movement seen at involved joints

Note: The final posture of the hand and fingers does not influence scoring as long as the heel of the hand is in contact with the table



6. Hand to box (front)

SET UP	TASK	VERBAL INSTRUCTIONS
<u>Starting position:</u> • Subject seated in chair facing table; chair centred on template as for task 5. • Hand not being tested on thighs. • Hand to be tested placed on table, heel of hand just beyond the line 2 cm from front edge of table (i.e. just past taped line, in circle – as in final position on last task). • Box centred on table; front edge aligned with 20 cm line. • Box should be stabilised by someone during the trial • Filming position (side)	<u>Task description:</u> • Subject attempts to place hand on the box. The heel of the hand must be placed past the front edge of the box. The palmar surface of the hand need not be flat. <u>Timing Procedure:</u> • Starts on the word "Go" and ends when the heel of the hand and fingers touch the box past the edge of the box. <u>Measure:</u> • The time elapsed from starting point to moment the heel of the hand and fingers touch box past the edge of the box.	<u>Verbal Instructions:</u> • "When I say "Go" lift your hand from the table and place it on the box as quickly as you can, like this (examiner demonstrates). • Make sure your hand goes all the way onto the top of the box Ready, Go."

Task specific scoring guidance

Score 0=

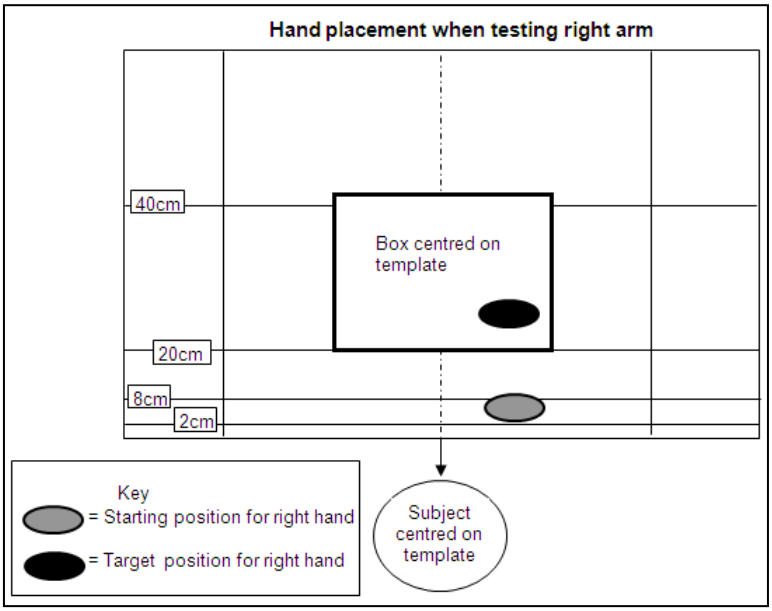
No voluntary movement seen at involved joints.

I.e. if movement seen only in hand and there is no reaching movement then subject scores a 0

Score 1=

Movement seen at involved joints

Note: The final posture of the hand and fingers



8. Reach and Retrieve

SET UP	TASK	VERBAL INSTRUCTIONS
<u>Starting position:</u> • Move chair closer to the table so that front legs of chair are approximately 11 cm further in than front edge of table. Check the position by asking the Subject to reach to the 40 cm line with their non-paretic arm and check their fingers cross the line (if not move the chair in closer or further away) (record chair position on scoring sheet). • 1 lb weight centred on table and positioned just beyond 40 cm line • Hand not being tested on thighs • Arm to be tested: elbow extended with palm of hand in contact with weight and forearm positioned in midrange between pronation and supination. • Hips against chair back • Subject must be able to maintain starting position while the tester states "Ready, Go" • Filming position (side)	<u>Task description:</u> • Subject attempts to pull 1 lb weight across the 8 cm line. Task object is a cuff weight folded in half and kept in place with a Velcro fastener. <u>Timing procedure:</u> • Start on the word "Go." End when the leading edge of the weight crosses the 8 cm line. <u>Measure:</u> • The amount of time elapsed from the starting point to the moment the leading edge of the weight crosses the 8 cm line.	Verbal Instructions: • "When I say "Go" slide the weight across the table so it passes this line as quickly as you can. Do the task by bending your elbow like this (examiner demonstrates). The weight should remain in contact with your hand until it crosses the line. Ready, Go."

Specific Scoring guidance

For this task the examiner is allowed to assist the subject in achieving the starting position

Score 0 = No voluntary movement /no active control of elbow joint (flexion) observed

Unable maintain starting position without physical assistance

Score 1 = Starting position achieved through compensatory movement, i.e. excessive trunk flexion or restricted range of elbow extension / shoulder flexion.

Score 2 = Subject loses contact with weight or pronates forearm or excessive upper arm or hand movements (i.e., swatting the weight with the hand) to achieve task

Score 3 = Minimal compensation movements of the trunk, upper arm or hand and / or lacks fluidity

Note: Some subjects may need to reach forward in order to reach 40cm line. Allow for appropriate trunk flexion but not if subject uses this as compensation for limited elbow extension / shoulder flexion.

9. Lift Can

SET UP	TASK	VERBAL INSTRUCTIONS
<u>Starting position:</u> • Subject seated in chair facing table; chair centred on template. • Chair returned to earlier position – tasks 5 & 6 • Hands on thighs • Unopened 12 oz soft drink can placed on table at subjects midline with front edge of can just beyond 20 cm line • Filming position (side-close)	<u>Task description:</u> • *Sub task 9a:* subject to lift the can and bring it close to lips with a cylindrical grasp • *Subtask 9b*: subject to lift the can and bring it close to lips with disc grip • *Subtask 9c:* subject to lift the can and bring it close to lips with a cylindrical grasp, unaffected hand to stabilize can. • *Subtask 9d:* subject to lift the can and bring it close to lips with disc grip, unaffected hand to stabilize can. <u>Timing procedure:</u> • Start on the word "go." End when can is within approximately one inch of subject's mouth. <u>Measure:</u> The time elapsed from starting point to the moment the can comes within approximately one inch of the subject's mouth.	<u>Verbal instructions:</u> • "You may be asked to do this task four different ways. <u>Subtasks a & b</u> • When I say "Go" lift the can to your mouth without touching your lips, like this (demonstrate). Do this as quickly as you can. Ready, Go." <u>Subtasks c & d</u> • When I say "Go" lift the can to your mouth without touching your lips, you may support the can with your other hand like this (demonstrate). Do this as quickly as you can. Ready, Go."

Task specific scoring guidance

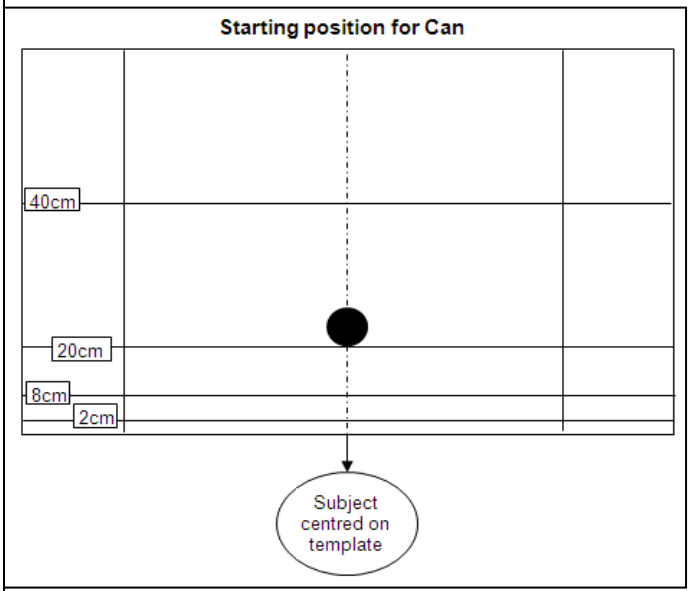
For all tasks requiring hand function, i.e. grasping, lifting and manipulation of objects, there must be some movement of the fingers / thumb to score a 1.

Score 0 = No movement at fingers / thumb

Score 1 = Movement must be initiated at hand / fingers. Unable to use specific grip given in instructions to complete the task

Score 2 = Achieves task using correct grip but with abnormal movement pattern (e.g. poor opening of the hand, lifting and trajectory control) moving of the object around the table, and/or more than 1 attempt to complete task

Score 3 = Achieves task but with minor difficulty opening hand / lifting the object, or slightly slower than normal



10. Lift Pencil

SET UP	TASK	VERBAL INSTRUCTIONS
<u>Starting position:</u> • Subject seated in chair facing table; chair centred on template • Hands on thighs • Hips against chair back • 7 inch pencil placed parallel to front edge of table, centred on subject's midline and with front edge of pencil at 20 cm. line • Filming position (side-close)	<u>Task Description:</u> • *Subtasks 10a:* subject attempts to pick up the pencil using 3-jaw chuck prehension (thumb and first two fingers). • *Subtask 10b:* subject attempts to pick up the pencil using 3-jaw chuck prehension with unaffected hand stabilizing the pencil Note: The pencil should be picked up off the table and not over the edge of the table. If the patient performs the task by lifting the pencil over the edge of the table once, repeat the task one more time. Assign a 120+ if the task cannot be accomplished in the correct manner • *Subtask 10c:* subject attempts to pick up the pencil by sliding it to the edge of the table and then using a palmar grasp <u>Timing Procedure:</u> Starts on word "Go" and ends when entire pencil (all surfaces) is raised from the table by at least an inch	<u>Verbal instructions:</u> • "You may be asked to do this task 3 different ways <u>Subtask a</u> • When I say "Go" pick up the pencil like this (examiner demonstrates). The pencil should be picked up on the table and not over the edge of the table. Do this as quickly as possible. Ready, Go." <u>Subtask b</u> • When I say "Go" pick up the pencil like this (examiner demonstrates). You may use the other hand to support the pencil Do this as quickly as possible. Ready, Go." <u>Subtask b</u> When I say "Go" pick up the pencil like this (examiner demonstrates). Ready, Go."

Task specific scoring guidance

For all tasks requiring hand function, i.e. grasping, lifting and manipulation of objects, there must be some movement of the fingers / thumb to score a 1.

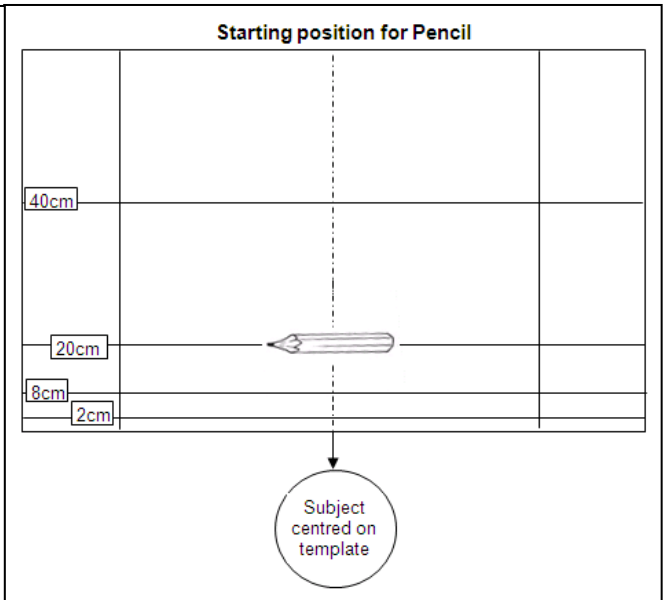
Score 0 = No movement at fingers / thumb

Score 1 = Movement must be initiated at hand / fingers Unable to use specific grip and/or pick up the pencil in the correct manner given in instructions (assign 120+)

Score 2 = Achieves task using correct grip but with abnormal movement pattern (e.g. poor opening of the hand and lifting control) moving of the object around the table, and/or more than 1 attempt to complete task

Score 3 = Achieves task but with minor difficulty opening hand / lifting the object, or slightly slower than normal

Note: take in to account control of clasp.



11. Pick up paper clip

SET UP	TASK	VERBAL INSTRUCTIONS
<u>Starting position:</u> • Subject seated in chair facing table; chair centred on template. • Hands on thighs • Hips against chair back • 2 in paper clip placed parallel to the edge of the table, centred on subject's midline, and with front edge of clip at 20 cm line; the wider end of the paper clip should be facing towards the side to be tested. • Filming position (side-close)	<u>Task description:</u> • *Subtask 11a:* Subject attempts to pick up the paper clip using a pincer grasp (pads of thumb and index finger opposed). • *Subtasks 11b:* Subject attempts to pick up the paper clip using a pincer grasp with unaffected stabilizing the paper clip Note - The paper clip should be picked up on the table and not over the edge of the table. If the patient performs the task by lifting the paper clip over the edge of the table once, repeat the task one more time. Assign a 120+ if the task cannot be accomplished in the correct manner. <u>Timing procedure:</u> • Start on the word "go." End when entire paper clip is off the table. <u>Measure:</u> • The time elapsed from the starting point to the moment the entire clip is raised from the table surface.	<u>Verbal instructions:</u> <u>Subtask a:</u> • When I say "Go" pick up the paper clip like this as quickly as you can (examiner demonstrates). The paper clip should be picked up on the table and not over the edge of the table. Ready, Go." <u>Subtask b:</u> • When I say "Go" pick up the paper clip like this as quickly as you can (examiner demonstrates). You can use your other hand to support the paper clip. The paper clip should be picked up on the table and not over the edge of the table. Ready, Go." <u>Special Consideration:</u> Fingernail length can significantly affect performance; therefore, patient should be instructed when making test arrangements to not clip fingernails for at least three days before test session.

Task specific scoring guidance

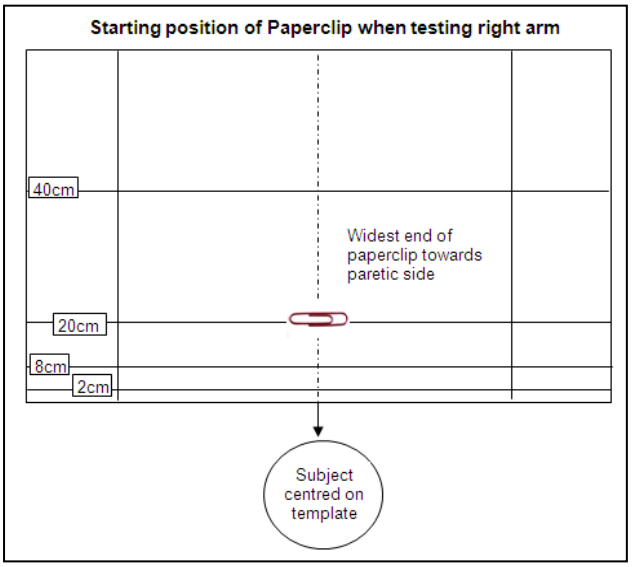
For all tasks requiring hand function, i.e. grasping, lifting and manipulation of objects, there must be some movement of the fingers / thumb to score a 1.

Score 0 = No movement at fingers / thumb

Score 1= Movement must be initiated at hand / fingers**.** Unable to use specific grip given in instructions to complete the task (120+ sec given)

Score 2 = Achieves task using correct grip but with abnormal movement pattern (e.g. poor opening of the hand and lifting control) moving of the object around the table, and/or more than 1 attempt to complete task

Score 3 = Achieves task but with minor difficulty opening hand / lifting the object, or slightly slower than normal



12. Stack Checkers

SET UP	TASK	VERBAL INSTRUCTIONS
<u>Starting position:</u> • Subject seated in chair facing table; chair centred on template • Hands on thighs • Three checkers are placed in a line parallel to front edge of table with front edge of each checker just beyond 20 cm line. Checkers spaced 4.5 cm apart with middle checker at subject's midline. • Filming position (side-close)	<u>Task description:</u> • Subject attempts to stack the two end checkers onto the centre checker. The task can be executed by picking up either checker first. <u>Timing procedure:</u> • Start on the word "Go." End when subject has placed the third checker in prescribed position. <u>Measure:</u> • The time elapsed from the starting point to the moment the third checker is in place.	<u>Verbal instructions:</u> • "When I say "Go" stack the two checkers on the end onto the middle checker like this (examiner demonstrates). Do this as quickly as you can. Ready, Go." Note: Checkers may be out of alignment, but, in order for the task to be considered completed, the top two checkers may not be touching the table surface.

Task specific scoring guidance

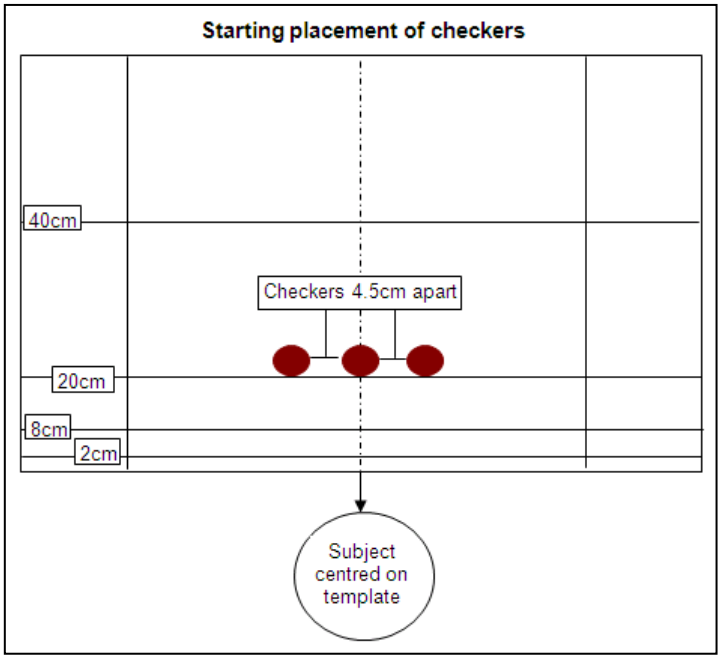
For all tasks requiring hand function, i.e. grasping, lifting and manipulation of objects, there must be some movement of the fingers / thumb to score a 1.

Score 0 = No movement at fingers / thumb

Score 1= Movement must be initiated at hand / fingers

Score 2 = Achieves task but poor control in clasping checkers, drops checkers etc

Score 3 = Achieves task but with minor difficulty with precision or fluidity, or slightly slower than normal



13. Flip cards

SET UP	TASK	VERBAL INSTRUCTIONS
<u>Starting position:</u> • Subject seated on chair; chair centred on template • Hands on thighs • Hips against chair back • 3, 3 X 5 in index cards placed in a line parallel to front edge of table, with short edge of card closest to subject just beyond 20 cm line. Cards spaced 3 cm apart with middle card at subject's midline.	<u>Task description:</u> • *Subtasks 13a*: Using a pincer grasp on the near edge of the cards, subject attempts to flip each of the cards over. This task should be done by sliding the front edge of the card just past the front edge of the table with some or all of the fingers and then grasping the card edge protruding past the table edge between the palmar surfaces of thumb and index finger. Cards should be flipped over from side to side (for supination, rather than from front to back). The cards do not have to be straightened or adjusted after they have been turner over. The subject should first flip over the card on the side being tested, then the centre card and then the card on the opposite side. Subject should be prevented from wetting fingers by licking. • *Subtask13b:* Slide the cards towards the body and then flip them, end over end, with the dorsum of the hand.	<u>Verbal description:</u> <u>Subtask a:</u> • "When I say "Go" flip over each card from side to side. Start with the card on your (state side being tested) side, then the middle card, and then the card on your (state opposite side) side. • Watch me first (examiner demonstrates). Do this as quickly as you can. Ready, Go." <u>Subtask b:</u> • "This time you will flip the cards from end to end like this (examiner demonstrates). • Do not lick your fingers and do the task as quickly as you can when I say Go Ready, Go."

Task specific scoring guidance

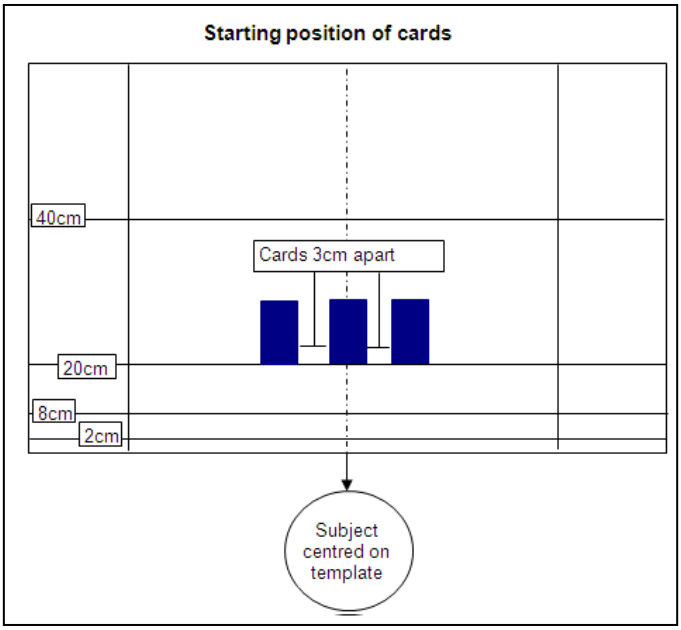
For all tasks requiring hand function, i.e. grasping, lifting and manipulation of objects, there must be some movement of the fingers / thumb to score a 1.

Score 0 = No movement at fingers / thumb

Score 1= Movement must be initiated at hand / fingers Unable to use specific grip given in instructions to complete the task (120+ given)

Score 2 = Achieves task using correct grip but with poor dexterity of the fingers, and excessive compensation of the trunk or upper arm and/or more than 1 attempt to flip any card

Score 3 = Achieves task but with minor difficulty with fluidity and precision, or slightly slower than normal



15. Turning Key in Lock

SET UP	TASK	VERBAL INSTRUCTION
<u>Starting position:</u> • Subject is seated in chair facing table; chair centred on template. • Chair returned to original position • Hands placed on thighs. • Hips against chair back • Examiner holds lock and key board, preventing board from moving when used by subject; board held parallel to front edge of table, just beyond 8 cm line and centred on subject's midline. • Filming position (side-close)	<u>Task description:</u> • Using a lateral pincer grasp, subject attempts to move the key in the lock from the vertical position first to the side being tested, then to the opposite side and finally back to the vertical starting position. Tumblers of the lock are set so that the key moves through a 180 degree arc (only), with 90 degrees of that arc on either side of the midline <u>Timing procedure:</u> • Start on the word "Go." End when the key is in the starting position again. <u>Measure:</u> • The time elapsed from the starting point to the moment the key is returned to the starting position.	<u>Verbal instructions:</u> • "When I say "Go" Grasp the key between your thumb and your first finger (examiner demonstrates) • Then turn the key, first to the (state side being tested) until the key is horizontal then to the (state the opposite side) until the key is horizontal and finally return the key to the original vertical position. • Do this as quickly as you can. Ready, Go."

Task specific scoring guidance

For all tasks requiring hand function, i.e. grasping, lifting and manipulation of objects, there must be some movement of the fingers / thumb to score a 1.

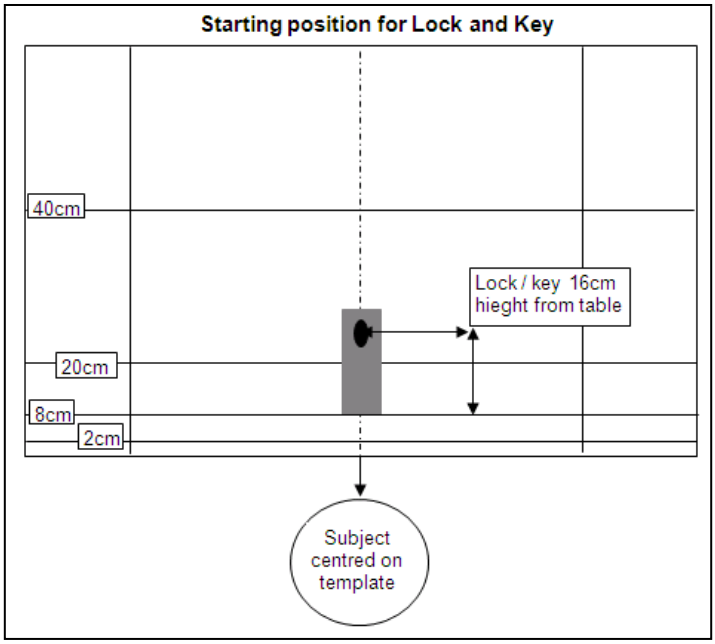
Score 0 = No movement at fingers / thumb

Score 1= Movement must be initiated at hand / fingers

Score 2 = Achieves task using a grasp other than pincer. Incorrect sequence used for turning key

Score 3 = Achieves task but with minor difficulty with fluidity and precision, or slightly slower than normal

Note: Take into account the extent of pronation and supination observed at forearm to achieve task



16. Fold Towel

SET UP	TASK	VERBAL INSTRUCTIONS
<u>Starting position:</u> • Subject is seated in chair facing table; chair centred on template. • Chair returned to original position • Hips against chair back • Hand towel is placed flat on table centred on subject with short edge of towel at 8 cm line. • Start with both hands gripping the closest corners of the towel between the thumb and index finger. • Filming position (side-close) Ensure trunk and both upper limbs in view	<u>Task description:</u> • Subject folds the towel in half lengthwise on the table. Using the affected hand the towel is pulled closer to the subject and then folded in half in the other direction, from the affected side to the unaffected side. The folding does not need to be exact, but ends of the towel need to be approximately aligned (within 1.5 inches). <u>Timing procedure:</u> • Start on the word "Go." End when the towel is completely folded on the table. <u>Measure:</u> • The time elapsed from the starting point to the moment the towel is completely folded on the table.	<u>Verbal instructions:</u> • "When I say "Go" Fold this towel in half length wise and then in half again, like this (examiner demonstrates). Do this task as rapidly as possible. Ready, Go."

Task specific scoring guidance

Score 0=

No attempt / unable to grip towel, i.e. no movement seen in fingers / thumb

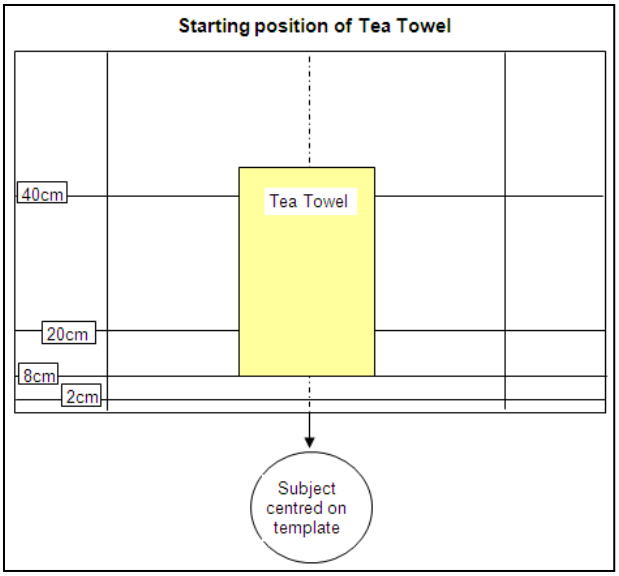
Score 1= Movement seen in fingers but unable to grip and/or release towel

Assisted to position towel in fingers prior to starting task

Score 2=Towel may be poorly folded or need smoothing / straightening out**.** Over use of non-paretic hand in the first fold. Excessive use of trunk flexion to compensate for reduced elbow extension. Abnormal grip to fold towel.

Score 3 = Achieves task but with minor difficulty with fluidity and precision, or slightly slower than normal

NB allow trunk flexion to reach towel as long as it is not compensating for reduced elbow extension / shoulder flexion. If towel is pulled towards subject in a normal functional manner during first fold do not penalize subject.



17. Lift Basket

SET UP	TASK	VERBAL INSTRUCTIONS
Starting position: • Subject standing and facing table. • Rolling bedside table (15" higher than table) placed over the desk on subject's side to be tested. The rolling bedside table extends across the length of the desk from the edge nearest the subject to the edge farthest from the subject • Basket at 8 cm line on the test table template, leading edge 14 cm from side edge of table of side to be tested, handles (taped together) lined up with centre of body. • Three pound weight placed in basket. • Filming position (side or front)	Task description: • Subtask 17a: Subject to pick up basket by grasping handle (from underneath the handle) and placing the basket on far edge of the rolling bedside table. The far edge of the basket should touch the far edge of the table. • Subtask 17b: Subject to pick up basket by hooking forearm under the handle and placing the basket on far edge of the rolling bedside table. The far edge of the basket should touch the far edge of the table. Timing procedure: • Start on the word "Go." End when any portion of the base of the basket extends beyond the far edge of the bedside table. Measure: • The time elapsed from the starting point to the moment the basket has been placed on the cart in the required position. (Note: release of the basket is not included in the time measure).	Verbal Instructions: • "When I say "Go" Pick up the basket with your (state the side being tested) hand and place the basket on the rolling table. The far edge of the basket should touch the far edge of the bedside table (examiner demonstrates). Try not to move your feet while you do this task. Do this as quickly as possible. Ready, Go."

Task specific scoring guidance

Score 0= Unable to stand

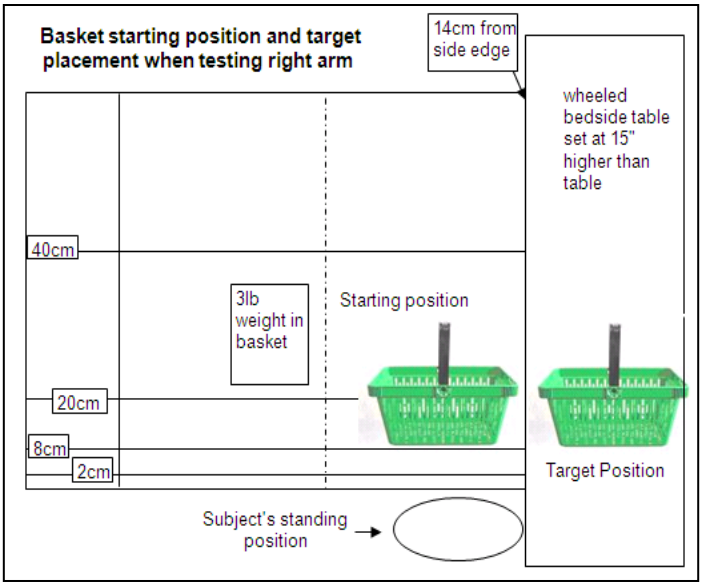
No movement at hand to grasp basket (subtask a)

Score 1= Hand movement seen but unable to grasp basket handle (subtask a)

Score 2= Achieves task but hits basket on side or bangs it onto shelf in uncontrolled manner or abnormal grasp on basket. Movement out of original foot position or use of non-paretic hand to maintain balance. Over compensation from significant extent of trunk rotation to complete task

Score 3= Lacks precision when placing basket on shelf

Slight loss of balance when achieving task (but no use of non-paretic hand or foot movement for support)



WMFT scoring sheet

Distance between top of table and chair seat (with table positioned at mid abdomen height)	cm	**Scoring scale** 0 = Does not / unable to attempt with the involved arm 1 = Involved arm does not participate functionally and the task is not achieved; however an attempt is made to use the arm 2 = Arm does participate and the task is achieved, but movement is influenced to some degree by compensatory movements and/or abnormal movement patterns or performed slowly and/or with effort 3 = Arm does participate and the task is achieved in one attempt; movement is close to normal but slightly slower; may lack precision, fine co-ordination, or fluidity 4 = Arm does participate; movement appears to be normal, timely (pay attention to expected normal times) and controlled.
Chair position sideways (items 1 - 4)	cm	
Chair position facing table (items 5, 6, 9-13, 15, 16)	cm	
Chair position facing table (item 8)	cm	

Item	**Time (0 – 120 s)**	**Functional ability score**	**Notes:**
1. Forearm to table (side)		0 1 2 3 4	
2. Forearm to box (side)		0 1 2 3 4	
3. Extend elbow (side)		0 1 2 3 4	
4. Extend elbow to side with weight		0 1 2 3 4	
5. Hand to table (front)		0 1 2 3 4	
6. Hand to box (front		0 1 2 3 4	
8. Reach and Retrieve		0 1 2 3 4	
9a. Lift Can subtask 1		0 1 2 3 4	
9b. Lift Can subtask 2		0 1 2 3 4	

9c. Lift Can subtask 3		0 1 2 3 4	
9d. Lift Can subtask 4		0 1 2 3 4	
10a. Lift Pencil subtask 1		0 1 2 3 4	
10b. Lift Pencil subtask 2		0 1 2 3 4	
10c. Lift Pencil subtask 3		0 1 2 3 4	
11a. Lift Paperclip subtask 1		0 1 2 3 4	
11b. Left Paperclip subtask 2		0 1 2 3 4	
12. Stack Checkers		0 1 2 3 4	
13a. Flip Cards subtask 1		0 1 2 3 4	
13b. Flip Cards subtask 2		0 1 2 3 4	
15. Turning Key in Lock		0 1 2 3 4	
16. Fold Towel		0 1 2 3 4	
17a. Lift Basket subtask 1		0 1 2 3 4	
17b. Lift Basket subtask 2		0 1 2 3 4	
Total Score			
Mean of total score			
Median of total score			

Appendix G - Main Study Statistical Results

Table G- 1: The list of motor impairment indices included in the main study analysis

Indices included in the main study analysis (measurement unit)	Wrist rig tests
Extensor AROM (degrees)	Active range of movement
Extensor PROM (degrees)	Passive range of movement
Extensor IF (Nm)	Maximal voluntary contraction
Sine tracking index (cross correlation) (degrees^2)	Active sinusoidal tracking
Sine coactivation index (correlation coefficient)	
Step tracking index (total Mean Absolute Error) (degrees)	Active step tracking
Path length (degrees/sample)	
Step coactivation index (correlation coefficient)	
Extensor onset timing (seconds)	
Stretch index (3.5Hz)	Fast passive sinusoidal tracking (stretch response test) - 3.5Hz
Stretch index (0.5Hz)	Fast passive sinusoidal tracking (stretch response test) - 0.5Hz
Mean torque index (Nm)	Slow passive ramp and hold tracking (torque test)

Table G- 2: Impairment measures that were found not to be normally distributed in the different patient groups of the main study

Group	Impairment measures which were not normally distributed
Impaired n=26	TI step, Ext onset, SI 3.5, SI 0.5
Unimpaired n=14	CI sine, Ext onset, SI 0.35, SI 0.5
Acute n=13	TI step, Ext onset, SI 3.5, SI 0.5
Chronic n=13	TI step, Ext onset, AROM ext, SI 0.5
Low MCA n=6	IF ext, SI 0.5
High MCA n=13	SI 3.5, SI 0.5

Table G- 3: Median (Interquartile range) values for all impairment indices and *P* values comparing the impaired and unimpaired groups. Statistical significance was tested using the non-parametric Mann Whitney *U* test. Statistically significant between group differences ($p<0.05$) are in bold.

	Impairment Indices	Group		*P* values
		Impaired (N=26)	Unimpaired (N=14)	Unimpaired - Impaired
Negative Impairments	Sine tracking index ($degrees^2$)	118.2 (31.7, 193.5)	222.3 (213.8, 236)	**<0.001**
	Step tracking index (degrees)	6.36 (5.57, 11.28)	3.97 (3.52, 4.23)	**<0.001**
	Path length (degrees/sample)	0.022 (0.016, 0.025)	0.009 (0.007, 0.010)	**<0.001**
	Active ROM extension (degrees)	22.1 (-15, 36)	57.8 (53, 65)	**<0.001**
	Extensor IF (Nm)	1.18 (0.2, 2.6)	4.95 (3.1, 6.8)	**<0.001**
	Extensor onset [a] (seconds)	0.41 (0.31, 0.56)	0.29 (0.26, 0.34)	**0.006**
Positive impairments	Coactivation (sine tracking) (correlation coefficient)	0.11 (-0.30, 0.30)	-0.34 (-0.45, -0.20)	**0.024**
	Coactivation (step tracking) [b] (correlation coefficient)	-0.05 (-0.27, 0.17)	-0.12 (-0.28, 0.05)	0.558
	Stretch index [c] (3.5Hz) (ratio SR area: LBL	1.24 (1.05, 1.76)	1.00 0.98, 1.02	**<0.001**
Secondary impairments	Passive ROM extension (degrees)	60.1 (42.4, 65.7)	70.09 (65.5, 73.9)	**<0.001**
	Mean torque [d] (Nm)	0.49 (0.33, 0.87)	0.45 (0.39, 0.65)	0.109

ROM – Range of movement; IF – isometric force; SR – stretch response; LBL – local baseline [a] Impaired group n=24; [b] Impaired group n=25; [c] Impaired group n=24; [d] Impaired group n=22, unimpaired n=11

Table G- 4: Between-days repeatability for the measurement indices from the active tests for 17 participants* from the impaired group (9 acute, 8 chronic) showing the range of values for this group, mean day 2 – day 1 difference, Bland and Altman limits of agreement and coefficient of repeatability

	Impairment Indices	Range of values (min – max)	Between-days repeatability		
			Mean difference [95% CI]	Limits of agreement	Coefficient of repeatability
Negative Impairments	Sine tracking index [a] ($degrees^2$)	2.0 - 229.6	3.13 [-6.6, 12.9]	(-33.5, 39.8)	±35.32
	Step tracking index (degrees)	4 - 16.42	-0.21 [-0.7, 0.29]	(-2.14, 1.72)	±1.88
	Path length (degrees/sample)	0.012 - 0.050	-0.002 [-0.006, 0.002]	(-0.016, 0.013)	±0.014
	Active ROM extension (degrees)	-52.3 - 51.2	4.4 [1.4, 7.4]	(-7.3, 16.1)	±14.1
	Extensor IF (Nm)	0 - 4.8	0.1 [-0.1, 0.4]	(-0.9, 1.2)	±1.1
	Extensor onset [b] (seconds)	0.22 - 1.28	-0.008 [-0.12, 0.11]	(-0.39, 0.38)	±0.37
Positive impairments	Coactivation (sine tracking) [b] (correlation coefficient)	-0.54 - 0.73	0.05 [-0.15, 0.24]	(-0.60, 0.69)	±0.61
	Coactivation (step tracking) [b] (correlation coefficient)	-0.50 - 0.71	-0.10 [-0.19, -0.01]	(-0.40, 0.21)	±0.34
Secondary impairments	Passive ROM extension (degrees)	21 - 69.8	2.3 [-1.1, 5.7]	(-10.9, 15.5)	±13.4

*Unless stated otherwise; [a] N=16; [b] N = 13; Data was missing due to technical reasons on one day assessment;

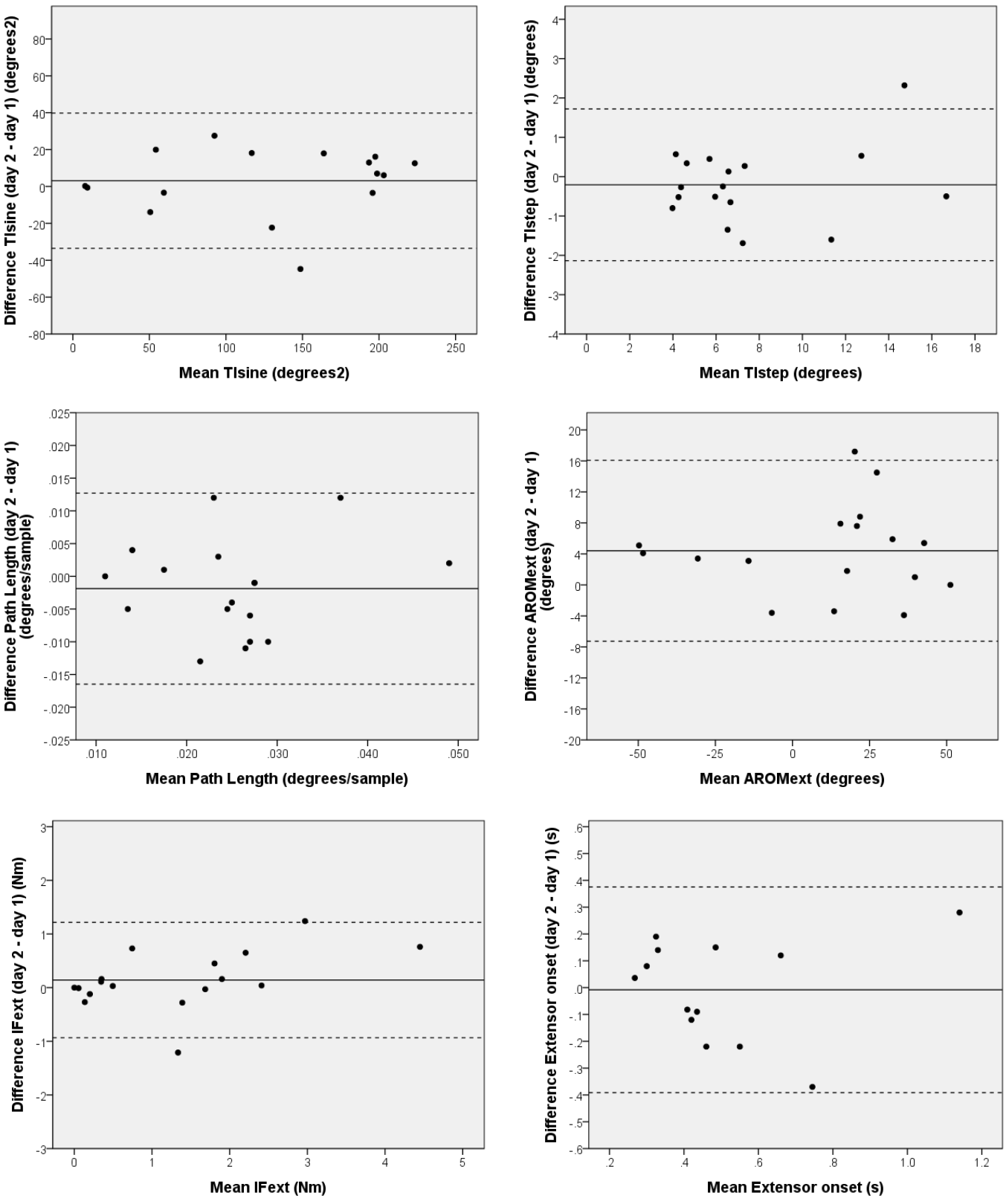


Figure G- 1: Bland Altman Plots for between-days test retest reliability for 17 impaired participants in the reliability sub-group, showing mean difference (bold line) and 95% limits of agreement (dashed): negative impairments – Sine (N=16) and step tracking indices, path length, active range of movement extension, extensor isometric force and extensor onset timing (N=13)

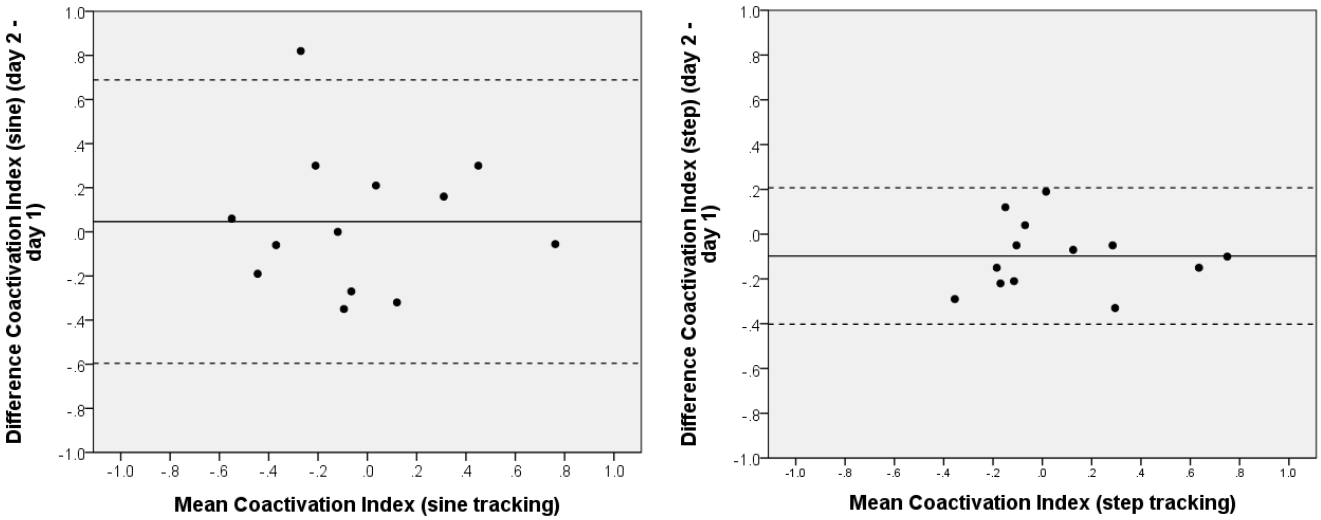


Figure G- 2: Bland Altman Plots for between-days test retest reliability impaired participants in the reliability sub-group, showing mean difference (bold line) and 95% limits of agreement (dashed): positive impairments – coactivation indices (sine and step tracking), N=13.

Table G- 5: Median (Interquartile range) values for all impairment indices and *P* values comparing the acute and chronic groups with the unimpaired group. Statistical significance was tested using a Mann Whitney *U* test. Statistically significant between group differences ($p<0.05$) are in bold

	Impairment Indices	Group			*P* values	
		Acute (N=13)	Chronic (N=13)	Unimpaired (N=14)	Unimpaired - Acute	Unimpaired - Chronic
Negative Impairments	Sine tracking index (degrees^2)	107.8 (41.3, 174.7)	178.8 (6.8, 201.1)	222.3 (213.8, 236)	**<0.001**	**<0.001**
	Step tracking index (degrees)	6.51 (6, 10.8)	5.90 (4.8, 12.0)	3.97 (3.52, 4.23)	**<0.001**	**<0.001**
	Path length (degrees/sample)	0.024 (0.022, 0.029)	0.017 (0.015, 0.022)	0.009 (0.007, 0.010)	**<0.001**	**<0.001**
	AROM extension (degrees)	19.5 (0.6, 34)	28.8 (-41, 37)	57.8 (53, 65)	**<0.001**	**<0.001**
	Extensor IF (Nm)	0.51 (0.23, 1.38)	1.98 (0.17, 3.71)	4.95 (3.1, 6.78)	**<0.001**	**0.002**
	Extensor onset [a] (seconds)	0.5 (0.32, 0.64)	0.4 (0.30, 0.50)	0.29 (0.26, 0.34)	**0.008**	**0.043**
Positive impairments	Coactivation (sine tracking) (correlation coefficient)	-0.2 (-0.45, 0.07)	0.14 (-0.19, 0.42)	-0.34 (-0.45, -0.20)	0.356	**0.003**
	Coactivation (step tracking) [b] (correlation coefficient)	-0.09 (-0.33, 0.12)	0.04 (-0.20, 0.31)	-0.12 (-0.28, 0.05)	0.884	0.237
	Stretch index [c] (3.5Hz)	1.15 (1.05, 1.76)	1.34 (1.04, 1.93)	1.00 0.98, 1.02	**<0.001**	**<0.001**
Secondary impairments	PROM extension (degrees)	48.9 (31.2, 55.8)	60.1 (42.4, 65.7)	70.09 (65.5, 73.9)	**<0.001**	**0.007**
	Mean torque [d] (Nm)	0.18 (0.07, 0.27)	0.49 (0.33, 0.87)	0.45 (0.39, 0.65)	**0.002**	0.853

AROM – active range of movement; IF – isometric force; PROM – passive range of movement; [a] Chronic group n=11; [b] Chronic group n=12; [c] Acute and chronic group n=12; [d] Acute group n=10, chronic n=12, unimpaired n=11;

Table G- 6: Median (Interquartile range) values for impairment indices and *P* values comparing the low and high MCA and unimpaired groups. Statistical significance was tested using a Kruskal Wallis Test and Mann Whitney *U* test. Statistically significant between group differences (p<0.05) are in bold.

Impairment Indices	Group median (IQR)			Kruskal Wallis Test *P* values	Mann Whitney *U* test *P* values		
	High MCA (N=17)	Low MCA (N=9)	Unimpaired (N=14)		High – Low MCA	Unimpaired – High MCA	Unimpaired – Low MCA
Negative Impairments							
Extension AROM (degrees)	31.0 (21.7, 42.8)	-55 (-29, 1)	57.8 (53, 65)	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Extensor IF (Nm)	1.67 (0.81, 3.71)	0.06 (0.01, 0.58)	4.95 (3.1, 6.78)	**<0.001**	**0.001**	**0.001**	**<0.001**
Extensor onset [a] (seconds)	0.4 (0.29, 0.50)	0.75 (0.35, 1.28)	0.29 (0.26, 0.34)	**0.002**	**0.022**	0.052	**0.002**
Positive Impairments							
Coactivation (sine) (correlation coefficient)	-0.22 (-0.45, -0.08)	0.28 (0.07, 0.59)	-0.34 (-0.45, -0.20)	**0.001**	**0.001**	0.311	**0.001**
Coactivation (step)[b] (correlation coefficient)	-0.13 (-0.36, 0.09)	0.30 (0.01, 0.58)	-0.12 (-0.28, 0.05)	**0.010**	**0.003**	0.551	**0.017**
Stretch index [c] (ratio SR:LBL)	1.15 (1.03, 1.48)	1.38 (1.13, 2.21)	1.00 0.98, 1.02	**<0.001**	0.178	**<0.001**	**<0.001**
Secondary Impairments							
Extension PROM (degrees)	60.1 (44.4, 65.5)	60.1 (42.4, 65.7)	70.09 (65.5, 73.9)	**<0.001**	**0.022**	**0.002**	**<0.001**
Mean torque [d] (Nm)	0.23 (0.15, 0.46)	0.52 (0.26, 0.84)	0.45 (0.39, 0.65)	0.067	0.142	**0.021**	1.00

AROM – active range of movement; IF – isometric force; PROM – passive range of movement; SR – stretch response; LBL – local baseline; [a] Low MCA group n=7; [b] Low MCA group n=8; [c] Low MCA group N=8 and high MCA group n=16; [d] High MCA group n=14, unimpaired n=11

Table G - 7: Spearman's correlation coefficients between all the variables for acute stroke group (N=13), statistically significant values in bold (p<0.05)

	Variable	Sine TI	Step TI	Path length	Ext onset	AROM ext	IF ext	CI (sine)	CI (Step)	SI (3.5Hz)	SI (0.5Hz)	PROM ext	MTI
Negative impairment	Step TI	**-0.912 (p<0.001)**											
	Path length	-0.011 (P=0.971)	-0.011 (P=0.971)										
	Ext onset	**-0.619 (P=0.024)**	**-0.619 (P=0.024)**	-0.071 (P=0.818)									
	AROM ext	0.368 (P=0.216)	-0.291 (P=0.334)	0.537 (P=0.058)	-0.110 (P=0.720)								
	IF ext	0.368 (P=0.216)	-0.286 (P=0.344)	-0.147 (P=0.632)	-0.085 (P=0.782)	**0.775 (P=0.002)**							
Positive impairment	CI (sine)	**-0.878 (P<0.001)**	**0.880 (P<0.001)**	0.097 (P=0.752)	**0.763 (P=0.002)**	-0.242 (P=0.426)	-0.206 (P=0.4.99)						
	CI (Step)	**-0.571 (P=0.041)**	0.538 (P=0.058)	-0.117 (P=0.562)	0.495 (P=0.085)	-0.473 (P=0.103)	-0.225 (P=0.459)	**0.748 (P=0.003)**					
	SI (3.5Hz)	0.042 (P=0.897)	-0.105 (P=0.746)	0.382 (P=0.221)	0.245 (P=0.442)	0.063 (P=0.846)	0.182 (P=0.572)	0.144 (P=0.656)	0.245 (P=0.442)				
	SI (0.5Hz)	-0.067 (P=0.854)	0.310 (P=0.383)	0.233 (P=0.536)	0.032 (P=0.923)	-0.077 (P=0.812)	-0.217 (P=0.499)	0.361 (0.249)	**0.573 (P=0.051)**	0.182 (P=0.572)			
Secondary impairment	PROM ext	0.253 (P=0.405)	-0.022 (P=0.943)	0.507 (P=0.077)	0.127 (P=0.680)	**0.758 (P=0.003)**	**0.555 (P=0.049)**	0.055 (P=0.858)	-0.225 (P=0.459)	0.182 (P=0.572)	-0.098 (P=0.762)		
	MTI	-0.067 (P=0.854)	0.310 (P=0.383)	0.223 (P=0.536)	-0.177 (P=0.625)	0.188 (P=0.602)	0.274 (P=0.444)	0.146 (P=0.688)	-0.012 (P=0.973)	-0.213 (P=0.555)	-0.118 (P=0.960)	0.298 (P=0.403)	
Activity	mWMFT	0.539 (P=0.057)	-0.371 (P=0.212)	0.214 (P=0.483)	-0. 273 (P=0.367)	**0.787 (P=0.001)**	**0.707 (P=0.007)**	-0.347 (P=0.245)	-0.476 (P=0.100)	-0.056 (P=0.863)	-0.035 (P=0.914)	**0.624 (P=0.023)**	0.541 (P=0.106)

Statistically significant correlation - Bold shaded cells ($P \leq 0.004$ level), bold un-shaded cells ($P \leq 0.05$ level); TI: Tracking Index; Ext: extension; AROM: active range of movement; IF: Isometric force; CI: coactivation index; SI: stretch index; PROM: passive range of movement; MTI: mean torque index; mWMFT: modified wolf motor function test

Table G- 8 Spearman's correlation coefficients between all the variables for chronic stroke group (N=13), statistically significant values in bold (p<0.05)

	Variable	Sine TI	Step TI	Path length	Ext onset	AROM ext	IF ext	CI (sine)	CI (Step)	SI (3.5Hz)	SI (0.5Hz)	PROM ext	MTI
Negative impairment	Step TI	**-0.863 (p<0.001)**											
	Path length	0.213 (P=0.484)	-0.169 (P=0.581)										
	Ext onset	**-0.661 (P=0.027)**	**0.638 (P=0.035)**	-0.074 (P=0.829)									
	AROM	**0.681 (p=0.010)**	**-0.676 (p=0.011)**	0.319 (P=0.289)	-0.369 (P=0.264)								
	IF ext	**0.846 (p<0.001)**	**-0.780 (p=0.002)**	0.141 (P=0.645)	**-0.651 (P=0.030)**	**0.725 (p=0.005)**							
Positive impairment	CI (sine)	**-0.725 (P=0.005)**	**0.615 (P=0.025)**	-0.061 (P=0.843)	0.487 (P=0.128)	**-0.692 (P=0.009)**	**-0.698 (P=0.008)**						
	CI (Step)	**-0.669 (P=0.017)**	**0.795 (P=0.002)**	-0.069 (P=0.831)	0.555 (P=0.076)	-0.490 (P=0.106)	**-0.834 (P=0.001)**	**0.592 (P=0.043)**					
	SI (3.5Hz)	-0.531 (P=0.075)	0.336 (P=0.286)	0.177 (P=0.583)	0.382 (P=0.276)	-0.531 (P=0.075)	-0.420 (P=0.175)	0.531 (P=0.075)	0.218 (P=0.519)				
	SI (0.5Hz)	-0.275 (P=0.364)	0.132 (P=0.668)	-0.125 (P=0.685)	0.241 (P=0.474)	-0.412 (P=0.162)	-0.275 (P=0.364)	0.170 (P=0.578)	0.042 (P=0.897)	**0.776 (P=0.003)**			
Secondary impairment	PROM ext	0.552 (P=0.067)	-0.456 (P=0.117)	0.191 (P=0.532)	0.077 (P=0.821)	**0.720 (P=0.006)**	**0.566 (P=0.044)**	-0.467 (P=0.108)	-0.396 (P=0.203)	-0.168 (P=0.602)	-0.121 (P=0.694)		
	MTI	-0.021 (P=0.948)	0.210 (P=0.513)	-0.470 (P=0.123)	-0.127 (P=0.726)	-0.441 (P=0.152)	0.056 (P=0.863)	0.189 (P=0.557)	0.055 (P=0.873)	0.209 (P=0.537)	0.301 (P=0.342)	-0.287 (P=0.366)	
Activity	mWMFT	**0.863 (p<0.001)**	**-0.835 (p<0.001)**	0.263 (P=0.385)	**-0.647 (P=0.031)**	**0.791 (P=0.001)**	**0.758 (P<0.003)**	**-0.786 (P=0.001)**	**-0.697 (P=0.012)**	**-0.720 (P=0.008)**	-0.527 (P=0.064)	0.445 (P=0.128)	-0.266 (P=0.404)

Statistically significant correlation - bold shaded cells (*P*<0.004 level), bold un-shaded cells (*P*<0.05 level); TI: Tracking Index; Ext: extension; AROM: active range of movement; IF: Isometric force; CI: coactivation index; SI: stretch index; PROM: passive range of movement; MTI: mean torque index; mWMFT: modified wolf motor function test

Table G- 9: P values for each impairment variable entered individually into a linear regression and quantile regression with the mWMFT function score.

	Impairment variables	Acute group		Chronic group	
		Linear regression		Quantile regression	
		P value		*P* value	
Negative impairments	TI Sine	0.067	0.221	**<0.001**	**<0.001**
	TI Step	0.066	0.123	**<0.001**	**<0.001**
	Path length	0.458	0.343	0.239	0.825
	Ext onset	0.075	0.187	**0.015**	**<0.001**
	Ext AROM	**0.016**	0.063	**<0.001**	**<0.024**
	Ext IF	**<0.001**	**0.003**	**<0.001**	0.145
Positive impairments	SI (3.5Hz)	0.295	0.691	0.114	0.060
	CI Sine	0.116	0.635	**0.002**	**0.057**
	CI Step	0.530	0.388	**0.003**	**0.037**
Secondary impairments	Ext PROM	**0.027**	0.144	**0.026**	0.155
	MTI	0.273	0.222	0.351	0.086

Appendix H - Wrist rig participant record form

Study	**Session 1 date:** **Participant file number 1:**		**Session 2 date:** **Participant file number 2:**	
Participant details	DOB: Time from Stroke:		R / L sided hemiplegia	
Clinical details	Hx of Unilateral neglect: Result of star cancellation test: Medication:			
Observation of wrist activity: Able to extend wrist and fingers >20˚ Mild severity high functioning		Able to extend wrist thumb and 2 digits > 10˚ Mild severity low functioning		Able to extend wrist 5˚ when supported in wrist rig Moderate severity
MAS score =	0 = No increase in muscle tone 1 = Slight increase in muscle tone, resulting in a "catch" and a "release" (brief increase in resistance) at the end of the range of motion 2 = Slight increase in muscle tone, resulting in a "catch", (increased resistance) followed by minimal resistance throughout the remainder (less than half) of the range of motion 3 = A more marked increase in muscle tone throughout most of the range of motion, however affected part can be easily moved 4 = Marked increase of muscle tone, passive movement difficult 5 = The affected part cannot be moved			
Tardieu Scale **V1 X=** **V1 Y=** **V3 X=** **V3 Y=**	0: No resistance throughout the course of the passive movt. 1: Slight resistance throughout the course of the passive movement, with no clear catch at a precise angle. 2: Clear catch at a precise angle, interrupting the passive movement, followed by release. 3: Fatigable clonus (<10 seconds when maintaining pressure) occurring at a precise angle. 4: Infatigable clonus (>10 seconds when maintaining pressure) occurring at a precise angle.			V1 – slow movt V3 – fast movt X – quality of muscle reaction Y – angle of muscle reaction (V1 end of passive range; V2 angle of catch)
Joint position sense Score:	0 – Absent: Patient does not detect the movement taking place. 1 – Impaired: Patient detects the movement taking place but the direction is not correct on all three occasions. 2 – Normal: Patient correctly detects the direction of the movement taking place on all three occasions.			
Test	**Files recorded/ comments/ problems** **Session 1**		**Session 2**	
1. AROM				
2. PROM				
3. MVC	**Ext:**	**Flex:**	**Ext:**	**Flex:**
0˚				
20˚				

4. Passive tracking	**Session 1**	**Session 2**
Force/angle test 5˚/s full PROM		
Stretch response 3.5Hz +/-5˚ (sin35_5_stretch) 0.5Hz +/-20˚ (sin_5_stretch)		
5. Active tracking	**Comments/ problems/ results Session 1**	**Session 2**
Sinusoidal without resistance 0.5Hz +/-20˚ (sin5_track)		
Random step without resistance (jump_c_track)		
Setting resistance files		
Sinusoidal with resistance (sin5_track)		
Random step with resistance (jump_c_track)		

Appendix I - Participant Information Sheet

Project Title:	**Arm movement problems and how they relate to arm function post-stroke**
Ethics Submission No:	**09/H0504/21**

Introduction

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. (Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study).
Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

Part one

1.1 What is the purpose of the study?

This study is being undertaken by Ruth Turk, an experienced Physiotherapist, as part of a PhD. Muscle weakness, tightness (known as spasticity) and loss of control of movement are common problems among people who have had a stroke. There is a need for better objective measures of movement problems to improve research of arm rehabilitation after a stroke. A better understanding of the underlying reason for improvement in arm activity after a stroke will enable better diagnosis of movement problems and more targeted therapy. The purpose of this study is to measure movement problems of the arm of older adults who have suffered a stroke, to understand how these movement problems are related to an individual's ability to perform activities such as reach and grasp, and understand how this relationship changes over time after a stroke.

1.2 Why have I been invited?

You have been chosen to take part in this study because you had a stroke either within the last four months or more than one year ago and you are over the age of 60. You are currently having treatment, or have had treatment in the past, from Physiotherapists or Occupational Therapists at one of the following hospitals: Western Community Hospital (Southampton), Farnham Hospital or Milford Hospital (Surrey); or you are registered on the School of Health Sciences research participant database. From your stroke you have some movement problems with your affected arm. If you decide to take part you will be one of up to 40 participants.

1.3 Do I have to take part?

It is up to you to decide. If you are interested please let the Therapy team who contacted you know by phone or by returning the reply slip in the stamped addressed envelope. The researcher will then contact you and will describe the study and go through this information sheet, which you are asked to keep. If you are still interested, you will be asked to sign a consent form to show you have agreed to take part and that you understand what is involved. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

1.4 What will happen to me if I take part?

You will be asked to take part in two assessment sessions which will take place at the Western Hospital, Southampton, or at Farnham or Milford Hospital, Surrey, depending where you are receiving or have received your care, or at the School of Health Sciences laboratory, University of Southampton. The tests will be conducted by the researcher and the sessions will last approximately one and a half hour with regular breaks (see schedule below). If you feel too tired to complete the session, the test of arm function can be undertaken at another time within a few days of the session. The researcher can assist you with any personal needs during that time but you may also like to be accompanied by a carer to assist with any needs.

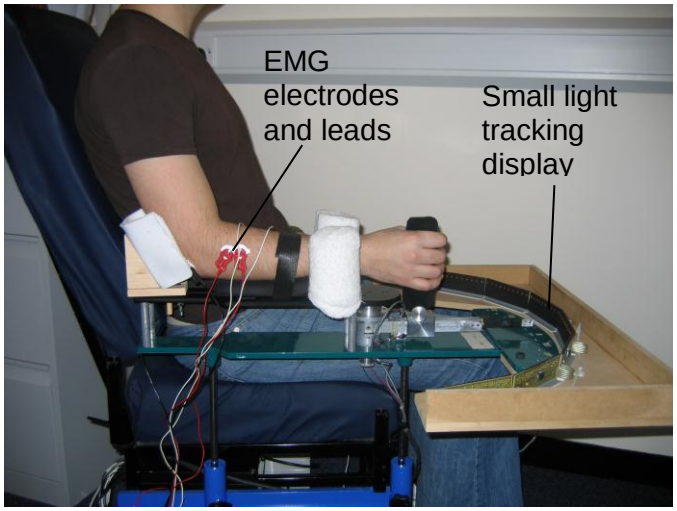
Testing schedule for participants

Session 1 Total time = 1 ½ hours	Complete neglect and spasticity tests, test movement in the rig (15 minutes)	Break (5 mins)	Set up and practice the rig tests, with two 5 min breaks (40 minutes)	Break (10 mins)	Test of arm function (20 minutes)
Session 2 Total time = 1 ½ hours	Set up and complete the rig tests with one 5 min break (60 minutes)	Break (10 mins)	Test of arm function (20 minutes)		

A wrist rig (see figure 1) designed to measure how the arm moves and how the muscles are working. This comprises:

- A chair with an arm-rest and a series of very small lights (LEDs) on a display placed in front. Your wrist joint is aligned with a pivot point to allow horizontal wrist movement.
- Electromyography (EMG) measurement (the electric signals from the muscles that move your wrist).
- An instrument in the arm rest that measures your wrist angle and an instrument that measures the strength you use to move your wrist.
- A Laptop computer that:
  - Records your movement data from each measurement session
  - Generates a moving target that you have to try and track with your movements
  - Analyses the information.

Figure 1 The wrist rig



At the first session the researcher will initially conduct two tests with you to ensure you fit the criteria for the study. Firstly you will be asked to cross out stars on a page in order to assess your ability to identify objects on both your right and left side. Then you will be asked to sit on the wrist rig chair with your arm placed on the rig armrest and secured with straps. The rig allows free movement of the wrist joint and you will be asked to move your hand towards you and away from you to ensure that you have enough strength to move in the rig. If you fit these two criteria, you will be asked to continue with the study. For the rest of the first session you will practise the wrist rig tests and then get to know a test of your ability to use your arm in a series of 15 tasks such as lifting and placing your arm on a table and on a shelf, lifting a drink can to the mouth, stacking some checkers, folding a towel and turning a key in a lock. At the second session firstly the assessor will move your wrist to assess your level of spasticity (muscle tightness), then you will be asked to perform the wrist rig tests followed by the test of arm function (see schedule).

To perform the wrist rig tests you will be sitting in the chair with your arm placed on the rig armrest and a series of very small lights (LEDs) on a display will be placed in front of the arm rest. You will be required to wear a loose short sleeved top, or one that can be rolled up to the elbow, so that your skin on your forearm can be cleaned with alcohol wipes and gel electrodes to measure your muscle activity can be placed on your arm. The researcher will again help you to place your arm in the rig in the correct position, and your arm will be secured with straps.

During the testing process you will be first asked to move your wrist towards you and away from you as far as you can. The researcher will then move your wrist through its full range.

You will then be asked to move your wrist to follow the LEDs as they light up in different sequences for a few minutes. These movements will be without, and then with, a small resistance. You will then be asked to push and then pull your hand against a resistance for five seconds. Lastly the assessor will move your wrist to follow a series of lights on an LED display while you relax your arm.

A recording of video information for the purposes of assessment, teaching and presentation of results, may be taken during the testing process. This will only happen if you agree to it and your face and other identifying marks will not be included or will be blurred.
If you take part in this study in the early stages after your stroke, you may be approached for a second follow-up stage of the project 8 to 12 months later.

1.5 Expenses

If you travel to the hospital where the testing will take place, your travelling expenses will be paid.

1.6 What are the possible risks of taking part?

There is a very slight risk of reddening of the skin on the hand and arm while it is held in the rig by Velcro straps; care will therefore be taken to ensure that the supports are not fastened too tightly and if you are undergoing tests for longer than 20 minutes the arm will be released and the skin checked for reddening at 20 minute intervals. If you become uncomfortable while in the rig, your arm will be released from the rig until any discomfort has eased.

1.8 What are the possible benefits of taking part?

There is no direct benefit to you from taking part. The information we get from this study may help us to improve the measurement of movement problems for future patients with stroke.

1.9 What if something goes wrong?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

1.10 Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

2.1 What will happen if I don't want to carry on with the study?

If you wish to withdraw from the study, you may stop the testing at any time without giving reason. If you agree, we will use any data we have collected up until the point of withdrawing from the study.

What if there is a problem?

If you have a concern or a complaint about this study you should contact Susan Rogers, Head of Research & Enterprise Services, at the School of Health Sciences (Address: University of Southampton, Building 67, Highfield, Southampton, SO17 1BJ ; Tel: +44 (0)23 8059 7942; Email: S.J.S.Rogers@soton.ac.uk). If you remain unhappy and wish to complain formally Susan Rogers can provide you with details of the University of Southampton Complaints Procedure. In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the University of Southampton, Southampton City Primary Care NHS Trust, or Surrey Primary Care NHS Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

2.3 Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you on report forms will have your name and address removed so that you cannot be recognised from it. You will be identified by unique number that connects your data to you. Your personal details will be kept separately from the research records. The data recorded, for the purpose of the research project, will be held on a password protected computer or as paper records kept in a locked filing cabinet.

2.4 Involvement of the Consultant

If you are currently under the care of a stroke Consultant in hospital, they have been informed that this research is taking place.

2.5 What will happen to the results of the research study?

The results of the study will be compiled in reports and published or presented at scientific conferences. If you participate in this study, you will not be identified in any report, presentation or publication. You will be sent a summary of the main findings.

2.6 Who is organising and funding the research?

The study is being organised through the University of Southampton and is funded by a Dunhill Trust Research Fellowship.

2.7 Who has reviewed the study?

The Southampton and South West Hampshire Research Ethics Committee have reviewed this study.

2.8 Contact for Further Information

Ruth Turk, PhD Student, 023 8059 8928, re@soton.ac.uk

Jane Burridge, Professor of Restorative Neuroscience, 023 8059 8885, jhb1@soton.ac.uk

Thank you for considering taking part in this study. You will be given a copy of the information sheet and a signed consent form to keep.

Appendix J – Consent form

Project Title: **Arm movement problems and how they relate to arm function post-stroke**

Ethics Submission No:

Participant ID No:

Principal Investigator: Ruth Turk **Tel: 023 8059 8928**

Please initial box

1. I confirm that I have read and understand the information sheet dated...7/9/09..... (version....5.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the University of Southampton and from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. I agree to a recording of video information for the purposes of assessment, teaching and presentation of results, although my face and other identifying marks will be blurred ☐
5. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Researcher	Date	Signature

1 for participant; 1 for researcher; 1 in medical notes