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THE USE OF MUSCLE MORPHOLOGY AND LOCAL DYNAMIC STABILITY IN THE CLINICAL ASSESSMENT OF TREATMENT OF NON-SPECIFIC CHRONIC LOW BACK PAIN

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1. This work was done wholly or mainly while in candidature for a research degree at this University;
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Signed:  .....

Date: 11th April 2020.....

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What a journey! One that I would have struggled to complete without the unwavering support from colleagues, family and friends.

"The smallest act of kindness is worth more than the grandest intention." - Oscar Wilde.

Firstly, to William and Emilie, my littlest biggest supporters, and possibly the youngest experts in chronic low back pain.

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ABSTRACT

This thesis investigated the use of a series of tests to examine local dynamic stability (LDS) of the trunk, morphology of lumbar multifidus muscle (LMM) and levels of pain and disability in non-specific chronic low back pain (NSCLBP) patients within a clinical setting.

Study one determined the reliability of a test for LDS of the trunk using maximum Lyapunov exponents (λ_{max}), calculated from 3-dimensional acceleration time series collected during a 3-minute kneeling cyclical tap-test. The test was found to be reliable (ICC=0.760) in healthy adults, thus providing evidence that the use of this testing protocol was valid for use in future studies with repeated measures design.

Study two established the reliability of using ultrasound imaging (USI) to measure LMM thickness on separate occasions. USI was shown to have excellent reliability (ICC=0.988) in measuring LMM thickness, thereby providing validity for use in future studies.

Study three examined the outcomes of a series of tests used in a cohort of NSCLBP patients and age matched healthy controls; aimed at assessing LDS of the trunk using a three minute cyclical tap test during single and dual task (motor + cognitive) conditions, LMM thickness, and levels of pain and disability. Differences between groups and relationships between measures were observed at baseline and at 3 months follow-up. Significant differences were found between healthy and NSCLBP groups when comparing LDS during single and dual task conditions. NSCLBP participants prioritised the motor task at greater expense of the cognitive task, whereas healthy participants showed no deficit in either task. No significant associations were found between LDS measures and pain or LMM thickness, although after 3 months and a significant reduction in pain, the NSCLBP group showed behaviour that was analogous to that of the healthy group during dual task conditions. The results of this study show that the series of tests were able to identify differences between healthy and NSCLBP populations and may provide a useful clinical tool in studies evaluating treatment efficacy and effectiveness.

Study four, a case study, explored the feasibility of using the series of tests in a patient receiving spinal cord and medial nerve stimulation – an intervention directly aimed at

reducing pain, rehabilitating LMM and restoring dynamic stability. The study demonstrated the practicability of using the protocol with patients and informed recommendations for a future, larger scale study.

The use of an innovative tap-test to measure LDS of the trunk during single and dual task conditions, in conjunction with LMM morphology, for clinical application in the assessment of NSCLBP patients are the novel aspects of this thesis and contribute new data and interpretations to this area of research.

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Definitions and Abbreviations

ADL	Activities of daily living
ANOVA	Analysis of variance
BMI	Body mass index
CLBP	Chronic low back pain
CSA	Cross-sectional area
CI	Confidence interval
CT	Cognitive task
DFA	Detrended fluctuation analysis
DST	Dynamical systems theory
EMG	Electromyography
FD	Fixed delays
FOA	Focus of attention
GMPT	General motor program theory
GSTT	Guys and St Thomas'
ICC	Intraclass correlation coefficient
ID	Individual delays
IMMPACT	Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials
LBP	Low back pain
LDS	Local dynamic stability
LMM	Lumbar multifidus muscle
LOA	Limits of agreement
LyE	Lyapunov exponent
m	Embedding dimension
MDC	Minimal detectable change

MeSH	Medical subject headings
MLE	Maximum Lyapunov exponent
MNS	Medial nerve stimulation
MRI	Magnetic resonance imaging
MSK	Musculoskeletal
MVC	Maximal voluntary contraction
NHS	National Health Service
NRS	Numerical rating scale
NSCLBP	Non-specific chronic low back pain
ODI	Oswestry disability index
p	Probability value
PGIC	Patient global impression of change
RMSE	Root mean square error
RUSI	Rehabilitative ultrasound imaging
$S(t)$	m-dimensional reconstructed state vector
$s(t)$	One-dimensional Euclidean norm series
SD	Standard deviation
SEM	Standard error of measurement
UCM	Uncontrolled manifold
USI	Ultrasound imaging
VAS	Visual analogue scale
VRS	Verbal rating scale
3D	Three dimensional
α	Significance level
Δ	Change
λ	Lyapunov exponent
τ	Time-delay

λ_{max}	Maximum Lyapunov exponent
λ_{max_DT}	Maximum Lyapunov exponent dual task
λ_{max_S}	Maximum Lyapunov exponent single task

Chapter 1 : Introduction

Low back pain contributes a huge, if not the greatest proportion of worldwide disability (Hoy *et al.*, 2014) and poses a major health problem in western industrialised populations (Chown *et al.*, 2008) with significant socio-economic consequences. Epidemiological research is generally vague due to the multifarious nature of the condition; however it has been estimated that LBP has a lifetime prevalence of up to 84% (Airaksinen *et al.*, 2006) with approximately a quarter of those going on to develop chronic low back pain where pain and disability persist beyond 12 weeks (Andersson, 1999). Furthermore, less than 15% of all low back pain has a specific cause (Airaksinen *et al.*, 2006) signifying that the majority of chronic cases have non-specific chronic low back pain.

Non-specific chronic low back pain is a complex biopsychosocial disorder with multiple manifestations (Airaksinen *et al.*, 2006) and despite extensive research into the disorder long-term prognosis does not appear to have been improved (Foster *et al.*, 2013). Regardless of there being numerous treatment options, success in treating these populations is limited; intervention outcomes have shown only moderate improvement with merely short-term beneficial effects (Balagué *et al.*, 2012). Due to the multifaceted nature of NSCLBP, accomplished treatment and management options for patients with NSCLBP are often obfuscated by the general lack of understanding of the condition.

Kinematic disturbances have been well documented in those with NSCLBP. From a biomechanical standpoint, it has been shown that patients with CLBP demonstrate neuromuscular and morphometric changes in lumbar paraspinal muscles (Le Cara *et al.*, 2014; MacDonald *et al.*, 2009; Wong *et al.*, 2014) which may lead to maladaptive recruitment patterns, distorted proprioception and accelerated muscle fatigue. In a healthy system, the central nervous system is capable of adjusting trunk muscle activation in response to the stability demands of the spine, however the capacity of this adaptive response is challenged in NSCLBP patients where the structural and functional health of structures is inherently suboptimal. In response to diminished motor function and dynamic stability, patients with NSCLBP have been found to require increased cognitive input for the execution of motor tasks (Sherafat *et al.*,

2014). The impaired dynamic spinal stability and loading is frequently identified in those with NSCLBP as a reason for their ongoing pain (Deckers *et al.*, 2015), yet the basis for such clinical labels is most likely unsubstantiated, with no specific diagnostic test able to objectively measure trunk stability.

In recent years there has been an increase in the use of a non-linear or dynamical systems theoretical approach to study motor behaviour; involving the analysis of kinematic data to evaluate the ability and robustness of the system to react against internal perturbations and maintain controlled movement over a sustained period of time (Dingwell *et al.*, 2000; Lee and Granata, 2008; Santuz *et al.*, 2018; Tanaka and Ross, 2009). Maximal Lyapunov exponents in particular have been shown to a be a reliable and valid way to compare local dynamic stability in patient groups compared to healthy controls (Arampatzis *et al.*, 2017; Asgari *et al.*, 2015, 2017), yet the utility of such methods has on the whole been through motion capture in laboratory settings thus limiting their clinical applicability.

Active rehabilitation programmes to improve pain and function in NSCLBP are commonplace, yet besides subjective assessment of range of movement and levels of pain and disability, there is no robust method to quantify change. In the context of physical interventions, it is the neuro-musculoskeletal capacity of an individual that is of interest within the clinical setting and the assessment of their stability under given conditions, in particular those that mimic real-life scenarios. Clinical tools to measure these parameters would not only augment existing diagnostic approaches, but also provide individualised performance indicators for prognosis and progression. Furthermore, such measures would facilitate the determination of treatment suitability as well as enabling the appraisal of effectiveness and efficacy of treatment interventions.

There is minimal evidence in the literature as to whether differences in local dynamic stability of the trunk exist between healthy people and those with NSCLBP, or whether this form of assessment would enhance clinical knowledge. This thesis aims to explore this gap in current knowledge, whilst acknowledging and addressing some of the current methodological challenges of reliably and validly measuring dynamic local stability of the trunk using kinematic data. Its overall purpose is to explore the use of an innovative and clinically useful method of measuring functional stability in patients

with NSCLBP as an adjunct to existing measures in order to potentially provide an objective means to measure effectiveness of interventions and patient progression.

Chapter 2 : Literature Review

The purpose of this literature review was to gain an understanding of the existing research in the field of neuromuscular control in non-specific chronic low back pain, and to enable development of relevant research questions based on this foundation of knowledge.

2.1 Literature search strategy

A broad range of literature was examined from an array of sources, including peer reviewed journal papers, conference proceedings and grey literature (unpublished theses).

Relevant search terms, including MeSH terms where appropriate, were entered into public databases (PubMed, Cochrane library, Web of Science, Scopus, CINAHL, AMED, PEDro and Google Scholar).

All retrieved articles were further searched by hand to identify other relevant literature.

The literature search was broadly divided into the following areas:

- Epidemiology and classification of NSCLBP
- Instability and motor control impairment in NSCLBP
- Measurement of spinal muscle morphology and functional dynamic stability

2.2 Chronic low back pain: An overview

2.2.1 CLBP: The scale of the problem

Low back pain (LBP) remains a condition of high prevalence (Koes *et al.*, 2010) and is a major health problem in western industrialised populations (Chown *et al.*, 2008). It is a common symptom thought to affect 70-85% of the population at some stage of their life (Andersson, 1999; Hong *et al.*, 2013). Furthermore, it accounts for an estimated 5 million General Practitioner consultations and 1.6 million hospital outpatient appointments in Britain each year (Chown *et al.*, 2008), and costs the NHS in excess of £1000 million per annum (NICE, 2009).

When LBP persists for longer than 3 months it is classified as chronic low back pain (CLBP). CLBP is thought to be prevalent in 23% of the population (Andersson *et al.*, 1993), having significant impact on peoples' lives, and resulting in considerable personal and public sector financial consequences (Rubinstein *et al.*, 2011). A major economic problem is posed due to the frequent use of health services and absence from work associated with CLBP (Ibrahim *et al.*, 2008). In 2011, the cost of chronic back pain to the economy was reported at being around £12.3 billion per year (Bridges, 2011). In addition, estimated lost production as a result of low back pain exceeded £3500 million per year (Maniadakis and Gray, 2000).

Disability from CLBP has been described as a 21st century epidemic (Kirk *et al.*, 2005) with the Global Burden of Disease study in 2010 reporting it as the leading cause of years lived with disability (Hoy *et al.*, 2014). Moreover, people with CLBP are more likely to experience negative outcomes, including depression, job loss, reduced quality of life, functional impairment and limited daily activities (Breivik *et al.*, 2006; Donaldson, 2009). People with CLBP lasting for more than a year are unlikely to return to their normal activities (Hong *et al.*, 2013), and according to Carter and Birrell (2000), those who have been off work with CLBP for 1-2 years are unlikely to return to any form of work in the foreseeable future, whatever form of treatment they receive.

The use of interventions, including surgery, pharmacological, and non-pharmacological approaches, for treating CLBP increased from 1995 to 2010 (Deyo *et*

al., 2014). However, despite increased utilisation of treatment interventions, the prevalence of CLBP symptoms and expenditures continues to rise (Deyo *et al.*, 2009).

2.2.2 Non-specific chronic low back pain

CLBP is deemed to be a multi-factorial problem rather than a diagnosis, with varying degrees of pain, disability and chronicity. The condition is termed 'non-specific' when the pain cannot be attributed to any specific pathological cause, for example inflammation, fracture, osteoporosis, malignancy, disc pathology or structural deformity (Balagué *et al.*, 2012) and a definitive diagnosis cannot be attained through radiological investigation. It is actually estimated that less than 15% of all back pain is due to specific causes (Airaksinen *et al.*, 2006).

In recent years there has been migration away from the notion that chronic pain is simply a continuation of an acute pain episode. It is more widely accepted that the concept of chronic pain is multidimensionally complex and involves other previously overlooked mechanisms such as neurophysiology, genetic expression and chemical release. Furthermore, there is clear evidence now that perception and circumstance can alter the way that pain is experienced.

Despite a plethora of research in the field, there has been little change to the long-term prognosis of NSCLBP (Foster *et al.*, 2013). Historically, treatment has been targeted at signs and symptoms (Dankaerts and O'Sullivan, 2011) where it is now believed that treatment addressing the underlying cause may be clinically more effective (Zimny, 2004). More recent approaches in treating NSCLBP involve multidisciplinary treatment modalities addressing various elements of the biopsychosocial model of back pain. For example, in addition to the use of pharmacological agents and physiotherapy, psychotherapeutic approaches may also be utilised, such as cognitive behavioural therapy and counselling. However, this style of management does not suit everyone and there remains a need for better identification of contributory mechanisms to pain and disability. The development and validation of such clinical tools will not only allow for advancement of available interventions but will stratify care by identifying which patients may best respond to specific protocols.

2.2.3 Models of chronic low back pain

The rise in the prevalence of NSCLBP, together with the spiralling associated costs has forced a review of the way this condition is regarded. There has been a shift away from the medicalisation of LBP towards a more holistic viewpoint; with consideration given to the role of psychological, social, occupational and lifestyle influences in chronic pain (Deyo *et al.*, 2009). The paradigm shift from the patho-anatomical model of back pain where physical or structural anomalies were sought to explain the source of pain started to take place when Waddell (1987) first proposed the biopsychosocial model of back pain. The diagram in Figure 1 illustrates how each domain of the biopsychosocial model can individually, or through interaction with other dimensions contribute to chronic pain.

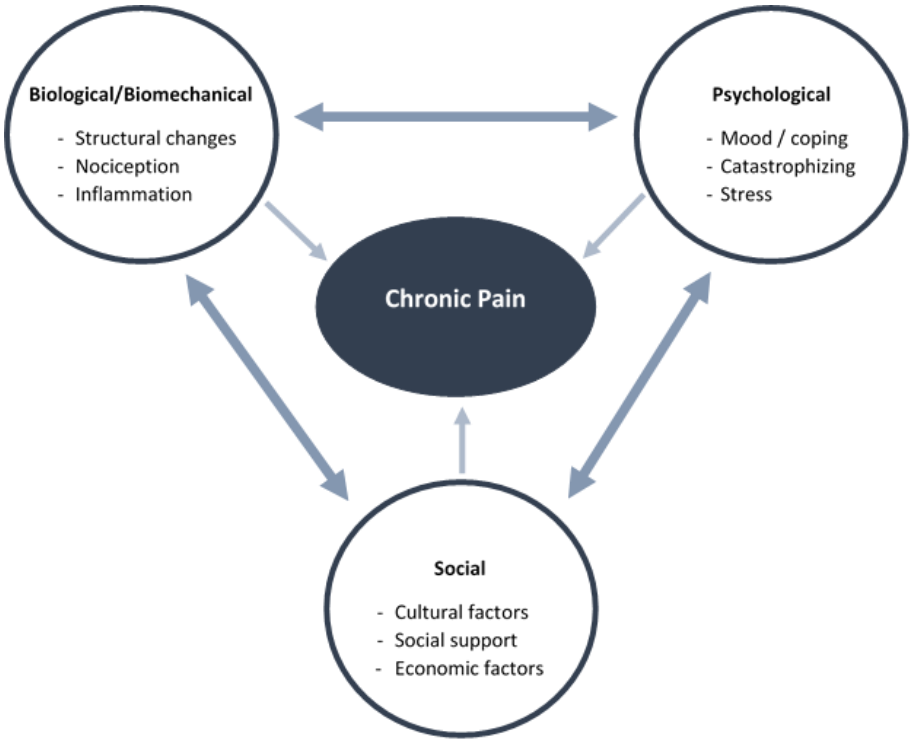


Figure 1: Diagram of the biopsychosocial model of chronic pain

Whilst the benefit of evaluating all aspects of this conceptual model in the management of NSCLBP should not be underestimated, O'Sullivan (2005) claimed that there may be

a tendency to wholly attribute NSCLBP to psychosocial factors in the absence of any known biological or biomechanical reasons.

Although NSCLBP is a complex and multifactorial process, it is well supported that the deconditioning of the lumbar paraspinal muscles can be an important risk factor for LBP (Beneck and Kulig, 2012; Steele *et al.*, 2015). Further models pertaining to the more biomechanical dimension have been proposed; such as the signs and symptoms model (Abbott *et al.*, 2009), the mechanical loading model (Kopec *et al.*, 2004) and the motor control model (Dankaerts *et al.*, 2007), all of which relate to the ongoing abnormal tissue loading, manifesting due to motor control impairments. There is a large body of evidence that demonstrates that the lumbar paraspinal muscles operate suboptimally in patients with low back pain (Fryer *et al.*, 2004). Previous research has found that patients with CLBP have demonstrated neuromuscular, morphometric, or histologic changes in paraspinal muscles (Le Cara *et al.*, 2014; MacDonald *et al.*, 2009; Roy *et al.*, 1989; Wong *et al.*, 2014). Evidence suggests that there is a change in muscle function associated with low back pain, such as reduced strength (Cassisi *et al.*, 1993; Lee *et al.*, 1995), increased muscular fatigability (Mannion *et al.*, 2001; Roy *et al.*, 1989), reduction in dynamic movements (Mannion *et al.*, 2001; Sihvonen *et al.*, 1991), as well as muscle architecture, such as cross-sectional area (Flicker *et al.*, 1993; Lee *et al.*, 2006b) and stiffness within the muscle fibres (Brown *et al.*, 2011; Solomonow *et al.*, 2003). Many studies have provided evidence to suggest that persistent motor control impairment can contribute to CLBP (Hodges and Richardson, 1996; Radebold *et al.*, 2000; Sihvonen *et al.*, 1997). Although the mechanisms behind the ineffectual motor control are not entirely clear, the self-perpetuating reflex inhibition as part of a cyclical mechanism for ongoing pain has been implied as one hypothesis (Panjabi, 2006). Pain within a joint is detected by mechanoreceptors or nociceptors, and afferent discharge is reduced through reflex inhibition (Hopkins and Ingersoll, 2000). A situation of decreased spinal stability becomes established due to the diminished neural drive to the muscles that stabilise the spinal joints, which in turn leads to reflex inhibition – the cycle continues.

There is no doubt that these changes, both structural and functional, along with accompanying pain will impact the other subsystems of the biopsychosocial concept. Indeed, in some cases it may be a chicken-and-egg scenario – pain causing stress, maybe depression and disability impacting the ability to work, or possibly a change in

work scenario or an episode of depression or bereavement may lead to changes in movement patterns which, over time lead to biomechanical alterations. Whilst it would be extremely short sighted to only consider one dimension of the model when assessing a patient, it may be contended that further understanding of where a potentially maintaining issue may exist could accelerate rehabilitation through access to the correct treatment intervention.

Extensive study in the field is ongoing; however, CLBP remains a condition that is relatively poorly understood. The observation made by Hirsch and Schajowicz over 60 years ago in 1952, that in spite of careful clinical examination, no pathologic changes can be found in the great majority of those seeking treatment for pains in the back, still resonates today. As a consequence, there has been a shift towards the consideration of functional issues, with many studies investigating the involvement of altered movement patterns, motor control impairment and dynamic stability as potential underlying problems.

2.2.4 Measuring pain & disability

The need to measure and quantify pain has potentially evolved from the necessity to prove efficacy of interventional protocols. This has seen the common use of pain measuring scales such as the McGill pain questionnaire (Melzack, 1975), the numerical rating scale of pain or the visual analogue scale (Hayes and Patterson, 1921). However, these measures are highly subjective as well as being very timepoint-specific - how an individual perceives their pain at that point in time. The reported pain score may also be influenced by a multitude factors - by their environment (for example, lack of sleep or stress at work) along with other potential side-effects of pain such as impairment in attention control, working memory and mental flexibility, depression, anxiety and fear. It is thought that using pain questionnaires in conjunction with other quality of life measures, such as the Oswestry Disability Index (Fairbanks *et al.*, 1980) helps to give a more rounded indication of the impact of pain on a person's life.

The lack of robust objective measures of disability due to pain has meant that pain and disability questionnaires are still extensively used both clinically and for research,

despite their questionable reliability. Typical clinical assessment may evaluate range of movement, however there is poor correlation between this and pain, and it is not necessarily indicative of any underlying dysfunction. Clinical gauges of movement ability and stability of movement are limited, and there remains a demand for such clinical tools.

2.3 The concept of instability in NSCLBP

Spinal instability has been subject to much debate over the decades, with ambiguity still surrounding its definition and clinical relevance. The evolution of concepts and improved understanding of spine function and back pain over the years has highlighted the importance of furthering our knowledge of spinal stability and its potential contribution to LBP. However, the complexity and multi-faceted elements of the spine makes study of spinal function and stability *in vivo* challenging.

According to Encyclopaedia Britannica (2016), the mathematical definition of stability is "the condition in which a slight disturbance in a system does not produce too disrupting an effect on that system". The clinical application of this definition, or variations thereof, has led to a widespread belief that a loss of normal pattern of spinal motion, or spinal instability, can cause pain and/or neurologic dysfunction (Panjabi, 2003). Indeed, back pain patients are often diagnosed with spine instability in the absence of any other identified pathology, even though there may have been no diagnostic tests performed that were specific to stability.

Instability may be presented in different forms:

- spinal instability due to structural pathological changes in anatomical structures, as in spondylolisthesis or degenerative disc disease (Knutsson, 1944) for example. This would cause overt instability of the spine, with excessive movement of certain vertebra that is identifiable by radiology (Friberg, 1987) and resulting in pain, deformity and potentially neurological deficits. This type of instability would generally require surgical intervention to fixate and stabilise the area.

- trunk instability during movement of the trunk as a whole rather than individual vertebral segments of the spine. This type of instability, in which excessive motion cannot be grossly demonstrated may be described as covert or micro instability (Pakzaban and Kopell, 2018). This functional instability tends to be diagnosed based on clinical findings; it is not so easily identifiable, with no obvious structural change to be seen or fixed.

The central nervous system is capable of adjusting trunk muscle activation in response to the stability demands of the spine, with both neural and mechanical coupling preventing erroneous motor control from producing segmental instability (Reeves *et al.*, 2019). However, in cases of injury or long-standing established pain, the neural and mechanical control may be altered and/or problematic.

Trunk stability would not exist without intersegmental stability, yet it is quite feasible to have a stable spine whilst exhibiting dynamic trunk instability. This type of functional dynamic instability could be due to mechanical and/or neural alterations and requires further contemplation. Furthermore, the evaluation of this type of stability *in vivo* is limited and requires development if we are to further understand the concept of dynamic instability in NSCLBP.

2.3.1 Spinal Stability

Mechanical stability of the spine is essential for it to perform basic biomechanical functions: allowing movements between body part, carrying loads and protecting the spinal cord and nerve roots (White and Panjabi, 1990). The spine as an osteoligamentous system is however inherently unstable and the spine in motion requires adequate neuromuscular coordination in order to maintain control stability (Cholewicki *et al.*, 2005; Radebold *et al.*, 2000; Reeves *et al.*, 2019).

Panjabi (1992) proposed a three-subsystem model to represent the spinal stabilising system and his conceptual model has continued to be adopted throughout the literature decades later. The three elements he describes are: the passive subsystem comprising the spine column - including bone, ligaments, facet joints, fascia and discs; the active subsystem consisting of the muscles surrounding the spine; and the neural

control subsystem which invokes control from the neural centres in response to musculotendinous feedback. Furthermore, he clarified that the passive system provides intrinsic stability, the active subsystem is responsible for dynamic stability and the neural subsystem evaluates and determines the requirements for stability and coordinates the necessary muscle response. These subsystems are represented schematically below (Figure 2) and illustrate that whilst each system is conceptually separate, they are functionally interdependent (Panjabi, 1992).

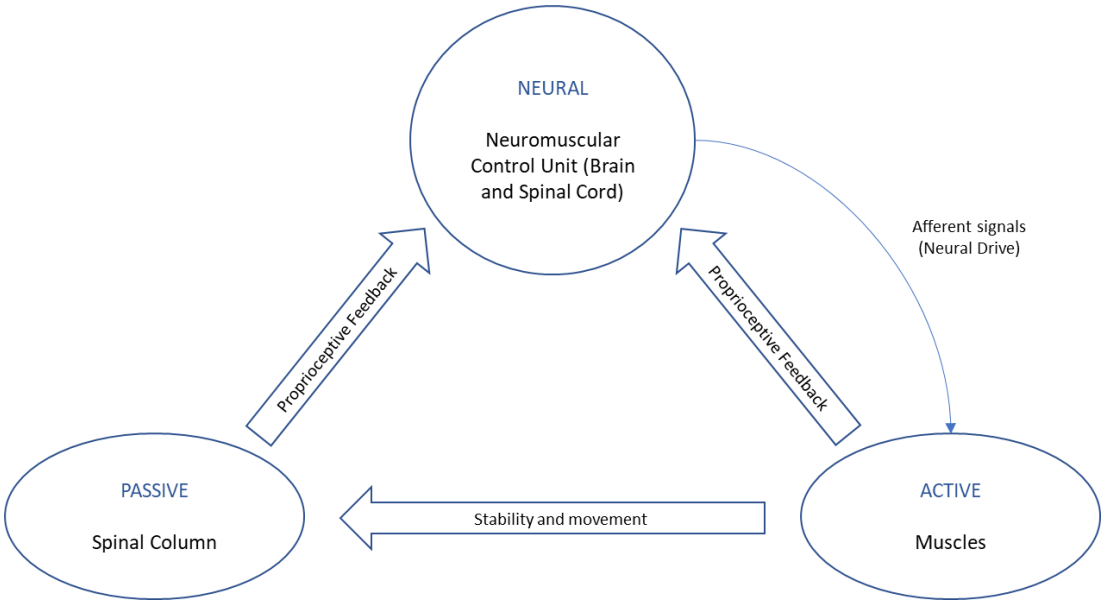


Figure 2: Model of the spinal stabilising system (Russo *et al.*, 2018)

The spine alone, despite the stabilising influence from passive structures such as discs and ligaments, has insufficient stiffness to counteract body mass (Crisco *et al.*, 1992; Reeves *et al.*, 2019). Therefore, static stability relies largely on the activation of paraspinal muscles to stabilise the spine. Empirical evidence suggests that a nominal level of paraspinal muscle activation is required to provide the stiffness necessary to support the upper body in the neutral unloaded spine (~ 2% maximal voluntary contraction; Cholewicki *et al.*, 1997).

The transverse abdominus and multifidus muscles are the most influential muscles in providing spinal stability and have been described as variable-stiffness springs, with

the level of stiffness increasing with activation due to the increased number of activated cross-bridges (Lee *et al.*, 2006a; Ma and Zahalak, 1985). Multifidus provides segmental stiffness and controls motion, and this muscle is solely responsible for around two thirds of spinal stiffness (Wilke *et al.*, 1995).

Dynamic stability is essential in maintaining equilibrium despite the presence of kinematic disturbances. The health of both the passive and active subsystems clearly affects spinal stability in motion, however the neural subsystem is principally responsible for effecting muscle control in this domain. Various sensorimotor pathways are necessary to ensure stable spine behaviour. In a study conducted by Moorhouse and Granata (2007) where the force response to position disturbance was measured in 11 healthy adults, they quantified the intrinsic and reflex responses by nonlinear systems-identification procedures. Analysis revealed a negative proportional intrinsic response that indicated that the intrinsic muscle stiffness was not sufficient to stabilise the spine without reflex response. They found that reflexes accounted for 42% of the total stabilising trunk stiffness, and both the intrinsic and reflex components significantly increased with trunk effort. They concluded that reflex dynamics are a necessary component in the control of spinal stability.

In summary, trunk stability is largely dependent on the combined behaviour of the active intrinsic muscle stiffness and the reflex response (Lee *et al.*, 2006a). These muscle reflex responses may include preparatory control in advance of predictable spine perturbations along with varying magnitude and timing of muscle activity (Stokes *et al.*, 2000; van Dieën *et al.*, 2003b, 2003a). Problems arise when unexpected perturbations occur and response rate is lacking, or when load exceeds the capabilities of the system. If neural control is not adequately regulated, then trunk instability can occur.

2.3.2 Dysfunction & Adaptation of the Spinal Stabilising System

Harmonious coordination of the neural, active and passive subsystems allows for optimised spinal stability within normal physiological ranges of movement and under

normal spinal loads (Panjabi, 1992). However, when there is disruption of any one of these subsystems then stability can be compromised.

Deficiencies within a subsystem may originate from trauma, age-related degeneration, muscle insufficiency or a combination of all these factors. Dysfunction may occur suddenly or develop gradually, and the neural subsystem must respond appropriately to ensure there is adequate active compensation to maintain or re-establish stability. The consequence of this shift and potential imbalance within the subsystem triad may be further injury, accelerated degeneration, muscle spasm and fatigue, and over time this may result in chronic dysfunction and pain (Panjabi, 1992).

In a healthy system, Panjabi (1992) suggested that there may be a functional reserve that can be called on to enhance spinal stability, for example in complex or excessive movements or in circumstances of increased load. The capacity of this adaptive response is largely dependent on the structural and functional health of structures within the system, for instance muscle size and strength, as well as other influencing factors, such as pain or cognition.

2.3.2.1 Pain and motor control

The literature suggests there is ambiguity surrounding the relationship between pain and motor control (Dankaerts and O'Sullivan, 2011; Hodges and Moseley, 2003). Studies to date have been unable to decipher whether suboptimal motor control strategies provoke pain, or inversely it is pain that impedes the adaptive changes in motor control; these antithetical hypotheses remain unproven.

Panjabi (1992) described a model of how motor control of the spine is achieved through the complex interaction of the active, passive and neural control systems, where dysfunction in any one system may lead to compensation by another subsystem (normal functional response). An adaptive response in another subsystem longer term (altered spinal stability) or a potential injury, may cause system dysfunction. For example, muscles exerting suboptimal stabilising forces on the spinal column will cause overload of the spinal joints and pain. The nociceptive pain signals result in

altered neural drive, affecting muscular function. The established negative feedback loop (Figure 3) may result in continual instability and pain.

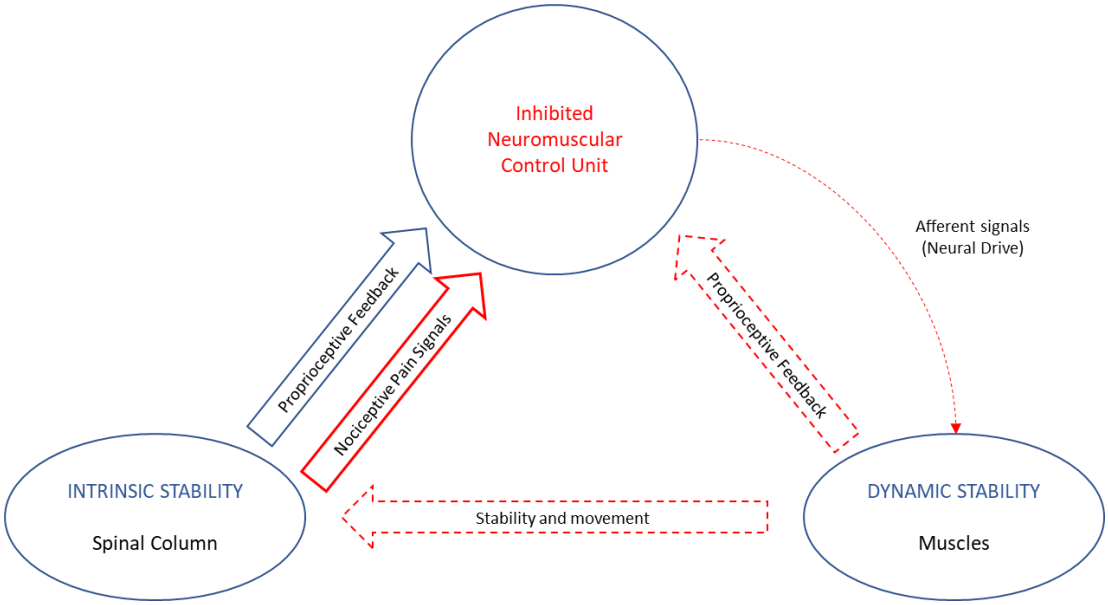


Figure 3: Negative feedback loop of neuromuscular control in response to pain (Russo *et al.*, 2018)

There appears no doubt that pain results in movement changes; however, how the trunk muscles respond to pain is highly variable (Hodges *et al.*, 2013). For example, in a study conducted by Hodges *et al.* (2013), EMG was used to analyse spinal stability and net trunk activity in healthy individuals performing a flexion-extension task whilst pain-free and whilst experiencing experimentally induced pain. Mechanical stability of the spine was quantified by the Stability Index based on the use of EMG data in a spinal stability model proposed by Cholewicki and McGill (1996). They found that the Stability Index and net muscle activity both increased in pain, although pattern of adaptation in muscle activity varied between subjects. This individual-specific response to acute pain is likely to provide spinal protection in the short-term but could have long-term consequences for spinal health. Previous studies have also reported similar findings (Moseley *et al.*, 2004; Moseley and Hodges, 2006).

It has been postulated that individuals who have previously experienced LBP may develop compensatory or adapted movements to avoid pain provocation (Hodges and Moseley, 2003; van Dieën *et al.*, 2003a), which may, over time, lead to maladaptation

and subsequent episodes of pain, or chronic pain. This was observed in subjects who demonstrated a reduction in postural strategy variability in response to pain, but failed to return to normal movement patterns following cessation of pain (Moseley and Hodges, 2006). Protective postural strategies have also been noted in individuals who have an expectation of pain (Moseley *et al.*, 2004).

Proprioception, balance and sensory impairments have been shown to be factors in CLBP (Hodges and Moseley, 2003; Silfies *et al.*, 2005). Reduced sensory input to the spine may result in reduced motion acuity (Gill and Callaghan, 1998) as well as slower psychomotor reaction times (Luoto *et al.*, 1995; Taimela *et al.*, 1993) in CLBP populations. In addition, it is thought that cortical effects such as changes in the central nervous system as a result of stress or fear may contribute to motor control impairments in the presence of pain (Hodges and Moseley, 2003).

2.3.2.2 Cerebral, cognitive & behavioural factors and motor control

There is growing opinion that cognitive factors play an important role in the development and maintenance of the chronic pain state (Apkarian *et al.*, 2009; Tracey and Bushnell, 2009). Various studies have identified structural, functional and neurochemical changes within the brains of people with chronic musculoskeletal pain, which are thought to contribute to the multifaceted psychological manifestations of CLBP.

There is extensive evidence that grey matter volume is significantly reduced in the brains of people with CLBP compared with healthy controls (Apkarian *et al.*, 2004; Buckalew *et al.*, 2008; Schmidt-Wilcke *et al.*, 2006). The magnitude of this decrease is thought to be related to pain duration (Apkarian *et al.*, 2004), and the regional reduction in neuron-matter has been linked to sensory and affective dimensions of pain (Apkarian *et al.*, 2004) as well as pain intensity and unpleasantness (Schmidt-Wilcke *et al.*, 2006).

Chronic pain has also been documented to accompany cortical reorganization (Flor *et al.*, 1997; Wand *et al.*, 2011). More extensive patterns of neuronal activation in pain-related cortical areas was seen in those with CLBP on the introduction of noxious

stimuli (Kobayashi *et al.*, 2009), which supports the occurrence of amplified central pain processing in patients with NSCLBP (Giesecke *et al.*, 2004). In addition, raised motor thresholds have been reported for the lumbar spinal muscles of CLBP patients (Strutton *et al.*, 2005). Evidence suggests there is reorganisation of trunk muscle representation at the motor cortex in individuals with CLBP, and this reorganisation may be associated with deficits in postural control (Tsao *et al.*, 2008).

Neurochemical profiling in CLBP patients has revealed significant changes in markers in the dorsolateral prefrontal cortex, thalamus and orbitofrontal cortex (Wand *et al.*, 2011). The magnitude of such changes seems to positively correlate with the duration and intensity of pain (Grachev *et al.*, 2000), anxiety (Grachev *et al.*, 2002) and depression (Grachev *et al.*, 2003). The observed shifts in neurochemistry are consistent with the established 'pain matrix' along with the exaggerated and ongoing neural activity seen in those with CLBP, suggesting that these neurochemical changes occur as a result of CLBP rather than vice versa (Wand *et al.*, 2011).

Within the context of the biopsychosocial model of LBP, cerebral changes observed in those with CLBP may have a wide-ranging effect. For example, there may be direct influence on the control of muscle activity and tension which may in turn alter spinal loading and initiate subsequent physiological changes in other spinal structures (Bergenudd and Johnell, 1991). Moreover, they may encourage the manifestation of psychological factors which directly influence cognition and behaviour; these include kinesiophobia and fear avoidance (Leeuw *et al.*, 2007), depression (Henschke *et al.*, 2008), catastrophising (Smeets *et al.*, 2006) and perception of illness (Foster *et al.*, 2008). These factors often result in the patient adopting altered movement patterns in attempts to avoid triggering pain, or in belief that less movement will prevent aggravation of the condition. The relationship between kinesiophobia and the mediated effects of pain catastrophising and functional disability is yet to be fully understood (Leeuw *et al.*, 2007). However, the maladaptive movement strategies are believed to be a key contributory factor to motor control dysfunction and chronic pain development and maintenance.

CLBP patients with motor control or movement impairment who show high levels of fear avoidance, paradoxically often adopt postures and movement strategies that actually promote increased pain (Dankaerts *et al.*, 2006), and furthermore, commonly

demonstrate a lack of awareness of assuming pain provocative postures (Burnett *et al.*, 2004). It has been proposed that proprioceptive deficits and an absence of the withdrawal reflex motor response (initiated in the presence of chronic pain) may be responsible for the development of these maladjusted postural strategies (Burnett *et al.*, 2004; O'Sullivan *et al.*, 2003), however this hypothesis is so far unsubstantiated.

In a similar way that a certain amount of cognitive resources for movement coordination or control are required in older adults (Loewenstein and Acevedo, 2010), patients with NSCLBP have been demonstrated to employ elements of cognitive control in the execution of motor tasks. Whilst the proprioceptive sensorimotor disturbances play a key role in motor control, the contribution of psychosocial factors in the performance of movement tasks should not be underestimated.

2.3.2.3 Changes in muscle morphology and motor control

Structural and functional changes in paraspinal muscles in people with CLBP have been well documented, but whether these changes are causes or consequences of low back pain remains unknown (Demoulin *et al.*, 2007). Furthermore, if muscular changes are not reversed swiftly, self-sustained motor control impairment can ensue. The patient's inability to effectively recruit the altered muscle can lead to atrophy, maladaptive recruitment patterns, distorted proprioception and accelerated muscle fatigue resulting in impaired dynamic spinal stability and loading (Deckers *et al.*, 2015). A cyclical mechanism of ongoing LBP becomes established.

The decrease in cross-sectional area of the paraspinal muscles has been repeatedly reported in patients with CLBP (Danneels *et al.*, 2000). The results of a systematic review conducted by Fortin and Macedo (2013) suggest that multifidus and paraspinal muscle groups are significantly smaller in patients with chronic LBP than in control patients who are healthy, and on the symptomatic side of patients with chronic unilateral LBP compared with the asymptomatic side. The cross sectional area of paraspinal muscles has also been associated to some degree with the muscle's capacity to generate force; any muscle force imbalance may lead to kinetic instability of the spine (Wan *et al.*, 2015).

Another morphological change associated with back pain is increased fat deposition. Through MRI assessment, intramuscular fatty infiltration has been reported in the paraspinal muscles of those with LBP (D'hooge *et al.*, 2012). Wan *et al.* (2015) reported that the reduction of the muscle cross sectional area and increased fatty infiltration occurred synchronously, and the extent of change is significantly greater in CLBP in the erector spinae muscles. Additionally, paraspinal muscle fatigability is increased in patients with LBP (Roy *et al.*, 1989). It is possible that this is due to the reduction of Type 1 (slow-twitch) fibres, as conversion of Type I fibres to Type II fibres is frequently seen in patients with CLBP (Demoulin *et al.*, 2007).

The stabilising function of trunk musculature is crucial in maintaining mechanical stability of the lumbar spine, especially around the neutral posture where the spine exhibits least stiffness (Cholewicki *et al.*, 1997). Therefore, any muscular dysfunction could be a critical element in dynamic instability of the spine, and thus motor control errors, movement impairment and continuing LBP.

2.3.3 Section summary

Lumbar spine stability relies on the health and harmonious interplay of the spine, ligaments, surrounding musculature and neural control system. Dysfunction within any of these structures, or disruption of neural feedback may result in clinical instability; which leads to increased loading of spinal joints and tissues of the trunk and ultimately pain. Reduced spinal stability is frequently diagnosed in patients with NSCLBP based on symptoms alone where there remains a lack of objective measure with which to formulate or quantify this diagnosis. In the absence of skeletal anomalies, the examination of trunk muscle morphology and neuromotor control in relation to spinal stability would enhance clinical diagnosis and facilitate appropriate treatment and management in NSCLBP.

2.4 Methodological approaches to assessing spinal muscle morphology

Spinal musculature may be viewed and measured using various types of imaging: magnetic resonance imaging (MRI), x-ray computerised tomography (CT) and ultrasound imaging (USI). Due to its accessibility, USI will be the focus of this review.

2.4.1 The use of USI in morphological assessment of muscle

The use of USI has increased significantly over the past 70 years or so, allowing for more widespread medical applications, including its diagnostic utilisation in morphological evaluation (Szabó, 2004). A key benefit of diagnostic ultrasound is that there are no absolute or relative contraindications, or any known adverse effects of the procedure. Whilst considered inferior to alternate gold-standard imaging techniques such as MRI and CT, USI has nonetheless become a valuable tool in the assessment of soft tissue, including muscle morphology.

The development of ultrasound imaging has seen its use extend beyond that of purely structural assessment to the evaluation of function, primarily focusing on the level and timing of muscle activation (Hodges, 2005). In 2006, at a symposium held in Texas, USA, the term 'rehabilitative ultrasound imaging' (RUSI) emerged. RUSI is used in relation to the procedure of evaluating 'muscle and related soft tissue morphology and function during exercise and physical tasks' (Teyhen, 2006).

Furthermore, many researchers are actively using USI in the assessment of lumbar multifidus muscles (LMM) following the observations of functional deficits and morphological changes of trunk musculature in individuals with low back pain (Hebert *et al.*, 2009). USI has been used to assess linear muscle thickness and cross-sectional area of LMM (Stokes *et al.*, 2005) , as well as thickness change in resting to contraction conditions (Kiesel *et al.*, 2007), and measurements have been used to make inferences regarding muscle activity and strength.

It has been demonstrated that USI is a non-invasive and safe clinical tool with which muscle morphology may be evaluated. The validity of USI is uncontested, but the high-level of operator-dependent accuracy associated this method may question the reliability of USI. Numerous studies have examined various aspects of USI reliability in relation to the assessment of LMM, including between-day measures (Pressler *et al.*, 2006), operator experience (Wallwork *et al.*, 2007; Wong *et al.*, 2013) and subject and transducer positioning (Coldron *et al.*, 2003; Larivière *et al.*, 2013).

2.4.2 USI principles and methodology

Ultrasound is capable of mapping both superficial and deep layers of tissue. Ultrasound waves are reflected differently by various tissue components according to their water content. Bone appears black or anechoic on ultrasound, with a bright hyperechoic rim. Muscles are hypoechoic with striate structure; fascia and other connective tissue strands and fascicles appear as hyperechoic lines. Fat is almost anechoic.

Spatial resolution is dependent on wavelength, and since the wavelength is shorter at higher frequencies, the obtainable resolution increases proportionally to the frequency. Ultrasound transducers of higher frequencies produce images of greater clarity but less depth. A low frequency transducer would be necessary for data acquisition of deeper structures.

A linear array transducer of 7.5MHz or above has the ability to produce high clarity images but is best suited to the imaging of more superficial structures. This type of transducer produces a parallel scan which, whilst limiting the width of the image to the footprint length of the probe, does minimise any distortion of image proportions, thus having the added advantage of making distance measurements more accurate.

A curvilinear transducer, with operating frequency 3.5 – 5MHz, provides a broader view and greater depth. It is therefore beneficial to use this type of transducer to image deeper structures, or when it is necessary to identify several reference points outside the scope of a linear probe. However, the size of the image produced is not a true reflection of reality. It is therefore important to consider that the only accurate

position to measure depth with a curvilinear transducer is with a vertical line drawn directly through the centre of the image.

In addition to the correct transducer type, accuracy is dependent on the angle at which the probe is applied to the skin. A close to perpendicular angle of incidence is important in both image clarity and true distance measurement. Stokes *et al.* (2005) claim that more of the sound beams are perpendicular to the muscle-fascia interface with the use of a convex transducer, making it preferable to a linear one. However, this would only be applicable if examining the width of LMM or for cross-sectional area (CSA) analysis, where the lateral borders of the muscle must be identified.

Many studies have used USI to evaluate LMM, yet there has been lack of consistency between studies with the type of transducer used. According to Worsley *et al.* (2012) measurements of LMM width, thickness and CSA made using linear and curvilinear transducers are not significantly different. This is supported by the work of Warner *et al.* (2008) who reported mean differences between linear and curvilinear transducers of 0.02cm (SD = 0.04cm) for thickness and -0.09 to 0.1cm (SD = 0.03cm) for width.

Selection of transducer is largely dependent on the depth of LMM according to the thickness of subcutaneous tissue lying superiorly. A linear probe will provide a higher clarity image allowing the most accurate measurement of thickness, but if greater depth is required, a curvilinear probe may be used, taking care to make measurements from the centre point of the transducer.

2.4.3 USI compared to gold-standard methods

Magnetic resonance imaging (MRI) is considered the gold-standard in musculoskeletal imaging and produces the most accurate means by which muscle size can be measured. Studies that have compared muscle thickness measurements using ultrasound imaging and MRI have found good agreement between the two methods, suggesting that real-time ultrasonography is a valid measure of muscle thickness (Dupont *et al.*, 2001; Hides *et al.*, 2006, 1995).

Dupont *et al.* (2001) studied both porcine muscles and shoulder musculature from human subjects. They measured muscle thicknesses using MRI and ultrasound and found correlation coefficients for measurements to be high (≥ 0.96) and furthermore, repeated sonographic measurements had a low coefficient of variation (≤ 3.1). They concluded that real-time sonography can accurately measure muscle thickness. Their findings were similar to those found in other studies (Hides *et al.*, 2006, 1995).

A study conducted by Hides *et al.* (1995) specifically studied the lumbar multifidus muscle and found that no significant difference was found between cross-sectional area measurements made with ultrasound and MRI. Conversely, Belavý *et al.* (2015) found that whilst ultrasound measures of cross-sectional area of lumbar multifidus 'agreed' with equivalent MRI measure, the correlation between the two measures was poor to moderate. All studies used relatively young, healthy participants, and most had small sample sizes. This potentially reduces the generalisability of the findings, however there is no specific evidence to suggest that ultrasound as a measure of muscle morphology is population- or condition-specific (Belavý *et al.*, 2015)

LMM is a reportedly difficult muscle to image using ultrasound, with the lateral borders lying adjacent to longissimus being difficult to depict (Stokes *et al.*, 2005). Calculation of CSA may therefore involve a level of subjectivity. LMM thickness is easier to delineate; measuring between the hyperechoic bony landmark of the facet joint and the clear fascial line. It has been documented that linear thickness measurements and CSA in LMM are highly correlated (Hides *et al.*, 1995; Stokes *et al.*, 2005). This cannot be assumed in all situations however, as the correlation weakens when the muscle becomes atrophied (Hides *et al.*, 1995). Nevertheless, a linear thickness measurement, when used in a longitudinal study may provide sufficient information on muscle health and size.

The evidence, and general consensus, suggests that as long as a strict protocol for ultrasound imaging is adhered to, real-time ultrasound is a valid and accurate method of measuring muscle thickness.

2.4.4 USI to measure muscle activity and strength

Measurement of muscle size provides diagnostic indicators of muscular atrophy and hypertrophy. Of additional interest is the fact that muscle size is believed to be closely correlated with the force generating capacity of a muscle (Maughan *et al.*, 1983; Rankin and Stokes, 1998). In addition, it has been claimed that clinically, RUSI may be used to quantify muscle thickness in resting and contracted states, and used as an indirect measure of muscle activation (Hebert *et al.*, 2009). However, whilst the use of ultrasonography to measure muscle thickness has face validity, the use of static images of muscle thickness to establish muscle activation is questionable, due to other confounding factors such as fascicle length, tendon stretch, and type of contraction.

Kiesel *et al.* (2007) specifically studied LMM with the use of RUSI and bipolar fine-wire electrodes inserted into LMM. They studied contraction within a limited range (19-34% of MVC) in healthy asymptomatic subjects and found a linear relationship between muscle thickness change and EMG activity. Related studies have looked at other muscles and found variability in outcomes. For example, one study found a linear relationship between muscle activity and muscle thickness (McMeeken *et al.*, 2004) whilst another found a curvilinear relationship, finding approximate linearity only with contractions below 20% of MVC (Hodges *et al.*, 2003). Koppenhaver *et al.*, (2009a) surmised that the measurement of muscle activation with ultrasound imaging is dependent on the level of contraction (percentage MVC) as well as contraction strategy, in addition to the competing forces of surrounding muscles.

Many studies have looked at the relationship between CSA and force production, and results are varied and inconsistent. Influencing factors include, but are not limited to, training status, sex differences and age. Equivocal results among studies deem the force-CSA relationship as complex and unpredictable (Jones *et al.*, 2008). This view is supported by Koppenhaver *et al.* (2009a), who conducted a systematic review on this topic and concluded that 'the results of studies comparing ultrasound measurements with electromyography (EMG) activity suggest that the ability of ultrasound to measure muscle activation is complex and probably context dependent'.

2.4.5 Reliability of USI in measuring muscle size

Reliability is the degree to which a measurement is consistent and free from error. Establishing adequate reliability is critical to any measurement (Bartko and Carpenter, 1976). There are many studies pertaining to the reliability of USI in the assessment of muscle morphology and more specifically LMM, with the general consensus being that USI provides an accurate and reliable method of measuring LMM thickness (Hebert *et al.*, 2009; Wallwork *et al.*, 2007). The degree of precision and reproducibility is to some extent operator-specific and clinically important values such as reliability, standard error of measurement and minimal detectable change should be determined per rater. This will be explored further in Chapter 6.

2.5 Functional variability and human movement

The study of variability of movement has been extensive over the years (Davids *et al.*, 2003) looking at the ability of the human system to organise individual components into articulate, coordinated patterns of action. Human movement can be achieved through numerous kinematic arrangements due to the many degrees of freedom in operation (Li, 2006), and it has been demonstrated that movement behaviours cannot be replicated from one trial to the next with complete accuracy, even with expert performers (Preatoni *et al.*, 2013).

Movement variability may be described as the normal variations in movement performance that occur across multiple repetitions of a task (Harbourne and Stergiou, 2009). Traditionally, random error or noise within the system was deemed responsible for movement variability (Schmidt, 2003). Many theoretical perspectives have been proffered when considering variability in motor performance (Newell and Corcos, 1993), with one prominent theory being the Generalised Motor Program Theory (GMPT). The GMPT considers variation in a given movement pattern to be the result of an error in the ability to predict the necessary parameters for employing the underlying motor program (Schmidt, 2003). Following this theoretical approach, increased variability indicates less cooperative behaviour whereas movement with decreased variability may be considered as skilled movement (Stergiou and Decker,

2011). Prediction error may be reduced over time with task-specific practice which will in turn optimise the accuracy and efficiency of the movement pattern (Stergiou and Decker, 2011).

The uncontrolled manifold (UCM) concept is another presented framework which essentially evaluates which variables are controlled in a motor system (Scholz and Schöner, 1999). Original thoughts were that of motor redundancy; having more elements than necessary to perform a task resulting in multiple ways to perform a task (Scholz and Schöner, 1999). It was proposed that the central nervous system finds a unique solution every time it has to produce movement by removing the unnecessary degrees of freedom from control (Latash, 2012). However, the premise behind the UCM concept is that the central nervous system does not remove the redundant degrees of freedom but rather uses the abundance to safeguard the stability and flexibility of movement (Scholz *et al.*, 2000); variables that influence task outcome are controlled and others are left to vary, allowing freedom in the operation of the movement. Several studies have investigated the coordination strategies of apparently redundant motor systems in motor tasks such as sit-to-stand, pistol shooting and bimanual pointing (Domkin *et al.*, 2002; Scholz *et al.*, 2000; Scholz and Schöner, 1999) with an aim to discover the functional purposes that variability plays in these motor tasks. Consensual findings were that kinematic task-relevant degrees of freedom were stabilised whilst the remaining degrees of freedom were allowed to fluctuate. Further validation that the UCM hypothesis allows quantitative assessment of stabilisation of selected performance variables was established, and this provides information on changes in the structure of a multi-joint synergy that may not be reflected in its overall performance (Domkin *et al.*, 2002).

Another theoretical perspective is the Dynamical Systems Theory (DST) which considers concepts of nonlinearity and stability in the investigation of movement patterns and variability (Harbourne and Stergiou, 2009). DST proposes that the human system is able to self-organise according to environmental, biomechanical and morphological constraints in order to find the most stable solution for producing a certain movement (Hamill *et al.*, 1999; Kelso, 1995). The brain and neuromuscular components are independent structures that collaborate to produce synergistically organised actions required to perform a task in the given environment (Kelso, 1995; Kurz and Stergiou, 2004). Through the development of coordinative structures or

collections of muscle complexes, it is thought that the number of degrees of freedom of the motor system is dramatically reduced, and that this reduction in dimensionality/complexity encourages the development of functionally preferred coordination or 'attractor' states to achieve certain actions (Glazier *et al.*, 2003; Turvey, 1990). Within each attractor region or neighbourhood, system dynamics are highly ordered and stable resulting in consistent movement patterns for each task. Flexible and adaptive behaviour is available however through the variability between multiple attractor regions. DST conceptualises increased variability in a movement pattern as a loss of stability, while decreased variability generally indicates more stable behaviour (Stergiou and Decker, 2011). Where DST differs from other theories is the phenomenon that increased variability can drive the system to new behaviourally stable solutions. DST purports that a system becomes highly unstable when increasing variability reaches a critical point, and at that point the system responds by switching to a new, more stable movement pattern with less variability. This supports the acquisition of stable motor systems and enhanced motor learning over time. The DST approach implies that a persistent lack of movement variability may indicate a system with inflexible motor behaviours and limited adaptability (Stergiou and Decker, 2011). However, the paradoxical relationship between stability and variability may suggest that DST is limited in its ability to account for the fact that some highly stable tasks may be performed in a variety of different ways, as demonstrated by elite athletes who are capable of persistence as well as adaptability during competition.

The human system has great capacity for adaptability due to its ability to exhibit control and stability through mechanical properties as well as movement pattern. When intact, the osteoligamentous arrangement of the spine together with supporting musculature provides mechanical stability, whilst the system relies on neuromuscular control and movement pattern to maintain dynamic stability whilst in motion. Papi *et al.* (2015) articulate that in order to stabilise movement performance, synergy of motor control is required, whereby neural organisation of a multi-element system optimally arranges the allocation of tasks and is capable of executing them efficiently. The presence of variability, often deterministic in nature is necessary to control the degrees of freedom but also to adapt in order to function in the environment. Evidence has alluded to the importance of variability, which should not be seen as error but rather as an essential output of a cooperative system (Davids *et al.*, 2003; Harbourne and Stergiou, 2009; Hristovski *et al.*, 2006). Stergiou *et al.* (2006) suggest proficient motor

skills and healthy states are directly linked to optimal movement variability, and this variability allows for diverse movement patterning. Optimal movement variability permits environmental adaptation as well as facilitating changes in coordination and reducing injury (Hristovski *et al.*, 2006).

Variability reflects the variety of movement options available that provide flexible, adaptive strategies able to cope with a multitude of tasks and changing environmental conditions. In the dynamic human system where movement and change are constant, a stable state is unachievable; it is healthy variability and adaptability that implies health (Rickles *et al.*, 2007). Optimal variability as a central feature of normal movement is consistent with a nonlinear approach (Harbourne and Stergiou, 2009). A complex dynamical system is in slight but constant disequilibrium with the environment (Price, 2004) - nonlinear theories recognise this disequilibrium as healthy. Harbourne and Stergiou (2009) state that health is indicated by a dynamic equilibrium that is not a static state.

Variability of movement provides continuous feedback to the central nervous system allowing for complex mapping of both the sensory and motor cortexes which in turn contributes to the neuroplasticity needed for achieving functional movement. Lack of variability may lead to abnormal mapping of the sensory cortex which in turn disturbs motor function and potentially predisposes to injury. It is possible however to have too much variability, and movement should be contained to within an acceptable range. This is critical with any cyclical task where if one movement falls outside the expected range, the next movement is perturbed leading to a cascade of random, uncontrolled movements and potentially a fall or injury. Optimal movement variability lies between too much variability and complete repeatability (Stergiou *et al.*, 2006).

2.5.1 Measuring human movement

Many techniques have been employed to assess human movement, such optical motion analysis, force plates and gait mats. However, specialist equipment is often lab-based and therefore of limited applicability to the clinical setting. As such, accelerometers have become more widely used for continuous, unobtrusive and reliable monitoring of

human movement (Godfrey *et al.*, 2008). Three-dimensional accelerometers measure the frequency and intensity of movement in three planes of motion: anterior-posterior, medio-lateral and vertical. They can measure body posture at a point in time by recording translational and rotational movements.

The small size of accelerometers allows for precise placement on the area under study. Location is one of the most important factors in ensuring accuracy and validity of recorded data. For example, signal attenuation may occur if the sensor is placed too close to the centre of rotation (Godfrey *et al.*, 2008). Signal noise can also be an issue; careful placement of the sensor on a rigid surface helps to reduce artefact due to soft tissue movement, and signal filtering can help to reduce spurious readings. Overall, accelerometery has proven itself to be an appropriate and viable means of measuring movement, and its portability and easy application makes it convenient for use in the clinical setting.

2.5.2 Measuring variability

In the context of measurement, variability can be determined as either end-point variability (i.e. the variability at the goal level) or as coordinative variability (i.e. how the performance was conducted over a number of iterations; van Emmerik *et al.*, 2016). End-point variability has typically been studied to evaluate the outcome of performance, whereas coordinative variability provides information on the adaptability of movement patterns. Various studies have observed coordination variability from a dynamical systems perspective (Hamill *et al.*, 1999; Heiderscheit, 2000) and have found that in instances of neurological disease and musculoskeletal injury that coordination variability has been reduced. This may imply that people with neuromuscular compromise lose flexibility in their use of coordination strategies when performing a task compared to healthy controls (Wilson *et al.*, 2008).

The DST introduced notions of stability and nonlinearity to explain variability; increased variability suggests a progressively unstable system that may shift to a new attractor, or a new behaviour (Harbourne and Stergiou, 2009). Traditionally, linear tools have been utilised to measure variability. Linear analysis involves statistics of

range, mean and standard deviation and allows for quantification of a signal, but will not provide information on the time-evolving nature or complexity of the signal – it will not reflect that every movement will be affected by the preceding movement and equally will affect the subsequent one. Harbourne and Stergiou (2009) state that by using the statistical mean, the temporal variations of the movement are removed and the true structure of variability present in the movement pattern is masked. Furthermore, an assumption of linear tools is that variations between repetitions of a task are random or independent, however studies have demonstrated that this is not the case (Harbourne and Stergiou, 2003; Hausdorff *et al.*, 1996). In contrast, nonlinear dynamics and mathematical models are tools that consider time and are capable of describing system complexity. Nonlinear tools capture how motor behaviour emerges over time and quantify the temporal organisation, or structure of variability, from which the concept of stability may also be computed (Harbourne and Stergiou, 2009).

2.5.3 Section summary

The complexity of the human movement system gives rise to variability in performance. The body, with multiple degrees of freedom may adopt multiple strategies to accomplish any given task, within the constraints of the individual system. Using a dynamical systems theoretical approach may expose how the system is able to self-organise according to environmental, biomechanical and morphological constraints, and may reveal the adaptability and flexibility of the system to employ the most stable solution. For those with chronic, well-established low back pain, variability may be lacking, movement patterns suboptimal and their ability to adapt and effectively coordinate or control movement compromised, resulting in a cyclical pain pattern that is difficult to disrupt. It is therefore important to further understand how movement patterns and dynamic stability differ in those with CLBP compared to healthy individuals in order to provide treatment strategies that can break the cycle of pain and address rehabilitation towards a healthy dynamic equilibrium.

2.6 Stability analysis of human movement

In dynamical systems, stability refers to the resistance of a coordinative movement pattern to change in response to a perturbation, as measured by deviation from the attractor state or the ability to return to an attractor state (Kelso, 1995). Stability within the human system may be conceptualised as the body's ability to counteract any slight disturbance in order to maintain dynamic equilibrium. Initial disruption may arise from both internal (e.g. neuromuscular) or external sources (e.g. trip on uneven surface), however various intrinsic factors influence the capability of a system to adapt in response to perturbations, or in fact just to maintain controlled movement over a sustained period of time. These may include the level of control or effort required to repeatedly move in a stable manner, the robustness of the system to accommodate larger disturbances before failing, and the speed at which the body can adapt and return to the initial operating range.

It is the neuro-musculoskeletal capacity of an individual that is of interest within the clinical setting and the assessment of their stability under given conditions. Stability may be classified as global or local, and various mathematical methods of nonlinear analysis have been developed in order to estimate the stability of a system.

2.6.1 Global stability measures

Global stability relates to the ability of the human system to maintain upright equilibrium by resisting large perturbations, such as slipping or tripping (Dingwell *et al.*, 2000). Typically, this would be assessed through the quantification of the body's centre of mass relative to the base of support (van Emmerik *et al.*, 2016). Measures able to evaluate global stability include margin of stability and time-to-contact and consider not only instantaneous position but also velocity and acceleration, which are vital components in a dynamical system. Such calculations may provide a quantitative valuation of the degree of stability and thus estimate the capacity of the system to withstand varying perturbations.

Various authors however have warned about interpreting stability based on variability as evidence of causality (of falls for example; van Emmerik *et al.*, 2016). For instance, research suggests that falls are associated with high gait variability (step length, step width and stride time), yet there is conflicting evidence. Hausdorff (2007) demonstrated that stride time fluctuations were associated with falls, and Brach *et al.* (2005) similarly found that too little or too much step width variability was also associated with falling. Yet Dingwell and Marin (2006) found that in even when greater kinematic variability was exhibited, adopting a slower walking speed increased local dynamic stability.

As already discussed, the amount and the structure of variability are quite different, so the paradoxical reasoning that equates variability with dynamic stability must be interpreted with caution. The analysis of local dynamic stability however, evaluates the change and structure of variability over a series of time, thus providing useful information on a system's sensitivity to small, intrinsic perturbations (Dingwell and Cusumano, 2000).

2.6.2 Local stability measures

Local dynamic stability refers to the ability of the human system to effectively respond to, or resist small, intrinsic fluctuations during locomotion. These fluctuations may be due to neuromotor noise or other internal perturbations, and must be attenuated in order to maintain global stability (van Emmerik *et al.*, 2016). To analyse nonlinear behaviour, or local stability, system topology and dynamics are necessary to describe the system mathematically (Choi *et al.*, 2019).

Various nonlinear measures have been used to assess local dynamic stability in humans, including maximum Lyapunov exponents (λ_{max}), maximal Floquet multipliers and Detrended Fluctuation Analysis (DFA). Maximum Lyapunov exponents convert kinematic or kinetic data from a time series to a state space and determines the rate of divergence/convergence of nearby trajectories. Maximal Floquet multipliers quantify the local orbital stability of a system in state space and determine whether the behaviour of the system is evolving to diverge/converge from the mean of the attractor

state from cycle to cycle. Detrended Fluctuation Analysis is a modified root mean square analysis across windows of a time series and assesses the fractal structure and long-range correlations of fluctuations.

Maximal Lyapunov exponents have been used repeatedly to compare local stability, in particular gait stability, in patient groups compared to healthy controls and elderly to young subjects. Through this research it seems reasonable to conjecture that λ_{max} is linked to real-life notions of stability. For instance, Lockhart and Liu (2008) reported greater maximal Lyapunov exponents in elderly subjects with a history of falls compared to elderly subjects with no such history, although walking speed was not controlled and could thus confound results significantly. Su and Dingwell (2007) investigated the hypothesis that λ_{max} quantifies the reaction to perturbation. They used a passive dynamic walking model with added noise and found that increasing noise led to increases in λ_{max} in the short term. Their findings may indicate that short term λ_{max} may be used to predict global stability and in turn detect an increased probability of falling. Similarly, other studies have experimentally induced unstable conditions for gait: walking over an unstable surface (Chang *et al.*, 2010), random application of varying galvanic stimulation (Sloot *et al.*, 2011) and introducing mechanical or visual perturbations (McAndrew *et al.*, 2011) and have shown that short-term λ_{max} does correlate with the reduction in global stability. Contrarily, long-term λ_{max} often suggested that global stability was improved. This finding has been attributed to the adaptations that occur in the longer term – short term movement is less stable whereas longer term movement pattern is more stable following adaptation by the human system.

Floquet theory is mainly applicable to periodic systems; it is questionable whether deterministic human locomotion, in particular gait or other cyclical actions fits this category, thereby challenging the construct validity of such mathematical models in biological systems (Bruijn *et al.*, 2013). Despite this, several studies have used this approach to study human stability. However, where maximal Lyapunov exponents were found to reflect the degree of experimentally induced chaos introduced into a system, studies using maximal Floquet multipliers appear to be more inconsistent in their outcomes. For example, whilst McAndrew *et al.* (2011) found the expected effect on the maximum Floquet multiplier following the introduction of surface or visual

perturbations, Sloot *et al.* (2011) found the converse effects of galvanic vestibular stimulation on maximal Floquet multipliers to those expected.

Detrended fluctuation analysis reveal long-range correlations between cycles of movement. However, the validity of the theoretical relationship between long-range correlations and dynamic (gait) stability is debatable (Bruijn *et al.*, 2013). All variations in movement are dependent on the preceding movement and likewise will influence future variations. All measured variations record not only deterministic variation but also reactions to perturbations such as impacts or sensory/motor noise, therefore there would always be some relationship between movements; thus, stronger correlations when the system may be responding to unstable movement. In opposition, Jordan *et al.* (2007) claims that less correlated gait allows more flexibility and thus greater stability. Inconclusive results have emerged from using DFA, for instance Chang *et al.* (2010) found there to be no differences in long-range correlations whether subjects walked over stable or unstable surfaces. Furthermore, the inconsistent results from the limited number of dynamic stability studies utilising this method of analysis questions its usefulness.

With all these measures it is possible to calculate local stability without any external perturbations from any kinematic time-series. This improves applicability and ease of use within a clinical setting, and for use with patients with CLBP. Conversely, it could be argued that in the absence of external perturbations, the stability levels within the system are not sufficiently probed. It is also important to be cognizant of the variability that different methods of analysis may produce in respect to local stability. For example, a positive λ_{max} may be suggestive of a locally unstable system, whereas the same individual may be considered locally stable based on maximal Floquet multipliers that are less than 1. It is thought that this inconsistency may be due to differences in time scales between analyses, with λ_{max} evaluating fluctuations over shorter time scales and Floquet multipliers over longer time periods. Dynamic stability should always be defined and considered within the context and demands of the task (van Emmerik *et al.*, 2016), and in turn this will inform the most appropriate measure to use.

Maximum Lyapunov exponent has a robust theoretical basis (Dingwell and Cusumano, 2000; Rosenstein *et al.*, 1993). λ_{max} is capable of describing the greatest rate of

expansion of any dimension during human movement over a relatively short time period and is well established in its use in the analysis of human movement. Table 1 details studies exploring local dynamic stability of the trunk/spine and it is clear that λ_{max} is the favoured method of choice in this field, perhaps due to its consistency. For this reason, maximum Lyapunov exponents will be described in further detail, with explanation of the calculation and its use in low back pain research.

Table 1: Selection of studies addressing local stability of the trunk/spine

Study	***Study aim***	***Motor task***	***Subjects***	***Measures***	***Findings***
Stability of dynamic trunk movement *Granata and England (2006)*	Determine whether movement pace and movement direction of dynamic trunk flexion & extension influence control of local dynamic stability.	Repetitive flexion-extension movements at different speeds.	20 healthy	Lyapunov exponent	Nonlinear dynamic systems analyses were successfully applied to empirically measured data, which were used to characterize the neuromuscular control of stability during repetitive dynamic trunk movements. Movement pace and movement direction influenced the control of spinal stability.
Local dynamic stability of trunk movements during the repetitive lifting of loads *Graham et al. (2012)*	Assess how varying the load-in-hands affects the neuromuscular control of lumbar spinal stability.	Repetitive lifting at 10 cycles/minutes for 3 minutes under two load conditions (zero load & 10% max. back strength.	30 healthy	Short- and long-term Lyapunov exponents	Improved dynamic spinal stability when lifting the heavier load; meaning that as muscular and moment demands increased, so too did participants' abilities to respond to local perturbations; supporting the notion of greater spinal instability during movement with low loads due to decreased muscular demand and trunk stiffness.
Fatigue influences the dynamic stability of the torso *Granata and Gottipati (2008)*	Test whether fatigue influences stability of dynamic torso movements.	Repetitive dynamic trunk flexion tasks before and after fatigue of extensor muscles.	10 healthy	λ_{max}	λ_{max} values increased with fatigue suggesting poorer dynamic stability when fatigued. Findings indicated that one mechanism by which fatigue contributes to low back disorders may be spinal instability.
Process Stationarity and Reliability of Trunk Postural Stability *Lee and Granata (2008)*	Characterise the reliability and establish the trial duration for torso stability assessment.	Maintaining seated posture on a wobbly seat pan.	12 healthy	Dynamic variability & Lyapunov exponent	Process stationarity and reliability were improved in more difficult balance conditions.

Table 1 (continued): Selection of studies addressing local stability of the trunk/spine

Study	***Study aim***	***Motor task***	***Subjects***	***Measures***	***Findings***
Precision of estimates of local stability of repetitive trunk movements *(Dupeyron et al. (2013)*	Assess the precision of λ_{max} in tasks involving the trunk as a function of the number of repetitions and determine the effect of time (fatigue) during prolonged sessions.	Repetitive flexion, rotation and combined movement tasks.	10 healthy	λ_{max}	Trunk local stability reached acceptable precision level after 30 repetitions. λ_{max} was higher (indicating lower stability) in flexion, compared to rotation and combined tasks. There was no time effect (fatigue). λ_{max} of trunk movement was lower and less variable than that of thorax and pelvis movements.
Sensor positioning and experimental constraints influence estimates of local dynamic stability during repetitive spine movements *Howarth and Graham (2015)*	Determine the influence of sensor positioning on estimates of local dynamic stability on spine movements.	35 consecutive cycles of spine flexion under both constrained and unconstrained conditions.	10 healthy	λ_{max}	Estimates for λ_{max} were significantly lower (i.e. dynamically more stable) for spine kinematic data obtained from the L3 sensor than those obtained from kinematic data using either the L1 or T11 sensors. λ_{max} was lower when the movement was constrained.
Evaluation of the threshold of stability for the human spine *Tanaka et al. (2009)*	Develop the threshold of stability and evaluate its potential to serve as a quantitative indicator for spinal stability.	Seated postural control on wobble chair, with eyes open and eyes closed.	8 adults	λ_{max}	Increasing task difficulty increased kinematic variability and decreased the basin of stability. Reduction of the size of perturbation decreased kinematic variability but had no impact on the basin of stability size.

2.6.3 Maximum finite-time Lyapunov exponent

As mentioned in the previous section, the maximum finite time Lyapunov exponent is a parameter that can be used to calculate local dynamic stability, or to determine the deterministic chaos in a system (Dingwell and Cusumano, 2000; Lee and Granata, 2008; Tanaka *et al.*, 2009). λ_{max} quantifies the maximum rate of exponential divergence or convergence of initial neighbours, or close points in the state-space of a dynamical system.

The premise on which λ_{max} is based is that a system would need to behave in exactly the same way (e.g. position, velocity or acceleration) time and again during a movement pattern for it to be regarded as a completely stable system. However, any level of variation may be considered as a perturbation for the following cycle. These perturbations may arise from internal (e.g. sensory-motor noise) or external (e.g. uneven surface) sources. The distance between nearest neighbouring points among the two states in time can be followed and if the distance increases exponentially this indicates instability. Conversely, should the distance decrease then this is an indicator of stability. The rate at which this divergence occurs gauges the level of stability/instability in the dynamical system: a larger value of λ_{max} suggests less stable behaviour.

2.6.3.1 Calculation

Wolf *et al.* (1985) proposed the first algorithm to determine the maximum Lyapunov exponent from experimental time series data. Limitations were associated with his method however and Rosenstein *et al.* (1993) and then Kantz (1994) later presented new algorithms which were purported to be better suited to smaller data sets. The differing mathematical models are beyond the scope of this thesis, however each procedure for calculating λ_{max} from kinematic data follows the same basic steps which are detailed below in Figure 4.

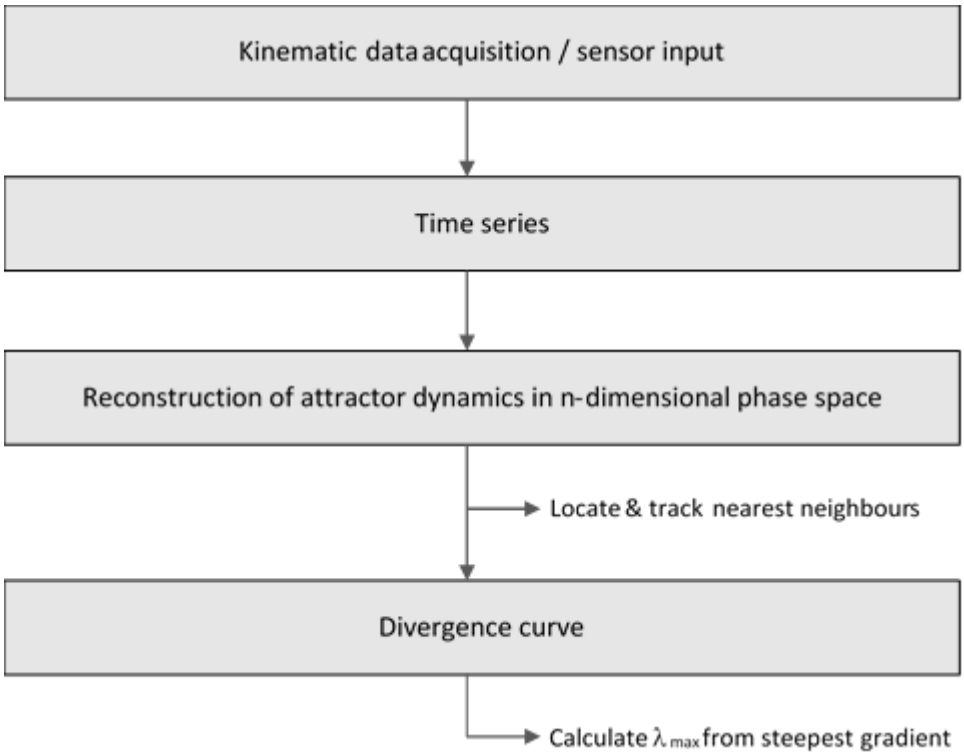


Figure 4: Basic steps for calculating λ_{max} from kinematic data

Before reconstruction of the selected state space, the data may be filtered and resampled. There are conflicting opinions on whether data filtering is appropriate and whether the reduction in noise also leads to loss of important information. In a systematic review conducted by Mehdizadeh (2018) examining different methodological approaches used to quantify Lyapunov exponents (λ), it was reported that of the 102 papers reviewed, 23% performed filtering before calculating λ, compared to 39% that did not. Moreover, analysis of these studies indicated that λ values calculated with or without filtering were in the same range suggesting that there is no adverse effect associated with filtering the signal before calculating λ.

Time series are used to build a proxy of the observed states. Therefore, signals collected from the system must be observed as a function of time (seeFigure 5-A). Time series length will affect the value of λ_{max}; a reduced λ_{max} is associated with shorter data

sets (Bruijn *et al.*, 2009; England and Granata, 2007). Studies have therefore suggested time-normalization of the time series by either fixing the number of data points in the whole time-series or normalizing the number of data points per cycle (for example per stride). Time-normalizing each cycle provides consistency regardless of velocity but removes any temporal variations between cycles which is an important component of nonlinear analysis. Resampling to a fixed number of data points for the entire time-series on the other hand normalizes the data whilst still allowing between-cycle temporal variation. England and Granata (2007) examined both methods and concluded that time-normalization of the entire time-series is most appropriate. Furthermore, they deemed the length of the data set to be more critical than sampling frequency providing that the sampling frequency is sufficient to characterise the kinematic variance. Regardless of which sampling rate or method of time-normalization is chosen, it is imperative that the same number of cycles is applied for every condition and subject (Bruijn *et al.*, 2009; England and Granata, 2007).

Subsequent state space reconstruction from the time series can be performed using time-delayed embedding. State space reconstruction offers geometrical and topological information about a dynamical attractor from observed kinematic data (see Figure 5-D). The concept of dynamical mapping in state space is founded on Takens Embedding Theorem (Takens, 1981). Reconstruction of the attractor requires an appropriate time delay (τ) and an elected embedding dimension (m), which can be used in the following equation:

$$S(t) = (s(t), s(t + \tau), s(t + 2\tau), \dots, s(t + (m - 1)\tau)$$

where *S(t)* is the m-dimensional reconstructed state vector, *s(t)* the one-dimensional Euclidean norm series, τ the time delay, and m the embedding dimension.

Arbitrary time delay may be sufficient to reconstruct the attractor; however, the process is enhanced by selection of the time delay τ according to the data set. Measures of autocorrelation and mutual information have been proposed as suitable methods for selecting an appropriate time delay (Fraser and Swinney, 1986). The most common approach to finding the time delay is from the first minimum of the mutual-information curve extracted from the average mutual-information function (Figure 5 -B; Myers *et*

al., 2013). The average mutual information function developed by Fraser and Swinney (1986) finds time delayed coordinates that are as independent from each other as possible. This allows the values of the time series to be plotted multiple times against themselves at a pre-determined delay (τ) to represent the phase-space of the multidimensional system from which the kinematic data was collected. Difficulties may arise when the function identifies a false-minimum, for example when there is significant noise in the time series. Careful inspection of the mutual-information curve is likely to expose any anomaly and the true local minimum can be redetermined (Figure 5-C). Further, there are differing opinions on whether time delays should be variable or fixed when calculating Lyapunov exponent for comparison. Gates and Dingwell (2009) advocate the use of individual delays whereas van Schooten *et al.* (2013) found that a fixed delay for all participants increased reliability in calculating Lyapunov exponent.

The embedding dimension *m* is usually determined through a global false nearest neighbour analysis (Kennel *et al.*, 1992). The value for *m* can be estimated by examining the change in distance between neighbouring points in phase space as the original time series is progressively embedded into higher dimensions (Wallot and Mønster, 2018). The difference in magnitude of neighbouring points should remain unchanged when the embedding dimension is sufficient. If embedding noticeably changes the distance between two neighbours then they are labelled false neighbours, and the data needs to be embedded further. Conversely, if the distance remains unchanged then the points are deemed true neighbours and further embedding should not affect the shape of the attractor. The embedding dimension *m* can be increased to the point where the number of false nearest neighbours drops to zero or where subsequent embeddings do not impact the number of false nearest neighbours (Wallot and Mønster, 2018). The selection of the embedding dimension is data-specific even when the same region (e.g. trunk) is under study - evident by the variety of values that are reported by studies using Lyapunov exponent to examine local dynamic stability of human locomotion. Reported *m* values for such studies include 3 (Arampatzis *et al.*, 2017; Ekizos *et al.*, 2018), 5 (Graham *et al.*, 2012; Granata and England, 2006) and 6 (Graham *et al.*, 2014; Howarth and Graham, 2015).

Lyapunov exponents can then be calculated by measuring the exponential rate of divergence of initially neighbouring trajectories in the reconstructed state space (Figure 5-E). Different algorithms analyse data slightly differently, therefore type and size of data sets should be considered when selecting a method for calculation. In Wolf's algorithm (Wolf *et al.*, 1985) nearest neighbour for data points are identified along a single reference trajectory, whereas the algorithm proposed by Rosenstein *et al.* (1993) and Kantz (1994) identify the nearest neighbour in state space for every data point. Further differences in methods exist in the time frame in which data points are followed – either throughout the entire time series (Kantz, 1994; Rosenstein *et al.*, 1993) or for a specified period that is a fraction of the time for one complete orbit of the attractor (Wolf *et al.*, 1985).

The logarithmic rate of divergence is plotted and the maximum Lyapunov exponent is estimated as the gradient of the line of linear best-fit. This has been seen in the literature to be calculated over a chosen time frame or number of samples. However, the true definition of λ_{max} is the maximum rate of separation which is observed as the initial rapid rate of divergence (Figure 5-F; Bruijn *et al.*, 2013).

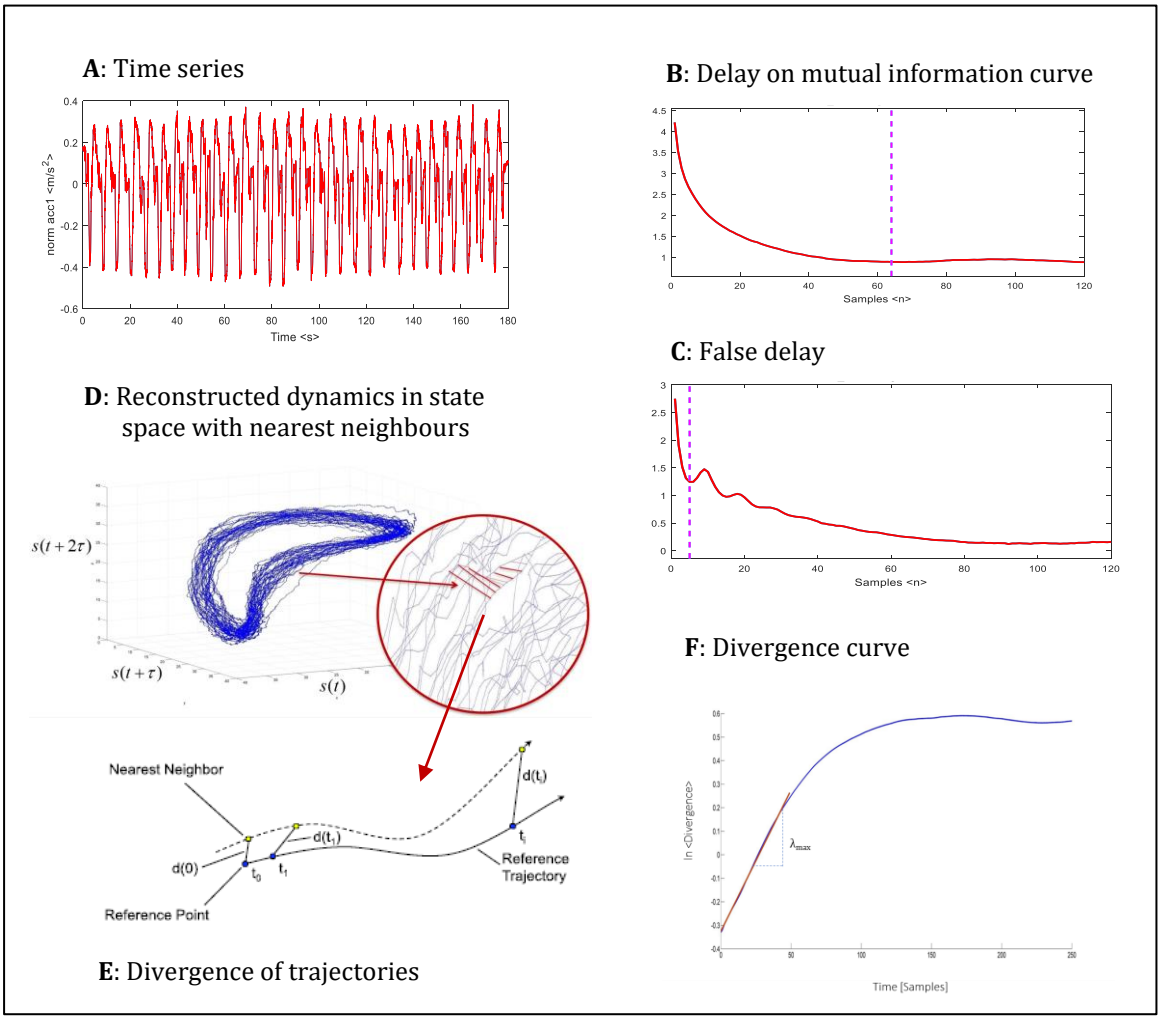


Figure 5: The process of calculating maximum Lyapunov exponents.

A: Time series data from accelerometer. **B**: Time delay from mutual-information curve. **C**: False-minimum on mutual-information curve. **D**: State space reconstruction in 3 dimensions with selected delay; with expanded view of a region on the reconstructed attractor displaying the increasing distance between nearest neighbours. **E**: Divergence rate of two trajectories. **F**: Average logarithmic rate of divergence of all nearest neighbour pairs. Gradient of line of best fit at slope of maximum divergence gives λ_{max}.

The diversity in methodologies associated with the calculation of Lyapunov exponent makes comparing values of stability difficult. Between study differences can occur within experimental design and data collection, for example video motion capture versus accelerometers, dissimilar sampling rates or disparate tasks. Moreover, the choice of algorithm used in calculation can significantly affect the value of λ_{max}. As a

consequence of the varied implementation of such methods there is a lack of population-specific reference ranges for λ_{max}. For such values to exist, there would need to be development and adoption of a standardised procedure to apply and calculate λ_{max} (Mehdizadeh, 2018).

2.6.4 The use of Maximum Lyapunov Exponent in measuring local dynamic stability in LBP

The last few decades have seen a rise in the number of studies utilising λ_{max} to assess neuromuscular control of the human system, and as popularity of this methodology has increased, it has been implemented in the study of low back pain patients. There appears to be more appreciation of the significances relating to reduced spinal stability, with many non-pharmacological therapies aiming to reduce pain and disability through improvement of neuromuscular control of movement. Research has thus been driven forwards in search of further understanding of NSCLBP with hope of future development of effective management strategies.

Despite the increased use of λ_{max} in low back pain research, there still remains a limited number of studies which have utilised and reported on this methodology. Table 2 displays studies which have used λ_{max} for local dynamic stability assessment in a low back pain population.

Table 2: Studies using maximum Lyapunov exponent to examine local dynamic stability in low back pain

Study	***Study aim***	***Motor task***	***Subjects***	***Measures***	***Findings***
Muscle Strength and Neuromuscular Control in Low-Back Pain: Elite Athletes Versus General Population *Moreno Catalá et al. (2018)*	Investigate the athletic-based specificity of muscle strength and neuromuscular control of spine stability in CNSLBP.	Repetitive lifting task inducing flexion and rotation of trunk, and quick-release experiments.	30 with LBP (15 athletes) and 29 with no LBP (15 athletes).	λ_{max}, MVC, EMG & VAS.	Local dynamic stability and trunk stiffness were no different between LBP and healthy groups. Both athletes and non-athletes with LBP showed the same level of muscular deconditioning and adopted similar strategies to ensure spinal stability following sudden perturbations.
The effects of movement speed on kinematic variability and dynamic stability of the trunk in healthy individuals and low back pain patients *Asgari et al. (2015)*	Evaluate whether the varying speed of motion affects the kinematic variability and movement control of the trunk. Test if LBP patients use altered trunk movement patterns and neurocontrol strategies compared to healthy.	Flexion/extension task at 3 different speeds.	14 with CLBP & 12 healthy.	Maximum Lyapunov exponent & Floquet multipliers.	Higher speed significantly reduced the kinematic variability, while it increased short-term Lyapunov exponents. Long-term Lyapunov exponents were higher at self-selected speed and lower in low back pain patients as compared to control volunteers. Floquet multipliers were larger at self-selected speed and during higher pace trunk movements.
The Effects of Experimentally Induced Low Back Pain on Spine Rotational Stiffness and Local Dynamic Stability *Ross et al. (2015)*	Assess if capsaicin-induced LBP affects spine stability & the neuromuscular control of repetitive trunk movements in healthy participants with no history of LBP.	Repetitive trunk flexion/extension task under different conditions.	14 healthy males.	λ_{max} & EMG.	Local dynamic stability and muscular contributions to lumbar spine rotational stiffness were significantly impaired during the LBP trial compared to baseline.
Comparing the local dynamic stability of trunk movements between varsity athletes with and without non-specific low back pain *Graham et al. (2014)*	Compare the dynamic stability of spine kinematics and trunk activations, as well as antagonistic muscle co-contraction, between athletes with and without LBP.	Repetitive trunk flexion with rotation task.	20 varsity athletes – 10 with LBP & 10 healthy.	λ_{max} & EMG.	There were significant reductions in the local dynamic stability of low back EMG in LBP participants, as well as trends for reduced dynamic spine stability and whole trunk EMG stability in these same participants

Table 2 (continued): Studies using maximum Lyapunov exponent to examine local dynamic stability in low back pain

Study	***Study aim***	***Motor task***	***Subjects***	***Measures***	***Findings***
Local dynamic stability of the spine and its coordinated lower joints during repetitive Lifting: Effects of fatigue and chronic low back pain *Asgari et al. (2017)*	Examine spinal and lower joint stability and response to fatigue of individuals with and without CLBP while performing lifting-lowering movements.	Repetitive trunk flexion/lifting task.	14 healthy & 14 NSCLBP	λ_{max} of spine and joints of lower extremity.	Spine and hip stability decreased as fatigue increased. CLBP was associated with more stable lower joints, especially the hip.
A random-perturbation therapy in chronic non-specific low-back pain patients: a randomised controlled trial *Arampatzis et al. (2017)*	Assess the effectiveness of a specific rehabilitation therapy for NSCLBP patients, based on random/irregular functional perturbation training induced by force disturbances to the spine.	Repetitive trunk movements (flexion & rotation) and quick-release experiments.	40 NSCLBP (20 control & 20 perturbation-based group)	λ_{max}, MVC, EMG & VAS.	The perturbation-based therapy reduced patient's low-back pain (35%), increased muscle strength (15–22%), and trunk stiffness (13%), while no significant changes were observed in the control group. There was an unchanged state in dynamic stability in both the experimental and control groups.
Effects of noxious stimulation to the back or calf muscles on gait stability *Van Den Hoorn et al. (2015)*	Investigate whether nociceptive stimulation (hypertonic saline injection) in a low back or calf muscle affects gait stability.	Walking under different conditions (pain/no pain).	16 healthy	Maximum Lyapunov exponent.	Experimental pain resulted in reduced gait stability at lower walking speeds – effects were larger for calf pain than LBP. However, gait became more stable with LBP at faster walking pace.
Pain catastrophizing moderates changes in spinal control in response to noxiously induced low back pain *Ross et al. (2017)*	Assess the direct effects of pain on spinal control and assess whether the relationship between pain and control is moderated by psychological features.	Repetitive spinal flexion under 3 conditions (no pain, pain & recovery).	16 healthy	λ_{max}.	There was no overall effect of pain on λ_{max}. Those with high pain catastrophizing scores became more stable with pain, whereas those with low pain catastrophizing scores destabilised with pain.

Eight studies were identified within the literature, all conducted within the last six years. All eight studies utilised maximum Lyapunov exponent calculations to explore local dynamic stability of the trunk in participants with LBP. The majority of studies implemented a movement task involving the trunk, principally a flexion/extension type movement (with or without the lifting of a weight). Three studies investigated stability through more movement planes by introducing trunk rotation as well as flexion/extension (Arampatzis *et al.*, 2017; Graham *et al.*, 2014; Moreno Catalá *et al.*, 2018). One study looked at changes in gait stability on the introduction of back and calf pain (Van Den Hoorn *et al.*, 2015).

Collection of kinematic data was similar in all studies. All but one study used 3D motion capture systems; Ross *et al.* (2017) used two 3D electromagnetic sensors placed on vertebral segments T12 and S1. Number of repetitive cycles varied from 20 to 40, with a most common test length of 30 or 35 cycles. Rates of movement were also mixed amongst studies, with some studies failing to report test speed. Two studies using flexion/extension tests reported using speeds of 0.25Hz or 15 cycles/minute (Graham *et al.*, 2014; Ross *et al.*, 2015), whilst the two studies that conducted tests that required flexion with rotation to both sides (additional demand during one cycle) used slower speeds of 0.2Hz or 12 cycles/minute (Arampatzis *et al.*, 2017; Moreno Catalá *et al.*, 2018).

All studies investigated the differences in dynamic stability with or without the presence of low back pain. Five studies recruited participants who had low back pain (Arampatzis *et al.*, 2017; Asgari *et al.*, 2015, 2017; Graham *et al.*, 2014; Moreno Catalá *et al.*, 2018) with two of those five recruiting athletes with and without low back pain (Graham *et al.*, 2014; Moreno Catalá *et al.*, 2018). The other three studies chemically induced low back pain through either topical capsaicin cream application to the skin of the lower back (Ross *et al.*, 2015), or injection of hypertonic saline solution - into the right erector spinae muscle at L3 (Van Den Hoorn *et al.*, 2015) or into the L4/L5 interspinous ligament (Ross *et al.*, 2017). Clearly the results of these studies need to be considered from a different perspective; the experimentally induced LBP will show any changes in dynamic stability only in relation to pain, whereas the participants with low back pain may have inherent morphological changes along with motor control

impairment that may further influence dynamic stability in these groups. Furthermore, the induced back pain groups were tested at baseline, in pain and again in recovery in a crossover design thereby reducing the influence of confounders as subjects acted as their own controls, whereas the natural LBP studies used separate healthy control groups.

The only longitudinal study which utilised an intervention providing rehabilitation therapy for NSCLBP patients was conducted by Arampatzis *et al.* (2017). In this study subjects followed a programme based on random/irregular functional perturbation training with the aim to increase muscle activation and thus strength, and also to increase the ability of the nervous system to perceive sensory signals and generate appropriate motor commands. Participants with NSCLBP were tested at baseline and again at 13-weeks having either followed a training programme or not (control group). Results showed that whilst there was a significant reduction in pain in the intervention group following therapy compared to the control group, there was an unchanged state in dynamic stability between timepoints in both groups.

All studies using participants with existing LBP (naturally occurring) found there to be no significant difference in λ_{max} between LBP and non-LBP groups (Asgari *et al.*, 2015, 2017; Graham *et al.*, 2014; Moreno Catalá *et al.*, 2018). Ross *et al.* (2015) however, who induced LBP with capsaicin, reported a significant correlation between λ_{max} and pain scores (p=0.002; baseline of no pain to induced pain). They found there to be significant positive correlations between λ_{max} and pain catastrophising scores in all trials (no pain, pain and recovery from pain); those with higher levels of kinesiophobia possessed the highest λ_{max} values. In contrast, a later study conducted by Ross *et al.* (2017) found there to be no overall main effect of pain on λ_{max} (p=0.564) and contrary to their earlier findings, those with higher pain catastrophising scores were reported to have lower λ_{max} values (i.e. stabilised) compared to lower pain catastrophising scores who were seen to destabilise (higher λ_{max} values). They attributed these conflicting results to the fact that different methods of pain induction were used, claiming that the different agents could have varied effects on proprioception and pain experienced (e.g. deep vs superficial).

Other notable outcomes included the unsurprising findings from Asgari *et al.* (2017) that lifting-induced fatigue had a significant effect on stability of the spine (increased λ_{max}; p=0.01). Contradictory reports on the effects of test speeds on stability were also noted. Whilst one study documented higher λ_{max} values when faster test speeds were used (in subjects with and without LBP; Asgari *et al.*, 2015), van den Hoorn *et al.* (2015) found there to be reduced stability with LBP when tested at slower test speeds, but recorded lower λ_{max} values with LBP when testing at higher movement speeds. They hypothesised that faster speeds may lead to more predictable trunk movements which may be necessary to compensate for potentially altered proprioception due to pain and/or less effective corrective strategies. Finally, Graham *et al.* (2014) observed that λ_{max} values were lower (less unstable) when participants performed an asymmetrical movement test, in both the healthy and LBP groups. They attributed this to higher trunk muscle co-contraction in tasks involving twisting and lateral flexion which they stated was supported by previously conducted studies in the field.

Various limitations were recognised in the studies reported in this section. Many of the studies had relatively low participant numbers, and the level of pain experienced by those with naturally occurring LBP was often low, potentially restricting any observed differences between groups. Secondly, the comparability of chemically induced pain studies with natural LBP studies is reduced; partly due to different pain types, potential functional differences and also the self-professed issues relating to inadequate time and rest periods between trials with the induced-pain protocols. Finally, some studies reported a lack of consistency with repetitive movement tasks, which would clearly affect observed variability and thus stability measures. Increased rigour and robustness of the movement task would undoubtedly improve the reliability of future studies.

Poor sensorimotor control has been documented in those with CLBP, and there is growing evidence to suggest that postural control is further impacted by deficits in higher-cognitive processes in this population. Several studies have looked at the influence of attentional demand and cognitive loading on dynamic stability of human movement; the results of which are discussed in the following section.

2.6.5 Attentional focus and the dual-task paradigm

Motor control and coordination is reliant upon proprioceptive afferents and complex sensorimotor actions. Contrary to the traditional view, which believed postural control to be automatic, it is now believed to be attentionally and cognitively demanding (Andersson *et al.*, 2002; Hemmati *et al.*, 2017; Huxhold *et al.*, 2006). Sensory integration for appropriate motor output is a supraspinal process which requires some degree of attentional resource (Shumway-Cook and Woollacott, 2000; Teasdale and Simoneau, 2001). The integrity between sensorimotor and cognitive processes is critical in maintaining stability and coordination of movement (Woollacott and Shumway-Cook, 2002). Yet the brain has limited capacity and so information processing of motor and sensory systems is highly competitive (Marois and Ivanoff, 2005); the brain only possesses limited resources and as such is unable to sustain simultaneous activation in all neural structures (Dietrich, 2003).

Within motor control literature, the focus of attention (FOA) has been shown to affect the accuracy of an individual's performance of a movement task. The constrained action hypothesis describes how internal FOA (focusing on body movements) may interfere with the automaticity of the body's movements, whereas external FOA (focusing on the effect of their movement) may enhance performance (Bourdon *et al.*, 2018). This has been shown to be the case in sports such as golf (Bell and Hardy, 2009) and standing long jump (Porter *et al.*, 2010) but was found to have no influence on gait local dynamic stability (de Melker Worms *et al.*, 2017). It has been postulated that the accuracy or performance of simple tasks may not be influenced by FOA (Wulf, 2013), and it is unclear whether FOA impacts trunk motor control. Bourdon *et al.* (2018) state that FOA should be controlled for in trunk stability research, for example by introducing targets to touch and maintaining external focus throughout the movement task, hence reducing variability and improving reliability.

The dual-task paradigm has been used to study the influence of a secondary cognitively demanding task on movement task performance. The competition for limited attentional resources may result in interference which affects the performance of one or both tasks (Woollacott and Shumway-Cook, 2002). Various theories of attention

have been proposed to explain changes in performance during the concurrent execution of two tasks, including:

The capacity-sharing theory - with limited attentional resources, if attentional requirements of simultaneous performance in a dual-task context exceed the information processing capacity of the system, decrements in performance of either one or both tasks would occur (Kahneman, 1973).

The 'bottleneck' theory - filtering of information occurs since only a certain amount can be processed at the same; two tasks requiring the same processing resources leads to impairments in performance of one or both tasks (Pashler, 1994).

The decrease of processing efficiency under dual-task conditions, compared to the processing of each single task in isolation, is observed as the dual-task cost (Künstler *et al.*, 2018). The dual task cost predictably rises with the increase of task difficulty or complexity.

Several factors may impact the performance of the postural control task, which may improve or decline; these include difficulty of postural and cognitive tasks as well as the attentional capacity of the individual (Fraizer and Mitra, 2008). Hypothetical reasoning varies when explaining an improvement in postural control performance. For instance, some authors have theorised that there is a distractor effect from the cognitive task which induces external focus of attention thus enhancing performance of postural control (Woollacott and Shumway-Cook, 2002). Other researchers have speculated that physical performance improvement is a selected strategy adopted to facilitate the execution of the cognitive task (Fraizer and Mitra, 2008). However, dual-tasking challenges may well be met differently by different populations (e.g. age or disease status; Bloem *et al.*, 2006; Rapp *et al.*, 2006; Simoneau *et al.*, 2008), with the prioritisation of either the postural or the cognitive task over the other.

It has been noted that impaired sensory integration, poor motor control and changes in neurocognitive function may exist in those experiencing low back pain, therefore the relevance of higher cognitive processes during postural control may be more prominent in this population. Furthermore, slower psychomotor speed and impaired short-term memory has been observed in those with CLBP (Luoto *et al.*, 1996, 1999),

which, together with pain and anxiety that interfere with executive functions (Leveille *et al.*, 2009) may well diminish dual-task capability in CLBP patients.

Conflicting findings have been reported in studies utilising dual-task methodologies in those with low back pain. Postural sway and centre of pressure was examined in several studies; one study used an auditory Stroop test as the cognitive task (Shanbehzadeh *et al.*, 2018) whilst others used a secondary task of reciting a string of memorised numbers backwards, with or without eyes closed (Mazaheri *et al.*, 2010; Salavati *et al.*, 2009). These studies found there to be no change in postural performance in those with LBP, and response to dual task was no different between groups. Other studies used a balance platform with a variety of cognitive tasks: auditory Stroop test (Etemadi *et al.*, 2016; Sherafat *et al.*, 2014), serial-3 task (sequential subtractions of 3 from a given number; Hemmati *et al.*, 2017) and reciting a string of memorised numbers backwards (Hemmati *et al.*, 2018). Hemmati *et al.* (2017) found there to be reduced balance in the dual-task condition, but there was no difference between the healthy and LBP groups. Sherafat *et al.* (2014) on the other hand found mixed results in the dual-task condition; reaction time increased in the healthy group, and stability (according to a Stability Index) decreased in the LBP group. Hamacher *et al.* (2014) analysed gait together with a word fluency test, where participants had to recite as many words as possible beginning with a given letter in the allocated time. Gait variability was reported to increase with the addition of the cognitive task in the CLBP group. Van Daele *et al.* (2010) conversely found that postural sway increased in healthy participants with the introduction of a cognitive task whereas in those with CLBP, postural sway was observed to decrease in dual-task conditions.

Several studies have also used λ_{max} to measure local dynamic stability in dual-task conditions, but only with healthy subject groups. Hamacher *et al.* (2016a) studied the reliability of measuring local dynamic stability (λ_{max}) during gait with simultaneous texting or serial-7 cognitive task (sequential subtractions of 7 from a given number) and demonstrated good to excellent reliability with their methodology. Focus of attention, subjectively measured on a visual analogue scale, was studied by Bourdon *et al.* (2018) whilst measuring λ_{max} during a repetitive spinal flexion task. They found

that λ_{max} was unaffected by FOA. Finally, Longo *et al.* (2018) measured spatial and temporal variability, and λ_{max} during a repetitive upper extremity motor task, with and without a simultaneous serial-3 task. Dual task conditions appeared to increase variability whilst reducing stability.

The evidence of cognitive impact on postural stability in people with NSCLBP remains unclear; the diverse experimental protocols employed in these studies may account for the wide-ranging differences found. There appears to be a gap in the literature and a need for further research to be conducted in this field to examine local dynamic trunk stability within the dual-task paradigm in NSCLBP patients. Furthermore, if these outcomes could be correlated with changes in spinal muscle morphology, clinical assessment and patient management would be augmented.

2.7 Chapter summary

There is unequivocal agreement that people with NSCLBP are biased towards disturbances in neuromotor control, which in turn may affect variability and stability of movement. However, it remains unclear if, and how cognition, muscle morphology, and pain influence dynamic control. To date, it appears that no study has investigated local dynamic trunk stability along with a cognitive task in a NSCLBP population. Furthermore, limited evidence links muscle morphology and pain to measures of stability.

The use of a non-linear or dynamical systems theoretical approach to motor behaviour within the constraints of NSCLBP would provide an individualised interpretation of performance, against which prognosis and progression could be gauged. Further profiling of cognitive effect, muscle morphology of key spinal stabilisers and pain would augment this assessment. Effective measurement of such outcomes would not only be clinically beneficial to the patient but could also improve efficiency in stratifying treatment options and enhance the appraisal of the efficacy of interventions.

Chapter 3 : Aims, Objectives & Hypotheses

3.1 Thesis Rationale

Low back pain continues to be the most prevalent of musculoskeletal conditions, with a high percentage of cases becoming chronic (pain persisting for over 3 months). The majority of chronic low back pain patients have no identified pathological cause for their pain and are commonly referred to as having 'non-specific chronic low back pain'; their care often resulting in pain management through the use of medications rather than a targeted treatment plan.

Changes in spinal muscle morphology have been well documented in those with CLBP, in particular atrophy of lumbar multifidus muscles – the key stabilisers of the spine that also provide proprioceptive feedback from the spinal column. As such, the concept that nociceptive pain is the result of poor spinal stabilisation due to reduced neuromuscular control is more than feasible.

Treatment options for these patients are limited. Physiotherapy and exercise programmes aim to improve functional stability through the rehabilitation of core muscles. However, voluntary contraction of LMM is often limited which, coupled with pain and patient compliance often limits success. The concept of implanting a neurostimulator to induce episodic contraction of LMM and thus restoring neuromuscular control has been explored, but there is no substantive evidence to date on the efficacy of this intervention.

Clinical assessment of NSCLBP patients is largely subjective in the absence of radiological findings. Mobility testing and palpation, together with patient reported measures (questionnaires) usually form the basis of evaluation. However, in evidence-based medicine, where the efficacy and effectiveness of emerging interventions are to be established, the need for functional diagnostic markers and objective assessment tools is apparent.

3.2 Aims

The aim of this thesis was to develop a series of objective clinical tests capable of assessing morphological and functional changes in muscle and movement that can be used to supplement subjective measures of pain and disability in measuring the effectiveness of treatment interventions for NSCLBP, and more specifically, neurostimulation of LMM (MNS).

The intention of MNS is to rehabilitate LMM and restore functional stability of the spine, with a consequential reduction in pain and disability, and improvement in mobility. The study protocol therefore needed to address each of these elements with the use of appropriate diagnostic markers for muscle morphology and functional dynamic stability.

3.3 Objectives

In order to understand how measures of muscle thickness, functional dynamic stability, pain and disability may contribute to a robust testing protocol, data were collected under experimental conditions from healthy subjects and those with NSCLBP at a series of time-points for longitudinal analysis. The testing protocol was then implemented using a patient receiving MNS to explore how the tests were tolerated and whether the use of such a testing regime may be feasible and appropriate in patients receiving this intervention.

Study objectives included:

i. Establishing the reliability of these tests.
ii. Investigating whether the tests can detect differences between healthy and NSCLBP populations.
iii. Investigating the relationship of test outcomes to levels of pain and disability.
iv. Investigating the feasibility of using the testing protocol in patients receiving MNS.

3.4 Hypotheses

The tests for local dynamic stability and LMM morphology will show:

1. Healthy participants are less unstable than those with NSCLBP.
2. Dual task condition reduces local dynamic stability (increases λ_{max}).
3. Lower LMM thickness in NSCLBP compared to healthy participants.
4. LMM thickness is positively related to local dynamic stability.
5. Local dynamic stability is negatively related to perceived pain.

Chapter 4 : General methodology

4.1 Chapter overview

This chapter gives an overview of the protocols and methods used throughout the studies in this thesis, together with justification for those methodologies. Specific methods used in each study will be discussed in more detail in the relevant chapters.

4.2 Methodological stance

Positivism is a philosophical ideology that recognises only that which can be scientifically verified. It develops hypotheses based on existing theory which can be tested during the research process.

The research reported in this thesis sits within a positivist paradigm – collecting and analysing quantitative data to discover differences between two populations (healthy and those with non-specific chronic low back pain) and using such data to prove or disprove specified hypotheses.

4.3 Study design overview

Figure 6 shows the phases of investigation reported in this thesis.

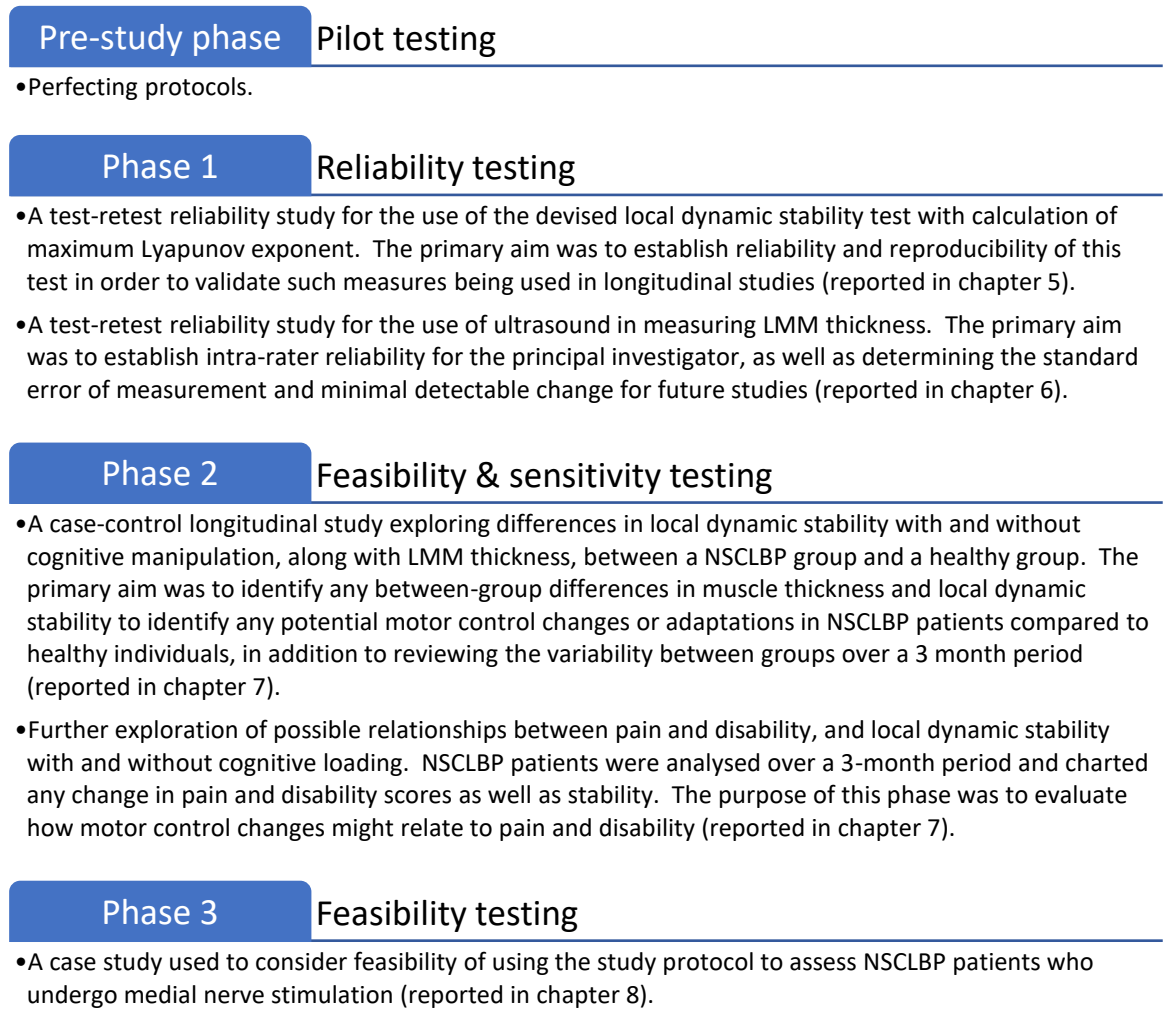


Figure 6: Phases of investigation and study details

4.4 Study populations

Study populations included people aged between 25 and 55 years of age, who were either healthy or had NSCLBP.

4.4.1 Recruitment

Convenience sampling was adopted for all studies; with confounding characteristics between groups, such as age and gender, being matched where applicable and feasible.

Participants were screened to ensure they met the inclusion/exclusion criteria and were then asked to consent to taking part in the study.

4.4.2 Inclusion/Exclusion criteria

A participant had to meet all the inclusion criteria and none of the exclusion criteria to be eligible for a study.

All criteria are detailed in Table 3.

Table 3: Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
• Aged 25-55 years. • CLBP >6 months *OR* no low back pain. • *If CLBP*: treatment plan is receiving medical management. • Capable of giving informed consent. • Able to meet requirements of the study (adequate mobility, can complete follow-up calls/visits). • Able to follow verbal instructions in English, as well as being able to read and speak English.	• Obvious mechanical instability related to pain, as identified by imaging. • Any previous spinal surgery or serious spinal injury, e.g. fracture. • Any connective tissue disorder that may affect muscle size and/or stability. • Pregnant/lactating or intending to become pregnant during the study. • Intense sports/fitness training during the previous 3 months or throughout the study. • Uncontrolled major comorbidities, e.g. psychiatric disorders.

CLBP is classified as low back pain that persists for more than three months (NICE, 2009), however CLBP may also be episodic which means pain experienced on at least half the days in the preceding period (over 6 months; Mason, 1994). On this basis, CLBP of ≥6 months was a prerequisite for the patient arm of this study to ensure the condition was long-standing enough that structural and functional alterations may be detectable. In addition, the predominant pain had to be low back pain - radiation of pain into the lower extremities was permitted as long as any structural cause had been ruled out with imaging.

Healthy control participants were required to have no low back pain. Each subject was questioned about any previous back pain that may have been experienced over the previous 2 years – maladaptive motor control strategies could still be in play and potentially confound results (Dankaerts *et al.*, 2006). They were excluded if there was any doubt over their ability to perform 'normal' pain-free movement.

Taking into account age-related changes, such as joint degeneration and changes in intervertebral motion (Wong *et al.*, 2004), whilst recognising the ability for a younger generation to compensate well for muscular weaknesses, participation was restricted to those aged between 25 and 55 years. This is consistent with other experimental literature exploring CLBP populations (Jubany *et al.*, 2017).

Pregnant or lactating females were excluded from the study due to physiological and biomechanical adaptations which may affect stability measurements.

Only 'virgin' backs, i.e. no previous spinal surgery, were included in the study. Any invasive intervention is likely to affect both structural and functional elements of the spine and may therefore confound measures. Furthermore, medial nerve stimulation is an intervention aimed at patients with virgin backs; in studying a relevant population, spinal surgery was therefore considered a reason to exclude.

4.5 Ethical considerations

Ethical approval was granted by the Health Research Authority (IRAS: 236346) and the School of Applied Sciences Ethics Committee at London Southbank University (reference number: SAS1825).

All photographs involving human subjects included in this thesis are with the permission of the individual.

It was important that there was no interference with the attached sensors during measurements, so male participants were asked to remove their top whilst female subjects were permitted to wear a vest top or open-backed hospital gown to maintain modesty. Participants were informed of this prior to giving consent.

4.5.1 Recruitment

An honorary research contract was obtained from Guys and St Thomas' NHS Trust thus allowing the principal researcher to work within the trust and have access to patient referrals and medical notes.

Potential NSCLBP participants were contacted following identification by members of the clinical care team within the pain management unit, or through the musculoskeletal (MSK) back pain physiotherapy clinic, both located at St Thomas' Hospital. The study was discussed with these patients and they were given the opportunity to ask further questions. In addition, they were given a participant information sheet which provided more detail on the study and outlined the time requirements of taking part. Patients were given as much time as they needed before committing to the study. Healthy control subjects were recruited from within St Thomas' Hospital in a similar process.

It was made explicitly clear that if they wished to discontinue their involvement in the study at any time, they were free to do so, and without having to give a reason. Their care would be in no way affected if they decided not to take part or chose to withdraw from the study at any time.

Patients were recruited according to the management plan within their standard care pathway. If the best course of treatment, in the clinician's opinion, changed during the study and they no longer met the inclusion criteria, then subjects would have been excluded at that point. Inclusion in the study did not preclude the patient from receiving best care.

4.5.2 Data Collection, Storage and Handling

All Subjects provided written informed consent prior to their participation in the study. Informed verbal consent was obtained before physical measurements were carried out, including palpation of anatomical landmarks, attaching the sensors and performing the ultrasound scan.

Participants were anonymised at source and allocated a unique study number which was used on all subsequent assessments. A list of names and corresponding identification numbers was kept separately and securely on an encrypted password protected server at London South Bank University.

All study forms (consent forms and questionnaires) were stored in the research and development allocated site file, which in turn was stored within a locked filing cupboard within a secure room at St Thomas' Hospital. This was only accessible by the researcher and other members of the research team.

Electronic data was stored on an encrypted USB stick for transfer to a secure encrypted password protected server at GSTT NHS Trust or London South Bank University.

Iron Mountain will be used to store anonymised study data for a period of 5 years following completion of the study. No personal data will be retained.

4.6 Instrumentation

Local dynamic stability measurement

- Biometrics Ltd data acquisition system comprising:
    - W4X8 DataLOG unit
    - ACL300 wired triaxial accelerometer
    - Bluetooth® USB dongle
- 2 x height-adjustable two-point tap posts and floor mats
- Developed sound test

Muscle measurement

- LOGIQ S7 (GE Healthcare) ultrasound machine
- 50mm broad-spectrum linear matrix array transducer (5-15MHz)
- 70 ° broad-spectrum convex transducer (1.8-5MHz)
- Ultrasound gel
- Adjustable plinth & pillow

Self-reported measures & study questionnaires

- Pain questionnaire using numerical rating scales (Appendix A)
- Disability questionnaire using Oswestry Disability Index (Appendix A)
- Patient Global Impression of Change Questionnaire (Appendix A)
- Informed consent form (Appendix A)
- Health questionnaire (Appendix A)

Software

- Microsoft Office – Word, Excel and PowerPoint
- IBM SPSS Statistics 21 (SPSS Inc, Chicago, IL)
- MatLab R2016b (The Mathworks Inc., Natick, MA, USA)
- Biometrics Ltd Bluetooth® DataLOG Windows application version 7.5

4.7 Data collection procedures

4.7.1 Local dynamic stability

The test protocol described below has been adapted from testing procedures developed by the research team at the Department of Training and Movement Sciences in Humboldt University, Berlin.

Participants performed a cyclical tap-test designed to promote movement through the trunk in multiple planes of motion – namely flexion, lateral flexion and rotation, principally engaging LMM muscles. Local dynamic stability of the trunk was examined using the maximum finite-time Lyapunov exponent (λ_{max}).

Participants knelt on a thin soft mat for comfort, between two posts each housing two tap-points (Figure 7-A & C). Each post was an adapted adjustable microphone stand with two moveable wooden blocks attached to act as the tap-points.

A wired triaxial accelerometer was attached to the skin using two-sided tape at the intervertebral space of T1/2 (Figure 7-B). The positioning of the tap points was standardised for all participants enhancing ecological validity by acknowledging anthropometrical measures. Each post, left and right, was positioned laterally along the arm length on the respective side at the point of the middle metacarpophalangeal joint. Both top tap-points were in line with the eyes and the bottom tap-points in line with the greater trochanter. Tap points were aligned with the aid of a laser light.

Participants were asked to adopt the kneeling-up position, keeping their knees and feet together. This position eliminated any contributory movement from the knees and ankles and ensured that it was primarily trunk movement that was being analysed (pilot testing revealed that kneeling vs standing whilst performing the tap test significantly impacted stability, p=0.001). A chair was placed around 6cm behind the subject to help prevent excessive posterior movement of the hips which helped keep movement focused within the trunk itself.

The test itself was a 3-minute repetitive tapping task whereby participants were asked to reach across with the right hand and tap the top left tap-point and then the bottom

left tap-point, and then repeat on the opposite side with the left hand (Figure 7-C). One cycle involved tapping top left (right hand), bottom left (right hand), top right (left hand) and bottom right (left hand). One test comprised 30 cycles at a rate of 10 (±1.5) cycles per minute. A frequency of 0.17Hz had previously been determined as suitable given the complexity of the task (2 targets on each side versus only one target on each side, or more simple flexion tasks used in other studies). This is not dissimilar to repetition rates (0.20-0.28 Hz) that have been previously reported to be adequate for the assessment of local dynamic stability (Dupeyron *et al.*, 2013; Graham *et al.*, 2014; Moreno Catalá *et al.*, 2018).

The tapping test was performed once under normal conditions and once with the introduction of a cognitive test (described below) with a short rest in between to allow participants to get up and move around. Order of tests was simply randomised with the toss of a coin (heads = single task, tails = dual task) to minimise any learning effect bias.

A familiarization phase of 1 minute took place before each test commenced. During this time participants practised the tapping routine alongside a metronome set at 40 beats per minute to ensure the tempo was accurately assumed. After this phase participants continued the test without acoustic signal in order to prevent normalisation of movement from external means. Each half cycle was timed (3 seconds ± 15%) and excessive deviation was reported to the subject during the measurement to guarantee a similar frequency for all participants performing the task. Each test was continued to 5-10% beyond the 3-minute mark and the final 30 continuous cycles were recorded for use in nonlinear analysis.

The dual task condition involved the introduction of an auditory cognitive task in addition to the repetitive tap task. A series of high-pitched and low-pitched sounds were delivered every 3-seconds. [The timing of these had been pre-determined during a pilot test. Sounds were tested at regular intervals, at mid-cycle or at a specific tap-point. Delivering sounds every 3-seconds caused the least amount of confusion to the rhythm of tapping. Participants were not told of the regularity of the sounds to prevent them changing their natural movements in accordance with the timing of the sounds.] The cognitive task involved simple arithmetic in response to hearing the high- and low-pitched sounds. From a starting number of 20, each high-pitched sound signified the

addition of 1 and each low-pitched sound required the subtraction of 1. Participants were required to keep a running total of the figure in addition to maintaining the regular tapping movements. Prompts were given if timing of the taps started to deviate, but otherwise verbal intervention was avoided. The verbal answer at the end of the sound test was recorded.

The cognitive task was devised to challenge mentally whilst not rendering the tap test impossible. Visual secondary tasks were not viable; therefore, an auditory or mathematical test was needed. An auditory Stroop requires specialist recordings to measure reaction time, or else constant monitoring throughout the test, thus limiting suitability in the clinical setting. Serial-subtractions are challenging but can be manipulated by the subject, such as slowing down the counting. It has also been suggested that speech can affect dual-task cost, and having an 'in-mind' test helps minimise confounding effects (Hemmati *et al.*, 2018). Pilot testing revealed that the test required constant cognitive processing through the short-interval delivery of sounds, interpretation and mathematical calculation, as well as allowing execution of the motor task.

A short while after completion of the tap-tests, the cognitive task was performed in isolation. The participant sat quietly whilst listening to the high and low-pitched sounds delivered at the same rate and in the same order as during the dual task test. The answer from this test was recorded and used as the reference value against which answers from dual task conditions were normalised.

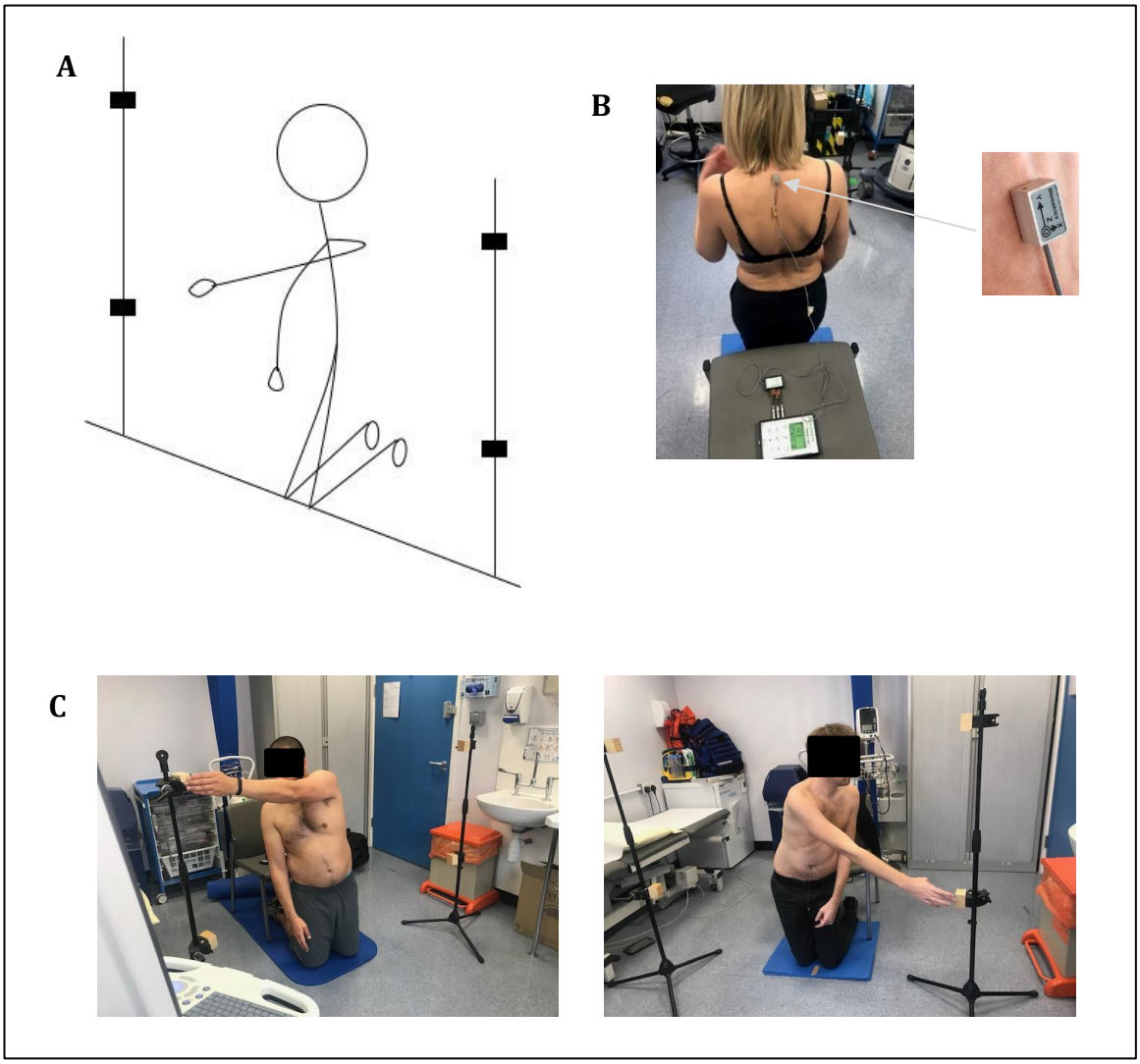


Figure 7: Tap test to measure local dynamic trunk stability.
A: Schematic drawing of setup. **B**: Positioning of accelerometer at T1/2.
C: Reaching to touch top and bottom tap-points.

4.7.2 Measurement of LMM thickness

The procedure utilised by the studies in this thesis has been based on the clinical protocols proposed by previous research in this field (Kiesel *et al.*, 2007; Stokes *et al.*, 2005; Wallwork *et al.*, 2007).

LMM thickness was measured using a LOGIQ S7 (GE Healthcare) ultrasound machine. Where feasible a 50mm broad-spectrum linear matrix array transducer (5-15MHz) was used. When deeper imaging was required a 70° broad-spectrum convex

transducer (1.8-5MHz) was used, making sure the image section to be measured was centred on the transducer to improve measurement accuracy. Static B-mode images were acquired.

Subjects lay prone with their forehead resting just above the breathing hole in the plinth, the head in the midline, and their arms resting on the plinth where comfortable. Pillows were placed under the hips/abdomen to reduce the lumbar lordosis to <10° to ensure optimal contact of the transducer.

Ultrasound gel was applied to the skin before the transducer was placed longitudinally over the midline for orientation. The spinous processes of L3, L4 and L5 were identified by moving the transducer cephalically from the sacrum and counting the vertebra. Reference points were marked on the skin. The laminae and spinous processes were then identified in cross-section by rotating the transducer through 90° whilst remaining centred on the midline. This allowed the lateral distance of the laminae from the spinous process to be noted.

The transducer was kept in the sagittal plane, moved laterally over the laminae on each side, and angled slightly medially to image the right and left multifidus muscles at L3-L4 and L4-L5 (Figure 8-B). Pressure of the transducer was kept to a minimum, whilst still maintaining good skin contact, to prevent compression of the muscle. The zygapophyseal joint was used as a consistent reference point to identify the deep border of the muscle.

Thickness of LMM was measured using on-screen callipers, between the posterior-most aspect of the zygapophyseal joint and the fascial plane between the muscle and subcutaneous tissue (Koppenhaver *et al.*, 2009b; Wallwork *et al.*, 2007) at each level (Figure 8-A & C). The mean value from 3 measurements was taken, as per the protocol suggested by the findings of the reliability study discussed in Chapter 6.

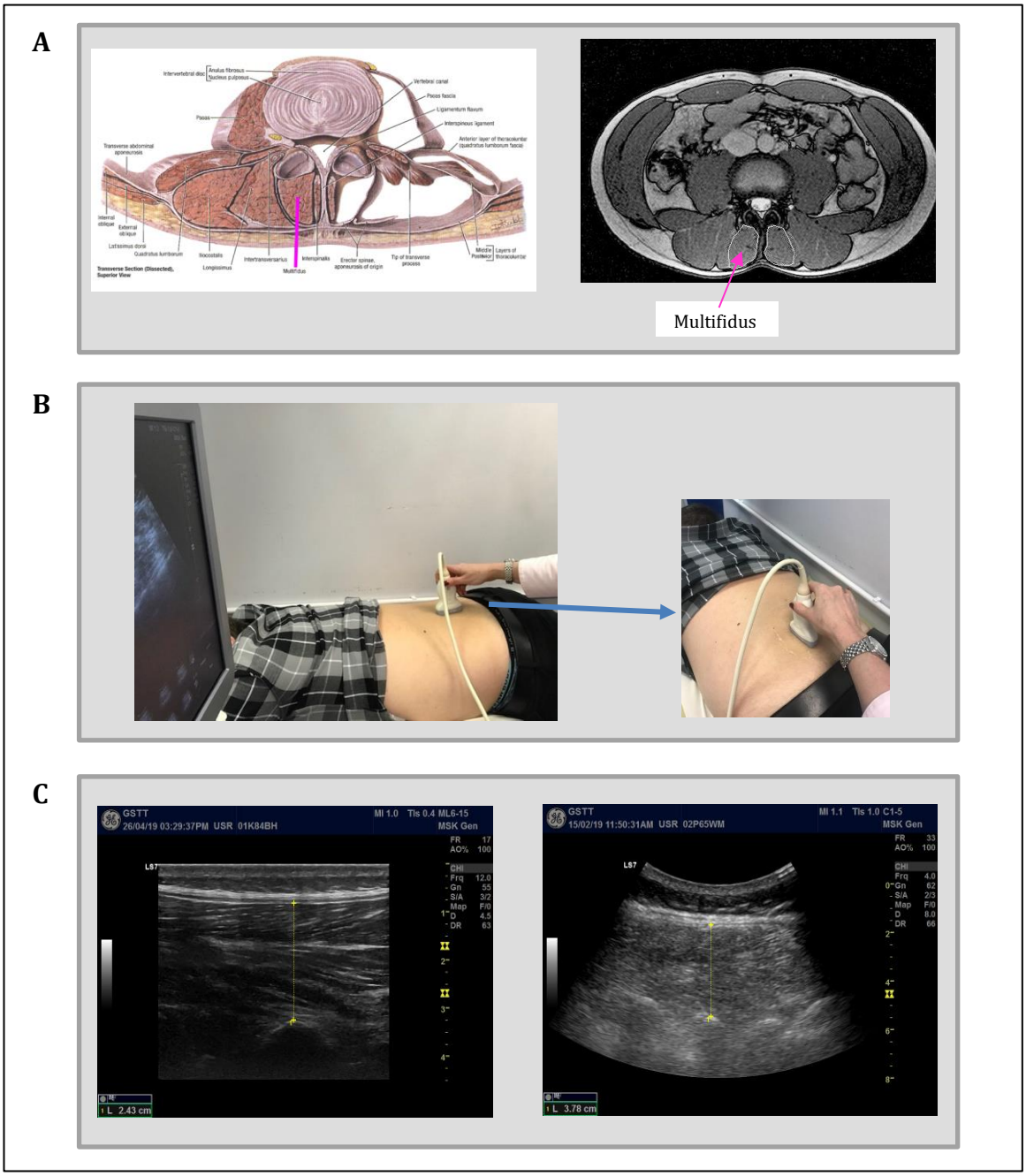


Figure 8: Measuring LMM with USI.

A: Anatomy of LMM. **B**: Positioning of ultrasound transducer. **C**: On-screen measurement of LMM thickness [Left image: linear transducer, Right image: convex transducer]

4.7.3 Pain, Disability & Global Impression of Change

Questionnaires were used to record patient reported measures (pain, disability and global impression of change).

4.7.3.1 Pain

IMMPACT recommendations state that self-report measures provide the 'gold standard' in addressing pain outcomes because they reflect the inherently subjective nature of pain (Dworkin *et al.*, 2005). Various unidimensional self-report measures of pain intensity are reported to be reliable and valid: Visual Analogue Scale (VAS), numerical rating scales (NRS) and verbal rating scales (VRS; Jensen and Karoly, 2001). However, there are important differences within VAS, NRS and VRS, such as consistency, patient preference, ease of data recording and ability to complete remotely (Jensen and Karoly, 2001) that must be considered when determining suitability of a specific scale for use within a study.

Reproducibility of NRS has been shown to be good irrespective of literacy levels (Ferraz *et al.*, 1990) whereas the test retest reliability of VAS proved higher in literate rheumatic patients ($r=0.94$, $p<0.001$) compared with illiterate patients ($r=0.71$, $p<0.001$; Ferraz *et al.*, 1990). The replicability of NRS allows scores to be completed verbally as well as written (Hawker *et al.*, 2011) and the ability to compare written and verbal pain scores with NRS has advantages over other methods. Furthermore, chronic pain patients have been shown to find NRS easier to understand and complete (de C Williams *et al.*, 2000). Overall the NRS is a simple and robust measurement method (Ostelo and de Vet, 2005).

Whilst NRS provides a snapshot view of a patient's severity of pain at that moment in time, some studies have found that NRS is less sensitive in describing the complexity of pain experienced by NSCLBP patients (Hawker *et al.*, 2011; Hush *et al.*, 2010) and consideration should be given to asking patients to rate various pain levels (e.g. least pain, pain on average and most severe pain) in varying time frames (e.g. current pain or pain over the last week; Dansie and Turk, 2013). Of course, there are some limitations with this as memories of pain may not be that accurate and are potentially influenced by changing context factors (Breivik *et al.*, 2008).

The Numerical Rating Scale (NRS) was most suited for use in this study as a patient reported measure of back pain due to data being collected both verbally and in the written format. NRS is an 11-point numerical pain rating scale that uses a 10cm line with the integers 0-10 placed at the corresponding distance, in cm, from the left end of

the line. Subjects are asked to score their pain by circling the number they feel most closely represents the level of pain they are experiencing. A score of zero indicates no pain at all, 5 resembles moderate pain, whilst 10 is ranked as the worst possible pain. Whilst the use of daily diaries is believed to be more accurate when asking about pain over a certain time period (Dansie and Turk, 2013), this was deemed an unnecessary burden for the patients in this study.

The pain questionnaire was therefore developed and given to NSCLBP participants at baseline and at 3-months. Four questions on the questionnaire required answering by marking the level of pain on the NRS as applicable. These questions were:

- How would you rate your LBP today?
- What is the worst your LBP has been in the last week?
- What is the lowest level of pain you have experienced in the last week?
- How would you rate your LBP on average?

Collected pain scores in response to these questions were to help give an overall impression of the level of pain experienced by participants and allow grouping into less severe or more severe pain groups. In addition, the pain they were experiencing on the day of testing may have had significant impact on kinematic behaviour and was therefore important to document.

Telephone questionnaires were conducted at 1-month and 2-months to maintain contact with participants. These questionnaires asked for a verbal rating of how they would score their back pain at that moment in time. This was to monitor their pain levels and track their progression during their study involvement.

4.7.3.2 Disability

Various measurements of pain related disability have been developed. Most commonly used scales to evaluate low back pain disability include Oswestry Disability Index (ODI), Roland Morris Disability Questionnaire (RMDQ) and the Quebec Back Pain Disability Scale. Davidson and Keating (2002) compared five methods of measuring low back pain disability and reported the ODI to be the most reliable and accurate in determining symptom change in patients. Furthermore, Roland and Fairbank (2000)

believe the ODI to be most clinically applicable and responsive to change in patients with persistent pain.

The ODI has been used extensively for clinical and research applications within LBP populations (Roland and Fairbank, 2000) due to its documented validity. A moderate correlation between pain intensity scores (VAS) and ODI (r=0.62) has been demonstrated (Grönblad *et al.*, 1993) and moreover, the ODI has been shown to be highly correlated with comparable test-retest reliability and internal consistency (Kopec and Esdaile, 1995).

The Oswestry Disability Index, also known as Oswestry Low Back Pain Disability Questionnaire, has proved to be a versatile questionnaire and is considered a valid and reliable method of measuring condition-specific disability (Fairbank and Pynsent, 2000). The ODI was therefore well suited for use in this study to measure the level of functional disability experienced during activities of daily living (ADL) in the chronic low back pain group.

The ODI has 10 sections relating to ADL: pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex life, social life and travelling. Patients select the most applicable statement for each activity and a score is allocated per response. An overall percentage score is calculated when all questions are answered.

ODI questionnaires were issued to NSCLBP participants at baseline and again at 3-months.

4.7.3.3 Patient Global Impression of Change

The Patient Global Impression of Change (PGIC) questionnaire is a 7-point Likert scale depicting a patient's rating of overall improvement of a condition from baseline. Patients rate their change as 'a great deal better', 'better', 'moderately better', 'somewhat better', 'a little better', 'almost the same', 'no change (or worse)'.

The use of the questionnaire is now commonplace both in clinical practice and within the research setting. Global ratings of change may be used to measure satisfaction with

treatment outcome (Ostelo and de Vet, 2005) as well as a patients perceived change in their own condition.

The reliability and validity of global ratings are still under scrutiny, and it has been suggested that global ratings often correlate with the patient's status at the time of questioning and are not an unbiased measure of change (Norman *et al.*, 1997). In fact, because of the global nature of the questionnaire, ambiguity surrounds which factors have contributed to the perceived worsening or improvement: pain, disability or mood, or a combination of these (Dworkin *et al.*, 2005). Nevertheless, Farrar and colleagues (2001) found there to be a consistent relationship between a change in pain intensity, measured by NRS, and how patients rated their improvement as measured by the PGIC. They saw this correlation regardless of study type, disease, age, sex, study result or treatment group. They purport that on average, a decrease of 2 or more points on the NRS was associated with the category 'much improved' on the PGIC, and a 4-point decrease corresponded to 'very much improved'.

PGIC was chosen for use in the study to provide some indication as to whether there was any relationship between the patients' subjective assessment of LBP progression and any changes in objective kinematic and morphological measures. In addition, stability in the cognitively loaded test may well be influenced by 'belief of wellness' and this measure may signpost any possible association.

PGIC was measured at 1-month, 2-month and 3-months. The purpose of monitoring at these time points was to gain an overall picture of a patient's perception of how, if at all, their low back pain may have changed throughout the study.

4.8 Data Processing

4.8.1 Spinal Kinematics

Three-dimensional kinematic data were collected using a Biometrics Ltd ACL300 wired accelerometer that fed into the W4X8 DataLOG unit. Data were transferred to specific DataLOG software on a PC via Bluetooth® technology. The accelerometer had

a sensitivity of ±100mV/g and an accuracy better than ±2% full scale. Calibration was performed for all components individually and normalised to 1g. Default sampling frequency was 1000Hz. Due to the small dimensions (19.0mmL x 12.7mmD x 10.9mmH), along with minimal mass (10g), it was possible to securely affix the sensor to the skin at T1/2 with double-sided tape so that activation of the paraspinal muscles did not significantly change the orientation of the unit.

DataLOG software displayed the live data graphically during testing which allowed screening for anomalies such as deviation of the sensor from its position at T1/2 or lead interference. At the end of each test, data were saved and then exported as a .txt file before being converted to a .csv file. A fourth order Butterworth 20Hz low-pass filter was applied to the measured 3D coordinates removing noise such as that caused by lead interference. This is in line with other studies measuring physiological movements of the trunk (Arampatzis *et al.*, 2017; Ekizos *et al.*, 2018).

A custom developed MATLAB programme utilised the .csv files to calculate the maximum finite-time Lyapunov exponent (λ_{max}) to assess the local dynamic stability of the trunk during the tap test. Data from the final 30 cycles were used for analysis, with the first cycles ignored to ensure that a steady-state movement pattern was achieved (Granata and England, 2006); they were resampled at 100Hz and time normalised to 18000 samples. λ_{max} was calculated according to the methods described in section 2.6.3.1.

Varying the values of the time delay, τ and the embedding dimension, m can result in very different state-space reconstructions (Kugiumtzis, 1996). It was therefore important to analyse each manipulable parameter in context, in order that they be optimised to the relevant series. Based on the notion that each dynamical system is unique, it has been postulated that each individual could be represented by a different set of parameters that would best reconstruct their data (Ekizos *et al.*, 2017). This may seem logical if a comparison of conditions is sought, i.e. within-subjects analysis, however when comparing between groups it appears preferable to use a fixed delay for all subjects (van Schooten *et al.*, 2013). Likewise, the same dimension should be used for all data to allow for comparative analysis.

For data within this thesis, *m*=3 was sufficient for all subjects, based on global false nearest neighbour analysis. This approach is supported by similar studies in the field (Arampatzis *et al.*, 2017; Ekizos *et al.*, 2018). Furthermore, high reliability has been demonstrated in studies analysing in dimension 3 (Ekizos *et al.*, 2018) arguably only in walking/running conditions, but in the absence of further evidence dimension 3 appeared suitable.

Every data set was carefully examined to ensure the algorithm had identified the true minimum value at the point where the delay was no longer increasing, and not a local minimum that may occur due to noise for example. τ was adjusted accordingly, on an individual basis, if this was found to be the case. τ ranged from 47 to 99 samples with an average of 74 samples (i.e. 1.2s). Following preliminary analysis, a fixed delay of 74, based on the overall average, was used for calculations in all subjects.

The average logarithmic rate of divergence of nearest neighbours in state space over time were calculated using the Kantz (1994) algorithm. The maximum Lyapunov exponent was then calculated from the slope of linear fit of the resulting average divergence curves in the range 0-0.5s. A smaller λ_{max} indicates a more stable system that is able to adapt locally in response to small variations or perturbations (Arampatzis *et al.*, 2017; Moreno Catalá *et al.*, 2018).

4.8.2 Ultrasound Data Processing

Three images at each level were captured, LMM thickness was measured using on-screen callipers (as described in section 4.7.2) and the mean value was recorded in an Excel database. Data entry was checked independently by a colleague for errors.

Image quality was generally assessed at the time of capture, however, where there was any ambiguity around the reference points between which to measure, a second opinion from an ultrasound-qualified colleague was sought, and agreement was made on thickness measurements.

4.8.3 Questionnaires

Questionnaire data was manually scored and inputted into an Excel database. All response data was double-checked for errors independently by a colleague.

NRS: Four scales were used to evaluate pain: pain right now, pain at worst over the past week, pain at best over the past week and typical or average pain. Each individual score was documented as well as calculating an average of the four scores to give each subject an overall pain rating. This allowed for individuals to be grouped accordingly for further analysis:

- In terms of severity: a score of 0 = no pain, a score of 1-3 = mild pain, 4-6 = moderate pain and a score of 7-10 = severe pain (Breivik *et al.*, 2008).
- In terms of change: pain stayed constant, pain worsened, or pain improved.

Various factors, including range of pain scores throughout the study (volatility of condition), overall pain score (severity of condition) and pain on day of testing were of interest in relation to kinematic measures.

ODI: Totalled ODI scores provide an overall percentage score of disability (Roland and Fairbank, 2000), with a score of 0-20% indicating minimal disability, 21-40% moderate disability, 41-60% severe disability, 61-80% crippled and 81-100% bed-bound or exaggeration of symptoms.

PGIC: A value of 1-7 was allocated to each answer, with 1 signifying no change or worsening of the condition through to 7 for much improvement. These scores provided a scale of overall perception of improvement that could be compared to kinematic measures particularly in relation to pain and disability scores.

4.8.4 Procedures to minimise bias

Due to the expertise required to operate the ultrasound machine and conduct/supervise the local dynamic stability testing, studies could not be blinded during the data collection phase. However, to minimise assessment bias, data were anonymised, and analysers were blinded to whether data related to NSCLBP or control participants.

4.9 Chapter summary

This chapter describes an innovative tap-test to measure local dynamic trunk stability through the calculation of λ_{max}, with and without dual-task conditions. These tests have been designed to be used within a clinical setting with NSCLBP patients in mind. Their use, in conjunction with other measures of muscle morphology, pain and disability, provide a battery of tests with which aspects of neuromotor control can be assessed and monitored in this patient group. Subsequent chapters will analyse reliability of the tool, along with its use in comparing healthy and NSCLBP groups.

Chapter 5 : Reliability of the maximum Lyapunov exponent in measuring local dynamic stability of trunk movement

5.1 Chapter overview

This chapter explores the reliability of repeated measurements of trunk stability through the use maximum Lyapunov exponent calculated from kinematic data collected during a kneeling cyclical tap test. Reliability values are reported with two-way mixed random effects absolute agreement intraclass correlation coefficient ($ICC_{(2,1)}$), and levels of agreement with standard error of measurement and a Bland and Altman plot.

5.2 Introduction

It is imperative that the reliability of any test or clinical tool, especially an unproven one, is established before its use for further research. Minimal measurement error is critically important during the collection of data during a longitudinal study if any trustworthy conclusions are to be drawn. Furthermore, if measures of human performance are sensitive enough to distinguish between small differences that may exist between different patient groups or following an intervention, it is essential that these potentially clinically meaningful differences are not confused with measurement error, or vice versa.

Reliability can be defined as the consistency of a test of measurement (Weir, 2005), or as the absence of measurement error (Portney and Watkins, 2014). Whilst all measurements involving human participants inherently contain a degree of error, an established acceptable level of reliability supports a test's internal validity and its effective practical use. In order to assess longitudinal within-subject changes in the clinical setting there are two types of reliability that are of most interest: absolute reliability and stability. Absolute reliability is described by Atkinson and Nevill (1998)

as the degree to which repeated measurements vary for individuals, and stability reliability similarly looks at the day-to day variability. A test-retest scenario will assess these types of reliability by analysing measurements taken on two separate occasions and determining the correlation or strength association of the two sets of data (Kimberlin and Winterstein, 2008).

Reproducibility of test outcomes are subject to measurement error, within which there are two components of variability: systematic bias and random error. Systematic bias refers to predictable errors in measurement (Portney and Watkins, 2014) with measurements differing in a particular direction (under- or over-estimation) between repeated tests (Atkinson and Nevill, 1998). Often this bias will occur because of natural performance predictors such as learning effects, insufficient recovery or fatigue, training effects or motivation (Atkinson and Nevill, 1998; de Vet *et al.*, 2006; Kimberlin and Winterstein, 2008) or due to the measurement instrument itself (Portney and Watkins, 2014). Whilst systematic bias tends to be more predictable, random error occurs owing to chance (Carmines and Zeller, 1980), and as such random errors differ in their magnitude and direction between subjects and occasions of testing (Bialocerkowski, 2008). Inherent biological or mechanical variation may be responsible for random differences between measurements, or they may arise due to inconsistencies in the measurement protocol, such as controlling posture during testing in a consistent way (Coldwells *et al.*, 1994). A robust protocol with strict procedure adherence will minimise the more obvious sources of error, but as random errors still tend to contribute more to the total error than the systematic bias the evaluation of reliability focuses on determining the amount of random error in measurements (Portney and Watkins, 2014).

The use of nonlinear time-series analysis to assess local dynamic stability of the trunk has become more popular over recent years. Many studies have employed the collection of kinetic and kinematic data from a variety of devised movement tests to calculate maximum Lyapunov Exponent to quantify the level of torso stability. If such empirical assessments are to be utilised in clinical and research environments, then the reliability of these methods must first be proven. However, there appears to be very few reliability studies demonstrating the consistency of such tests, and those that have been conducted have looked mainly at trunk stability during walking, running or use of a wobble chair. Many of these studies demonstrate wide ranging values of

intraclass correlation coefficients (ICC). For example, Lee and Granata (2008) used a wobble chair to assess trunk stability in a variety of tests of differing difficulty, each lasting between a few seconds and 40 seconds. They used 12 healthy subjects to test intrasession and intersession reliability and calculated ICC values ranging from 0.22 to 0.83. Similarly, Hamacher *et al.* (2016) and Reynard and Terrier (2014) found their ICC values ranged from poor to excellent depending on the complexity of the task. Conversely, Ekizos *et al.* (2018) calculated much higher ICC values of >0.9 during walking tasks and >0.75 in running tasks. They also found low root mean squared differences in both conditions. They do acknowledge that their ICCs were higher compared to other studies, and they attributed this in part to the fact that they recorded kinematic data over an extended time period (270 seconds) compared to the shorter collection time used in other studies. This notion has been supported by other researchers who reported that reliability increases substantially as the number of recorded steps/cycles increases (Bruijn *et al.*, 2013; Kang and Dingwell, 2006). Likewise, Lee and Granata (2008) suggested that longer trial durations may achieve improved test-retest reliability. They discussed the concept of stationarity, whereby the statistical properties no longer change over time, and state that 'brief transient movements in postural control can influence the mean and variance of a signal if the signal duration is short', which limits repeatability of stability measurements.

Reproducibility is an umbrella term that encompasses concepts of agreement and of reliability (de Vet *et al.*, 2006), both of which are important when considering the value of a test in the clinical environment. Measures of reliability are often used by researchers, with varying success, to report this level of reproducibility using a variety of statistical methods. Pearson's correlation coefficient is often seen to be used, however there is differing opinion on whether this is a suitable approach - it measures the strength of linear correlation as opposed to agreement and it is possible to have a high degree of correlation when agreement is poor (Maher, 1993). Intraclass correlation coefficient, another measure of reliability, relates to the variability between subjects and for repeated measures on a continuous scale is the most appropriate reliability parameter (de Vet *et al.*, 2006). ICC however gives no indication of the magnitude of disagreement between measurements and may therefore have less clinical relevance (Rankin and Stokes, 1998). Indeed, it has been purported that reliability measures are less important in an evaluative measurement instrument where the purpose of the clinical tool is to measure changes in health status within

patients over time; in which case parameters of agreement may be preferable (de Vet *et al.*, 2006; Guyatt *et al.*, 1987; Rankin and Stokes, 1998). Standard error of measurement (SEM) is a suitable parameter of agreement for measurements on a continuous scale, as well as Bland and Altman 95% limits of agreement tests (de Vet *et al.*, 2006; Rankin and Stokes, 1998). Whilst Bland and Altman limits of agreements (Bland and Altman, 1986) have traditionally been used to measure agreement between two different testing methods, its use within test-retest studies has been more widely observed in studies with clinical applicability (Atkinson and Nevill, 1998; Hamacher *et al.*, 2016; Rankin and Stokes, 1998; Weir, 2005).

The tap test protocol used in this test-retest study was devised to reflect the clinical situation whilst making attempts to optimise the level of reliability based on the factors highlighted above. The length of the test was set at 3 minutes, incorporating 30 cyclical movements in multiple axes. It is believed that this will provide data sets of sufficient length to improve repeatability and is in line with test-lengths used in studies utilising methods to assess stability with Lyapunov Exponent analyses (Ekizos *et al.*, 2018; Hamacher *et al.*, 2016; Reynard and Terrier, 2014). Whilst reliability may improve with more trials conducted over more days (Ekizos *et al.*, 2018) the practicality of implementing this in a clinical setting, with multiple appointments and patients in pain, is unrealistic. Therefore, this reliability study utilised a one-test-retest design which would mirror the reality of using such measures within the clinical environment or research setting using CLBP patients who may be limited in the time able to perform challenging movement tests.

The aim of this repeatability study is to establish and quantify reproducibility, and thus provide an indication of the test-retest reliability of the dynamic stability measurement.

The objectives are to calculate the intraclass correlation coefficient and the standard error of measurement, as well as look at the level of agreement between measurements taken during each session.

5.3 Methods

5.3.1 Study design

This was a single-group test-retest study that involved two testing sessions, one week apart at the same time of day.

5.3.2 Subjects

A convenience sample of twelve healthy individuals (6 male and 6 female) were recruited to take part in the study. None of the subjects had a history of low back pain or any reported spinal condition. Anthropometric data are detailed in Table 4.

Subjects provided written informed consent prior to their participation. The School of Applied Sciences Ethics Committee at London Southbank University had previously granted ethical approval of the protocol and consent form (reference number: SAS1825).

Table 4: Anthropometric data of participants

		Range
Gender	6M : 6F	
Age (yrs)	32.83 ± 9.45	25 – 53
Height (m)	1.74 ± 0.10	1.58 – 1.93
Weight (kg)	71.33 ± 13.05	53 – 92
BMI (kg/m^2)	23.47 ± 2.83	19.27 – 28.73

All figures are mean values ± standard deviation
BMI: Body mass index

5.3.3 Procedure

Participants attended two testing sessions, one week apart. Attempts were made to schedule the same day, and time of day was controlled for to minimise any potential

circadian variation in performance. They completed a demographic information sheet on their first visit and then performed one 3-minute tap-test as per the protocol described in section 4.7.1 during each session. No performance feedback was given after the first session or immediately before the second test to maintain the integrity of the test-retest reliability measure.

Following a short familiarisation period, one test under normal conditions (no dual task) was performed. Kinematic data were collected with the use of the Biometrics Ltd ACL300 wired accelerometer and W4X8 DataLOG unit. Data were processed and the maximum Lyapunov Exponent (λ_{max}) was calculated using a customised MATLAB programme. λ_{max} was calculated in dimension 3 using a fixed delay (74) as well as with individual delays. Statistical analysis was run on both data sets to determine the most reliable way to calculate λ_{max} in a longitudinal study.

5.3.4 Statistical analysis

Statistical analyses were conducted using SPSS version 21 software (SPSS Inc, Chicago, IL) and Microsoft Excel. The level of significance for all tests was set to $\alpha = 0.05$.

Descriptive statistics (mean and standard deviation) were determined for λ_{max} calculated with fixed and individual delays on two separate occasions for the group n=12.

The data were assessed for outliers, and the assumption of normality was calculated using the Shapiro-Wilk test, due to its suitability for small sample sizes (Razali and Yap, 2011).

Absolute difference in the λ_{max} values between session one and session two were found and root mean squared error (RMSE) was calculated to determine the magnitude of the variance in the calculated λ_{max} values between the two sessions. RMSE was calculated using:

$$RMSErrors = \sqrt{\frac{\sum_{i=1}^{n}(\hat{y}_i - y_i)^2}{n}}$$

Where n is the number of subjects (n=12) and $\hat{y}$ and y are the examined parameter values for each trial.

ICC estimates and their 95% confidence intervals were calculated based on a single-measures two-way mixed-effects absolute agreement model (McGraw and Wong, 1996) or ICC $_{(2,1)}$ (Shrout and Fleiss, 1979). Benchmark values for correlation coefficients, according to Portney and Watkins (2014) were as follows:

<0.25	Little or no relationship
0.25-0.5	Fair relationship
0.5-0.75	Moderate to good relationship
>0.75	Good to excellent relationship

The level of agreement between within-subject measures was quantified by standard error of measurement (SEM) calculations and visually illustrated via a Bland and Altman plot. For estimating the SEM, the standard deviation from the first session and the test-retest reliability index obtained were used (Beninato and Portney, 2011) in the following equation:

$$SEM = S_{baseline} \times \sqrt{(1-ICC)}$$

Where $S_{baseline}$ corresponds to the standard deviation of the first session.

5.4 Results

λ_{max} values calculated with fixed and individual delays at each time point for each subject, along with mean values and standard deviations are presented in Table 5.

Table 5: Individual λ_{max} values calculated with fixed and individual delays, with mean values and standard deviations

Subject	Fixed delay		Individual delays	
	Measurement 1	Measurement 2	Measurement 1	Measurement 2
1	5.448	4.874	5.481	4.860
2	4.751	4.024	4.904	4.018
3	5.550	5.606	5.754	5.683
4	4.767	4.615	4.753	4.485
5	5.455	5.132	5.495	5.173
6	6.724	6.015	6.777	5.897
7	4.981	5.011	5.075	5.088
8	4.244	4.352	4.376	4.400
9	4.413	4.049	4.708	4.255
10	5.496	4.885	5.478	4.759
11	4.652	5.364	4.640	5.224
12	4.546	4.471	4.720	4.581
MEAN	5.086	4.866	5.180	4.869
SD	0.688	0.608	0.661	0.568

SD: Standard deviation

Over the 24 trials λ_{max} ranged from 4.024 to 6.724 (fixed delays) and 4.018 to 6.777 (individual delays). Calculating λ_{max} with individual delays generally produced higher values. There was only one subject who produced a λ_{max} of >6, and with median values of 4.880 (FD) / 4.882 (ID) this suggests that this may be an unusually high reading. However, the data for this subject were not identified as outliers when calculated using fixed delays, and as repeat test data were similarly high, they were included in the analysis. Data were assumed to be normally distributed: $p>0.05$ for the Shapiro-Wilk test. Descriptive statistics are represented visually in Figure 9.

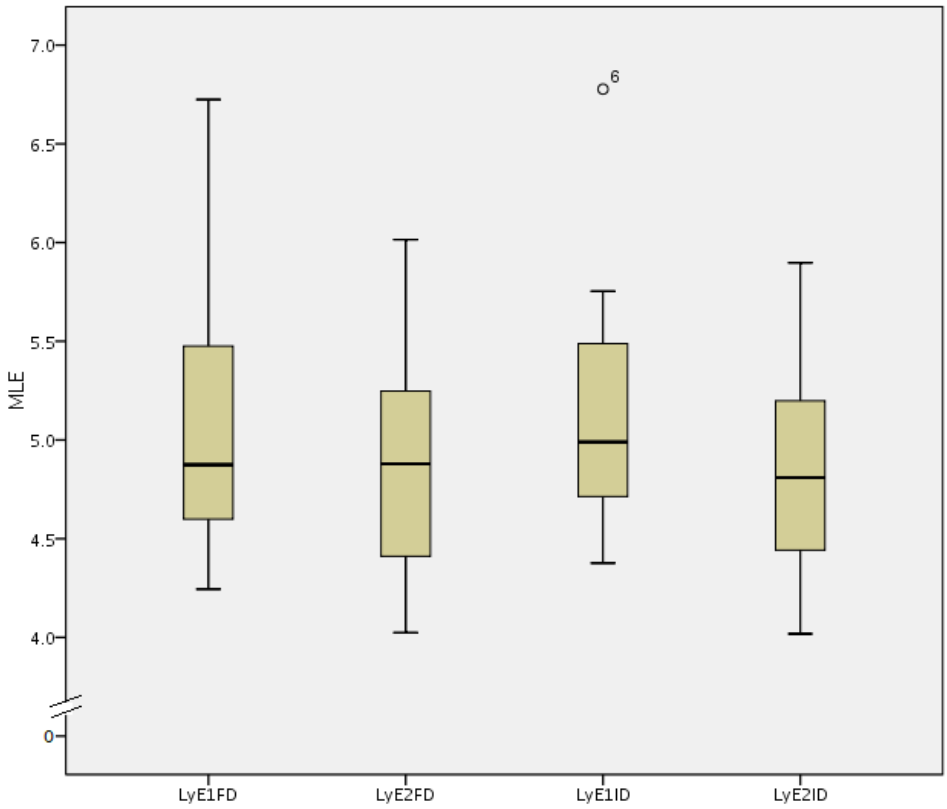


Figure 9: Boxplot depicting mean maximum Lyapunov exponent (MLE) values with standard deviation errors, collected in session 1 (LyE1) and in session 2 (LyE2) calculated with both fixed delays (FD) and individual delays (ID)

The Bland Altman plots shown in Figure 10 illustrate the bias and degree of agreement (± 95%) for λ_{max} calculated with fixed and individual delays. The plots show visually that the magnitudes of the differences are fairly constant throughout the range of measurement, i.e. differences are not related to the size of the λ_{max} value. The limits of agreement are wide; however, this could be influenced by the relatively small sample size used. The range of agreement is wider when using individual delays to calculate λ_{max}.

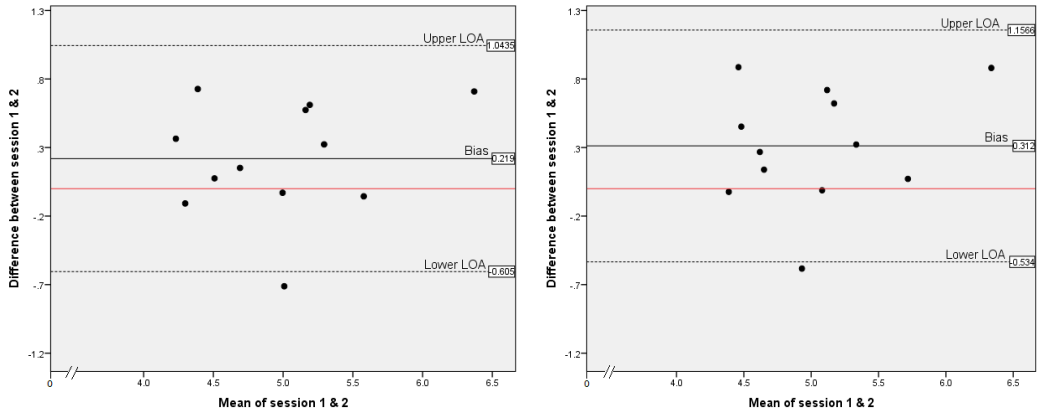


Figure 10: Bland Altman plot for MLE data
Calculated with fixed delays (left) and individual delays (right) with representation of Limits of agreement (LOA) from −1.96*sd* to +1.96*sd*

Within-subject reliability scores (ICC), absolute difference (RMSE), internal consistency (Cronbach's α) and Standard error of measurement are reported in Table 6.

Table 6: Within-subject reliability results for local dynamic stability during the tap test

	ICC (95% CI)	**RMSE**	**Cronbach's α**	**SEM**
λ_{max} FD	0.760 (0.362 - 0.924) p<0.05	0.458	0.883	0.337
λ_{max} ID	0.682 (0.159 - 0.900) p<0.05	0.517	0.860	0.373

FD: fixed delay, ID: Individual delays
ICC: Intraclass correlation coefficient, CI: Confidence intervals
RMSE: Root mean squared error
SEM: Standard error of measurement

Calculating λ_{max} using fixed delays improved the level of reliability, with an ICC value of 0.760, demonstrating a good to excellent relationship between repeated measures. Internal consistency of measures was also excellent (Cronbach's $\alpha = 0.883$).

Absolute difference between within-subject repeated measures ranged from 0.030 to 0.727, with a RMSE of 0.458. The SEM of 0.337 represented a measurement error of approximately 6.63%.

5.5 Discussion

Measurement of trunk movement and quantification of local dynamic stability is challenging due to vast differences in research methodologies as well as complexity and variability of postural coordination. Research in this field is further obfuscated when studying subjects in pain. It has been noted that postural coordination is altered in those experiencing low back pain, potentially due to a reduced capacity to make anticipatory adjustments (Jacobs *et al.*, 2009). Conversely, healthy individuals have demonstrated less deterministic (i.e. more random) spinal movement during weighted lifting tasks than NSCLBP subjects (Dideriksen *et al.*, 2014). It is therefore essential that the reliability of any measure of local dynamic stability, particularly a novel one intended for use in a clinical situation, is established before its use in further research.

The primary aim of this study was to evaluate the within-subject between-day consistency of measures of local dynamic stability using a 3-minute functional tap-test, with two slightly different methods of calculating λ_{max} (using fixed or individual delays). The examination of ICCs between tests is considered to be a valid statistical procedure to determine strength of relationship between measurements (Vincent and Weir, 2012). The results show a moderate to good relationship (ICC = 0.682) between repeated measures when using individual delays in the calculation of λ_{max}, with reliability improving to good to excellent (ICC = 0.760) when using fixed delays. The use of individual delays when measuring λ_{max} longitudinally within subjects seems logical, however, this method poses limitations when drawing comparisons between groups. It makes more sense to standardise elements of the calculation, by fixing the delays to minimise the error of measurement, thereby improving reliability.

Cronbach's alpha was high for both fixed and individual delays (α = 0.883 and 0.860 respectively) suggesting excellent internal consistency of measurements.

Using fixed delays to calculate λ_{max} generally produced slightly lower absolute differences between measurements taken in session 1 and session 2. Root mean squared error between test measurements is considered an appropriate criterion to describe the variation of a parameter in absolute terms (Aggeloussis *et al.*, 2010). The typical within-subject difference did not exceed 0.727, with the RMSE being 0.458. The magnitude of difference did not appear to be related to the value of λ_{max} suggesting that differences between measurements were subject specific. Analysis shows the 95% confidence intervals to be wide; likely due to the small sample size used in this study. Altman (1991) suggest that the sample size should be large enough, preferably >50, to estimate the limits of agreement well. Rankin and Stokes (1998) advise against calculating confidence intervals in studies with a small sample size as the wide values can be misleading. As such, the confidence intervals/limits of agreement provided in this analysis should be interpreted with caution.

Comparison of the reliability of λ_{max} with previous studies is difficult due to the use of a novel 3-dimensional tap test that demands flexion/extension, lateral flexion and rotation of the lumbar spine. Other studies have examined λ_{max} reliability during walking and have reported moderate to good (0.53 – 0.68; Reynard and Terrier, 2014; van Schooten *et al.*, 2011), and good to excellent (0.971 – 0.985; Ekizos *et al.*, 2018) intersession ICC values. Lee and Granata (2008) utilised a 40 second wobble chair task and reported a wide variety of inter-session reliability – they found little or no relationship (ICC 0.22-0.31) from kinematic data and good to excellent reliability (ICC 0.75-0.83) from kinetic data. The ICC values calculated from data collected in the current study are not dissimilar from those reported in previous studies. Reliability has been reported to improve when using longer testing cycles (Bruijn *et al.*, 2009; Kang and Dingwell, 2006). Ekizos *et al.* (2018) recorded kinematic data for 270 seconds which they suggest contributed to the higher ICC values, whilst Lee and Granata (2008) used a shorter testing cycle (40s) and recognised that this may have been a contributing factor to their low ICC values. Despite the tap-test being a complex manoeuvre, measuring over a 3-minute period may have improved the test-retest reliability in this study.

The test-retest ICC results suggest that the accelerometer consistently records trunk movement during repeated testing. Dissociation of measurement error from true movement variability is difficult, however the use of healthy subjects with no pain or musculoskeletal issues helps ensure that the natural variability in movement during the tap-test is captured. The complexity of the task may also lead to greater variability and decreased regularity. However, the RMSE of 0.458 and standard error of measurement was calculated at 0.337 which equates to approximately 6.63%, may suggest that healthy individuals perform the test in a relatively similar manner each time.

Differences in within-subject test-retest data may potentially be attributed to the nature of the theoretical concept of the used Lyapunov calculation whereby time series analysis tries to identify the true dynamics of a system from the observed time-ordered data (Ekizos *et al.*, 2018). λ_{max} may be altered by not only the state of the system but also the component of the system under measure. Ekizos *et al.* (2018) identified up to a 13.3% difference in λ_{max} values in a walking task when placing marker sets in different locations. Erroneous sensor placement could therefore affect approximation of the true dynamics of the system. Whilst several factors may influence the accuracy of the placement of the accelerometer, steps were taken to minimise these during the study design. The small size of the Biometrics 3D accelerometer together with its location helps to negate non-related movement of the device during the tap-test. The sensor sits in the intervertebral space of T1/2 to reduce the effect of contracting paraspinal muscles or spinous process rotation. Minimal anatomical knowledge or palpatory expertise is required to locate the T1 and T2 vertebrae, meaning accuracy of sensor placement should be fairly high. However, adipose tissue is cited as a source of potential error for sensor marker placement and accuracy (Peters *et al.*, 2010). The increased soft tissue thickness may reduce accuracy of palpation and may in turn also contribute to local movement or roll of the accelerometer. The mean BMI of subjects in this study was 23.47kg/m^2 $\pm$ 2.83, which sits within the healthy range (20-25kg/m^2). However, one subject had a BMI >27 and another >28, both classified as being overweight. On inspection of the data for these subjects the absolute difference of the λ_{max} measured at session 1 and 2 was 0.323 and 0.075, implying that in these cases sensor placement was accurate and there was minimal, if any, interference due to increased BMI.

The findings of the current study are further supported by the outcomes from the study described in Chapter 7. The healthy control group, n=17, performed repeated measures of the tap-test: at baseline and again at 3-months. Whilst the level of variability is likely to be higher over a longer period of time, the intraclass correlation coefficient remained good to excellent, ICC = 0.777, and had narrower confidence intervals, 0.507 – 0.910 (although this may be due to the larger sample size). Furthermore, the RMSE was 0.503 which is similar to that found in this study. These results were found from a larger sample with a wider age range and a higher mean BMI, with 3 participants registering as obese. These outcomes suggest that this measure of λ_{max} may be used in heterogenous groups and reinforce the reliability of this measure.

5.5.1 Limitations

It is generally accepted that approximately 5o subjects are required for true accuracy in reliability research (Altman, 1991; Hopkins, 2000). The small sample size (n=12) of this study therefore potentially compromises the precision and applicability of its findings. However, similar findings of reliability from another larger cohort (n=17) performing the same repeated measures, reinforces the validity of the findings in the current study.

The use of a single rater in this study limits the application of these results. Further study of inter-rater reliability would be useful in order to study the random effects. The main rater-effect would be the placement of the accelerometer. The precise objectivity of the protocol, together with minimal data interpretation should help to lessen any rater-error. For future research it would be prudent to conduct further reliability analysis using multiple raters, however, for the purpose of studies described within this thesis the reliability is valid due to the use of the same rater throughout.

The presence of a learning effect is possible, whereby subjects may have become accustomed to the tap-test and adjusted their natural movement strategies accordingly for the second test. Having minimal practise time and a week between tests helped minimise any potential effect. Moreover, the results appear to support the absence of

any learning effect as there was no trend identified in the difference direction of λ_{max} between sessions 1 and 2.

Both Reynard and Terrier (2014) and Ekizos *et al.* (2018) reported improved reliability when using averaged measures as opposed to single measures. The intended use of the protocol described in section 4.7.1 is for the clinical evaluation of patients with NSCLBP. The relatively demanding nature of the 3-minute tap-test, together with the presence of pain, naturally precludes the suitability of asking patients to perform repeated measures within one session. It may be possible in future research to conduct multiple tests during several clinic visits pre-intervention, days or weeks apart to provide a baseline measure, and again at certain intervals post-intervention. This may provide more accurate local dynamic stability data for patients.

5.5.2 Research implications

Interventional or prospective studies examining local dynamic stability require a valid and reliable tool for measurement. Tracking progress following intervention, both within clinical and research settings, generally utilises repeated measures experimental designs, during which the consistency of the measure is crucial. This method of capturing kinematic data and calculating maximum Lyapunov exponent provides a robust measure of local dynamic stability.

The protocol may be used to assess whether differences can be identified between different populations, for example, healthy versus NSCLBP, as well as measuring within-subject changes, with or without intervention. Further study may also be required to establish whether increasing the number of measures over a series of days may improve the accuracy of this measurement method.

5.6 Conclusion

The data presented in this study indicate that the local dynamic stability measure derived from kinematic 3-dimensional acceleration time series, from the 3-minute tap-test calculated with fixed delays is reliable in healthy adults and is suitable for use in studies with a repeated measures design.

Chapter 6 : Reliability of ultrasound imaging in measuring lumbar multifidus muscle thickness

6.1 Chapter overview

This chapter explores the intra-rater reliability and reproducibility of measuring LMM thickness using USI. Intraclass correlation coefficients, standard error of measurement and minimal detectable change are reported.

6.2 Introduction

The reliability of USI to measure LMM thickness has been well documented (Hodges, 2005) with intra-rater reliability generally being considered to be more reliable than between examiners. Nevertheless, inter-rater reliability has still been reported as being good (Skeie *et al.*, 2015), with the mean difference between examiners being low, and the Limits of Agreement narrow in range.

Several researchers have conducted studies of varying quality to examine the intra-rater reliability of muscle thickness measurements with USI, however, only a handful can be considered to be of high-quality (Hebert *et al.*, 2009). The range of intraclass coefficients for intra-rater reliability of acquisition and measurement was reported to range from 0.62 to 0.97 among the higher quality papers (Hides *et al.*, 2007; Hodges *et al.*, 2006; Pressler *et al.*, 2006; Teyhen *et al.*, 2005). These studies examined both trunk and abdominal musculature, and for those specifically evaluating LMM, the ICC coefficients were generally higher (Kiesel *et al.*, 2007; Van *et al.*, 2006).

It has been suggested that the accuracy of USI is largely operator-dependent, yet despite this, there appears to be little difference in the reliability between novice and experienced examiners. The results from a study by Wallwork *et al.* (2007) showed that a novice and experienced assessor were both able to reliably measure LMM

thickness using USI; using an average of 3 trials per rater produced high inter-rater reliability scores (ICC >0.96), with differences in measurements between the two raters equating to <0.07cm.

Some authors have suggested that by averaging measures of LMM thickness reliability is improved. Koppenhaver *et al.* (2009b) specifically studied the effect of averaging multiple trials on measurement error during USI measurements to calculate percentage thickness change between rest and contraction. They concluded that intra-examiner measurement precision appeared to be optimised by using an average of 3 consecutive measurements. Similarly, Wong *et al.* (2014) studied LMM at rest and reported that a reduction of standard error of measurement was observed when multiple measure averages were used. They reported mean reductions in SEM of 25.8% when using the mean of 2 measures, and of 32.6% when using the mean of 3 measures.

Whilst USI appears to be a reliable method of measuring LMM thickness, there remain questions over potential morphological between-day differences, such as those caused by circadian rhythm or levels of hydration; some of which may be difficult to control for.

The purpose of this study was to determine the operator (test-retest) reliability of measuring lumbar multifidus thickness using ultrasound imaging in preparation for the main study, in addition to establishing the measurement error that will be relevant to any changes in muscle thickness during future longitudinal studies.

The researcher has extensive clinical experience along with the necessary anatomical knowledge, has been professionally trained in the use of diagnostic ultrasound, and conducted all ultrasound imaging in all studies described within this thesis.

The study had two specific objectives:

1. To study the intra-examiner reliability of using ultrasound imaging to measure lumbar multifidus thickness on two separate occasions.

2. To calculate the standard error of measurement and establish the minimal detectable change, along with the least number of measurements required to provide reliable, meaningful parameter values.

6.3 Methods

6.3.1 Study design

The study was a single-group repeated-measures design, involving two visits a week apart, at the same time of day.

6.3.2 Subjects

A convenience sample of twelve healthy individuals, 6 male and 6 female, were recruited to take part in the study. None of the subjects had a history of low back pain or any reported spinal condition. Demographic characteristics of participants are detailed in Table 7.

Subjects provided written informed consent prior to their participation. The School of Applied Sciences Ethics Committee at London Southbank University had previously granted ethical approval of the protocol and consent form (reference number: SAS1801).

Table 7: Demographic Characteristics of Participants (n=12)

		Range
Gender	6M : 6F	
Age (yrs)	31.0 ± 6.2	25 - 43
Height (m)	1.69 ± 0.09	1.55 – 1.83
Weight (kg)	64.8 ± 12.5	44.0 – 89.5
BMI (kg/m^2)	22.6 ± 2.8	18.3 – 28.2

All figures are mean values ± standard deviation

BMI: Body mass index

6.3.3 Procedure

Participants completed a demographic information sheet before measurements were taken.

The full protocol for LMM measurement is described in section 4.7.2. In summary, subjects lay prone on an examination couch with the head in the midline and forehead, arms and legs resting on the couch. Pillows were placed under the abdomen to eliminate the lumbar lordosis and ensure optimal contact of the transducer. The spinous processes of L3 and L4 were identified though palpation and marked on the skin.

To view and measure multifidus, a 50mm linear array ultrasound probe, frequency 3-13mHz, was used to acquire B-mode static images (ultrasound device: Esaote MyLab™ Gamma, Genoa, Italy).

Parasagittal placement of the transducer verified the location of the L3 and L4 spinous processes. With the relevant spinous process located as the midpoint, the transducer was moved laterally, still in the longitudinal plane, to view the multifidus muscle (Figure 8-B). Pressure of the transducer was kept to a minimum, whilst maintaining good skin contact, to prevent compression of the muscle. The zygapophyseal joint was used as a consistent reference point to identify the deep border of the muscle.

For each subject, image acquisition of multifidus muscle thickness at L3 and L4 bilaterally was performed ten times at each level on one occasion and repeated a week later. Images were blinded by assigning a unique identification code. Multifidus thickness was then measured using a customised routine written in MatLab (version R2016b, The Mathworks Inc., Natick, MA, USA), by calculating the distance between the apex of the zygapophyseal joint to the plane between the thoracolumbar fascia and the subcutaneous fat (Figure 8-C; Koppenhaver *et al.*, 2009a; Wallwork *et al.*, 2007). The examiner was also blinded to measurement values at the time of measuring.

6.3.4 Statistical analysis

Statistical analyses were conducted using SPSS version 21 software (SPSS Inc, Chicago, IL) and Microsoft Excel.

Descriptive statistics (mean and standard deviation) were determined for LMM thickness at each level on the two separate occasions. Cronbach's alpha was calculated to indicate the internal consistency of measurements within subjects.

Intraclass correlation coefficients (ICC) with 95% confidence intervals were calculated to examine the intra-rater reliability of multiple lumbar multifidus thickness measurements in participants during a single session and between two sessions. ICC estimates were based on an absolute agreement, two-way mixed-effects model (ICC_3), with $ICC_{(3,1)}$ used for single measures and $ICC_{(3,k)}$ used for average measures. The two-way mixed-effects model was determined to be the most appropriate method of testing intra-rater reliability with multiple scores from the same rater, as no generalisation was required (Shrout and Fleiss, 1979). Similarly, this model is applicable in a test-retest scenario where repeated measures are not randomised.

The standard error of measurement (SEM) was calculated for measurements of within sessions and between days, using the equation:

$$\text{SEM} = S_x\sqrt{1 - r_{xx}}$$

Where: S_x is standard deviation and r_{xx} is reliability.

The SEM gives an indication of absolute reliability – it provides the measurement error in the same units as the actual measurement. This type of reliability could be deemed as being more clinically applicable when compared to a relative reliability co-efficient value, such as ICC (Donoghue *et al.*, 2009).

In addition, minimal detectable change (MDC_{95}) was calculated using the equation:

$$MDC_{95} = 1.96 \times \text{SEM} \times \sqrt{2}$$

Where 1.96 corresponds to the level of confidence adopted (95%) and $\sqrt{2}$ represents a correction factor for repeated measurements.

The MDC_{95} provides an estimation, with a 95% degree of confidence, of the smallest objective change in thickness that may be attributable to actual change rather than due to random measurement error. The MDC_{95} can be interpreted in the following way (Furlan and Sterr, 2018):

$-MDC_{95} \leq \Delta < +MDC_{95}$	Change due mostly to random measurement error
$-MDC_{95} > \Delta \geq +MDC_{95}$	Change due mostly to real modifications in performance

The least number of ultrasound measures (K) which could provide reliable thickness values was determined using the Spearman-Brown prophecy formula:

$$K_y = \frac{(ICC_{conf}\ (1-ICC_y)}{(ICC_y\ (1-ICC_{conf})}$$

Where: y is the examined parameter value, ICC_y is the calculated intraclass correlation coefficient of y, and the ICC_{conf} is the acceptable level of confidence. ICC_{conf} was set at 0.80 (Süptitz *et al.*, 2012).

A two-way repeated measure analysis of variance (ANOVA) was used to determine whether there was any interaction between day and measurement number, on muscle thickness values within subjects. If differences between measurements were found, a post hoc test (Bonferroni) was applied in order to determine where these differences occurred.

6.4 Results

Raw data is contained within Appendix C.

Mean values with standard deviations and intraclass coefficient correlations with corresponding 95% confidence intervals (lower bound and upper bound) are presented in Table 8 for within day and between-days measurements. Figure 11 visually represents between-day differences.

Table 8: Mean ± SD values for LMM thickness at each spinal level and Intra-rater reliability for within-day and between-day measurements.

	Within-day				**Between-day**	
	DAY 1		DAY 2			
	Mean ± SD	$ICC_{(3,k)}$ (95% CI)	Mean ± SD	$ICC_{(3,k)}$ (95% CI)	Mean ± SD	$ICC_{(3,k)}$ (95% CI)
L3_Left	2.73 ± 0.41	0.985* (0.968-0.995)	2.72 ± 0.42	0.991* (0.981-0.997)	2.72 ± 0.41	0.984* (0.967-0.994)
L3_Right	2.78 ± 0.42	0.992* (0.984-0.997)	2.79 ± 0.41	0.995* (0.990-0.998)	2.78 ± 0.41	0.988* (0.976-0.996)
L4_Left	3.02 ± 0.45	0.996* (0.991-0.999)	3.04 ± 0.47	0.996* (0.992-0.999)	3.03 ± 0.45	0.990* (0.980-0.997)
L4_Right	3.04 ± 0.46	0.996* (0.991-0.999)	3.08 ± 0.44	0.996* (0.992-0.999)	3.06 ± 0.44	0.991* (0.982-0.997)

Mean & SD (Standard deviation) reported in cm

$ICC_{(3,k)}$: Intraclass correlation coefficient

* ICC is statistically significant at $p<0.001$

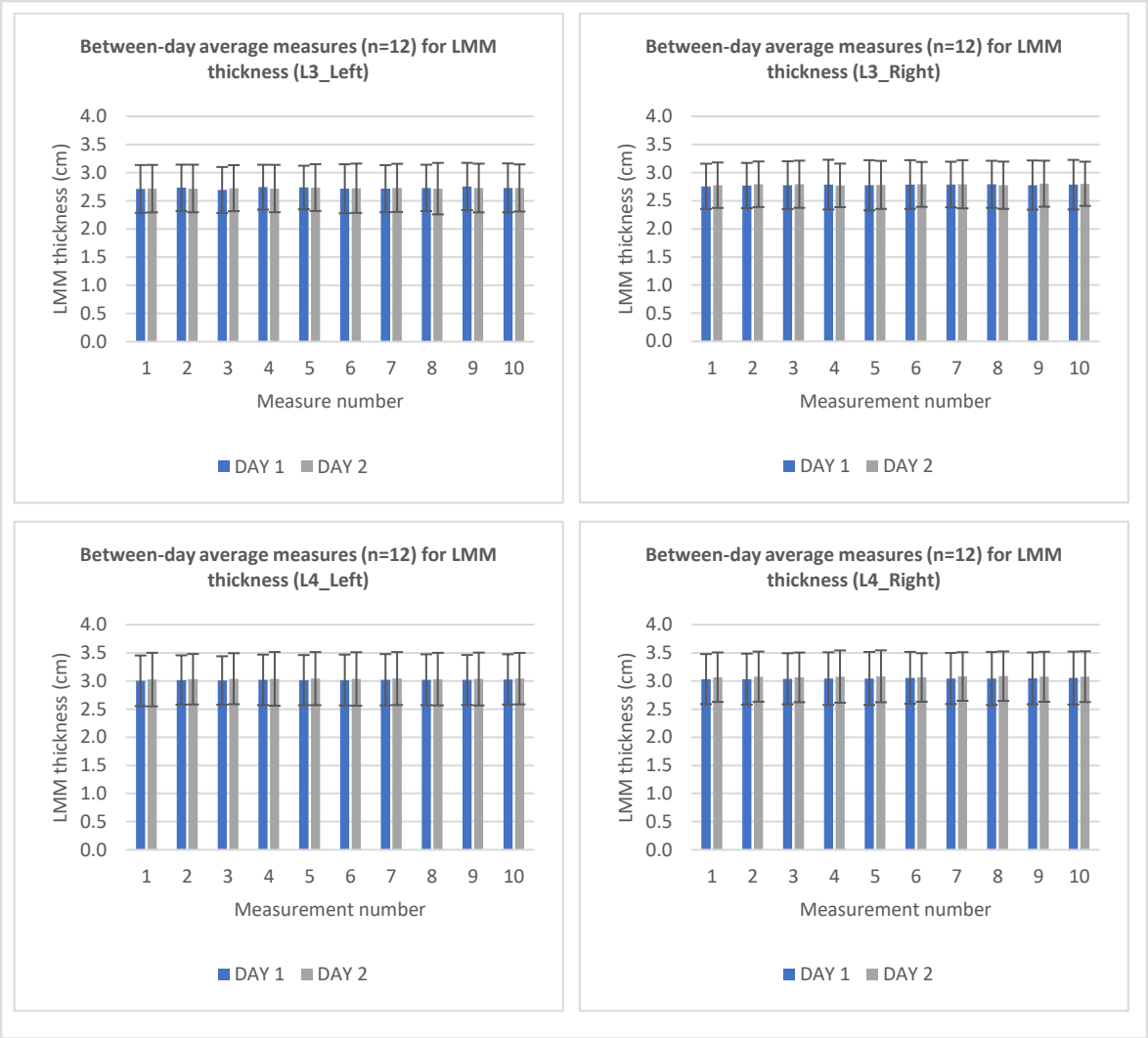


Figure 11: Between-day measures for repeated LMM thickness measurements for each spinal level.
Values are expressed as means with SD (error bars). No significant effects of trial number or time on measurements, or any significant trial*time interactions at any level.

LMM thickness data for each level was subjected to a two-way ANOVA with repeated measures, with measurement trial and time as within-subject factors. This revealed:

L3 Left LMM thickness

- No significant effect of trial number, $F(9,99)=.916$, $p=.514$, $\eta_p^2 =.077$.
- No significant effect of time, $F(9,99)=.015$, $p=.904$, $\eta_p^2 =.001$.
- No significant interaction of trial*time within subjects, $F(9,99)=1.034$, $p=.419$, $\eta_p^2 =.086$.

L3 Right LMM thickness

- No significant effect of trial number, $F(9,99)=1.584$, $p=.130$, $\eta_p^2=.126$.
- No significant effect of time, $F(9,99)=.201$, $p=.662$, $\eta_p^2=.018$.
- No significant interaction of trial*time within subjects, $F(9,99)=1.069$, $p=.392$, $\eta_p^2=.089$.

L4 Left LMM thickness

- No significant effect of trial number, $F(9,99)=.721$, $p=.688$, $\eta_p^2=.062$.
- No significant effect of time, $F(9,99)=.901$, $p=.363$, $\eta_p^2=.076$.
- No significant interaction of trial*time within subjects, $F(9,99)=.396$, $p=.934$, $\eta_p^2=.035$.

L4 Right LMM thickness

- No significant effect of trial number, $F(9,99)=.720$, $p=.690$, $\eta_p^2=.061$.
- No significant effect of time, $F(9,99)=3.880$, $p=.075$, $\eta_p^2=.261$.
- No significant interaction of trial*time within subjects, $F(9,99)=.879$, $p=.547$, $\eta_p^2=.074$.

Clinically important values: SEM, MDC_{95} and minimum number of trials required are reported in Table 9.

Table 9: Clinically important values

	Within day						**Between day**		
	DAY 1			DAY 2					
	SEM	MDC_{95}	SBP	SEM	MDC_{95}	SBP	SEM	MDC_{95}	SBP
L3_Left	0.05	0.14	1	0.04	0.11	1	0.05	0.14	1
L3_Right	0.04	0.10	1	0.03	0.08	1	0.04	0.12	1
L4_Left	0.03	0.08	1	0.03	0.08	1	0.05	0.12	1
L4_Right	0.03	0.08	1	0.03	0.08	1	0.04	0.12	1

SEM: Standard error of measurement in cm

MDC_{95}: Minimal detectable change (95% confidence) in cm

SBP: Spearman-Brown Prophecy – minimum number of trials required

6.5 Discussion

The primary aim of this study was to evaluate the intra-rater reliability of measuring LMM thickness with USI on separate occasions. The results show excellent reliability of USI to measure LMM thickness across continuous trials (mean ICC was 0.992 on day 1 and 0.995 on day 2) and equally excellent reliability in measures between-day, across two sessions (mean ICC of 0.988). These are similar findings to those reported by other researchers in this field (Koppenhaver *et al.*, 2009a; Van *et al.*, 2006; Wong *et al.*, 2013). Furthermore, there were no significant effects of trial number or time ($p>0.05$) or any significant trial*time interaction ($p>0.05$).

Between-day reliability can be influenced by hydration of tissues, subject positioning as well as location and angle of transducer application (Coldron *et al.*, 2003; Larivière *et al.*, 2013). Vigilance in controlling influential variables whilst conducting measures help to reduce potential sources of error. Using a similar time of day for repeated measures potentially helped mitigate the effect of tissue changes due to hydration (although water intake was not monitored) or diurnal variation. Whilst this was controlled for in this study, this may not be possible in future measurements, and should be considered if readings vary more than expected. A strict protocol should be adhered to when positioning the subject, ensuring that the lumbar lordosis is flattened as far as possible. Location and angle of transducer pose potential sources of error; however, it is thought that the easily defined superior-inferior boundaries of the LMM help minimise measurement inaccuracies. Adopting a strategy for the placement of the ultrasound transducer improves reliability: the facet joint of interest should be placed directly in the centre of the image and images should be optimised by altering transducer angle so that the bony facet joint and superior fascial lines are hyperechoic (Stokes, 2006). This will assist in placement replication between measurements.

Linear transducers are known to provide superior image clarity and improved accuracy of measurements compared to curvilinear probes. Whilst Warner *et al.* (2008) found there to be little difference in reliability of measures using linear and curvilinear transducers, the default probe should be linear to ensure true and accurate linear measures. However, anatomical factors such as an increased lumbar lordosis or significant adipose tissue lying superficial to LMM may require the use of a curvilinear

transducer. In these instances, centralisation of the zygapophyseal joint in the image is essential in acquiring a true and accurate measure of thickness.

In addition to determining reliability, clinically important values were calculated for use in determining a clinically meaningful change in future study. These included standard error of measurement, minimal detectable change and least number of measurements required to provide reliable parameter values. The standard error of measurement was generally low: mean SEM on day 1 was 0.04cm, 0.03cm on day 2 and between-day measures showed a mean SEM of 0.05cm. These SEM values are consistent with those reported in previous research (Koppenhaver *et al.*, 2009a; Wallwork *et al.*, 2007; Wong *et al.*, 2013). Mean minimal detectable change with a 95% degree of confidence ranged from 0.09cm (day 2) to 0.13cm (between-days); indicating a maximum relative MDC of 5.15%. The least number of trials required to provide reliable measurement data was 1 in all cases.

Calculations using the Spearman-Brown prophecy in this study suggest that only one measurement is required to provide a reliable LMM thickness measurement. Nonetheless, these are human measures that are open to human error and some studies have previously suggested that the reliability of measurements is increased by taking the mean of three readings (Koppenhaver *et al.*, 2009c; Wong *et al.*, 2013). It therefore seems reasonable to take three measurements to limit the risk of ambiguous readings, and to use the mean value. This strategy has been adopted in other studies (Van *et al.*, 2006; Wallwork *et al.*, 2009).

6.5.1 Limitations

This study was undertaken on a relatively small sample size (n=12). Hopkins (2000) states that approximately 50 subjects are required for greater precision in reliability research, thus the findings must be interpreted cautiously. Nonetheless, ICC values were consistently very high, so some reduction in reliability values would still prove more than acceptable.

The results are representative of a healthy population, and therefore generalisability to a population with NSCLBP is limited. That said, USI does not appear to be population or condition-specific (Belavý *et al.*, 2015) and previous studies that have studied reliability of LMM thickness measures using USI in individuals with LBP and in asymptomatic participants found there to be no significant difference in reliability estimates between groups (Wong *et al.*, 2013).

Finally, the study is limited by the analysis of measurements collected using only a linear transducer. Assessment of SEM and MDC using a curvilinear probe may have added value in the future evaluation of LMM thickness, although previous evidence has claimed that the shape of transducer has little effect on reliability (Worsley *et al.*, 2012).

6.5.2 Research implications

Given the high reliability of between-day LMM thickness measurements and relatively low SEM values, the use of USI provides an acceptable method with which to assess lumbar multifidus morphology within longitudinal studies. Furthermore, the results show that USI has the potential to detect changes in LMM thickness that are clinically meaningful should they exceed the MDC of 5.15%.

6.6 Conclusion

The results from this study provide data indicating that the use of USI to measure LMM thickness is a reliable method. This provides validity for future studies to utilise this measurement method by this examiner; the protocol for which will include using the mean value from 3 separate measurements. The minimal detectable change will be set at 5.15% signifying that any change in LMM thickness measurements must exceed this value in order to be considered clinically meaningful.

Chapter 7 : Longitudinal analysis of local dynamic stability and lumbar multifidus muscle morphology in NSCLBP patients and age matched healthy controls over 3 months

7.1 Chapter overview

This chapter examines the outcomes of a series of tests used in a healthy control cohort and in a group of subjects with NSCLBP; aimed at assessing local dynamic trunk stability and lumbar paraspinal muscle morphology in conjunction with levels of pain and disability where appropriate. Differences between groups and relationships between measures are explored.

7.2 Introduction

In the absence of any structural or pathological cause, altered neuromuscular control, along with psychological or social factors are known risk factors for both the onset and chronification of non-specific LBP (Niederer *et al.*, 2016). New treatment approaches for patients with persistent low back pain have emerged in recent years (Urits *et al.*, 2019), and the frequent inability of patients to complete active rehabilitation programmes has been recognised. Therefore, alongside multidisciplinary programmes to address the psychosocial aspects of chronic pain, more directed neuromodulatory interventions have been developed to target the deficient motor control and associated lack of dynamic stability often seen in this patient group.

Functional diagnostic markers are becoming increasingly important where the lack of radiological or clinical findings cannot explain the persistence of pain and restrictions of movement. Clinical management of neuromuscular dysfunction requires a diagnostic foundation upon which to construct a therapeutic strategy, as well as requiring a means for continual monitoring during the course of an intervention and beyond. Standard clinical evaluation in the longitudinal assessment of effectiveness of

treatment interventions is often largely dependent on subjective or patient-reported outcome measures. The conundrum that is NSCLBP continues to attract much attention in the field of research, and there has been an increase in the use of kinematic analysis in attempts to quantify differences in motor behaviour in this population compared with healthy subjects. However, these methods of investigation often involve specialist equipment within laboratory settings, thus limiting their clinical value. A critical step in progressing treatment options and in evaluating emerging new interventions is the development of clinically viable methods which are able to identify and monitor changes in motor behaviour in those with NSCLBP.

The use of accelerometery to collect kinematic data has been previously discussed in section 2.5.1, and is a favourable method of measurement in terms of clinical practicality. Such data can be utilised in the calculation of maximum Lyapunov exponents as an objective and quantifiable measure of dynamic stability. Several studies have previously employed λ_{max} to determine local dynamic trunk stability during a motor task and examine the differences between healthy and low back pain subjects. Inter-study methodologies were varied, limiting comparability, however overall there appeared to be minimal differences detected between healthy groups and participants with naturally occurring LBP (Asgari *et al.*, 2015, 2017; Graham *et al.*, 2014; Moreno Catalá *et al.*, 2018).

The criteria for motor task selection should be carefully considered. The movement test should be sufficiently demanding of the neuromuscular system, whilst not proving too difficult to excessively disrupt movement patterns beyond the system's capacity to be able to complete the task. The selected motor task varied between studies that investigated local dynamic stability using Lyapunov exponent, with most opting for a trunk flexion/extension task. However, the performance of a unidimensional task such as forward bending questions the applicability to every-day life where movement is more likely to be multidimensional. Challenging the human system through a motor task that demands combined movement through multiple planes may identify differences in stability of motor control between those with and without NSCLBP, as well as more closely reflecting real-life scenarios of movement.

It has also been recognised that an effective way to manipulate variability and stability during a cyclical motor task is through the addition of a secondary cognitive task

(Longo *et al.*, 2018), further challenging a neuromuscular system that may depend on cognitive assistance to maintain motor control. No study to date has explored the use of λ_{max} in the quantification of local dynamic trunk stability within a dual task paradigm in a NSCLBP population.

The aim of the present study was to test the feasibility of using the measuring instruments and test protocols described in Chapter 4 in the clinical setting with NSCLBP patients, and exploring the sensitivity of the combined test protocol in detecting differences between heterogenous groups (healthy and NSCLBP). Furthermore, the variability of longitudinal measurements was explored in order to assess the potential usefulness of such a test regime in the monitoring of patients following an intervention.

It is hypothesised that the healthy group will show greater local dynamic trunk stability (lower λ_{max}) overall compared with the NSCLBP group. In line with the view that tasks that demand more resources are less stable (Longo *et al.*, 2018), it is predicted that local dynamic stability will decrease (λ_{max} increase) in the dual-task condition in both groups, but more so in the NSCLBP group.

7.3 Methods

7.3.1 Study design

This is an observational study, measuring parameters at two timepoints, baseline and 3-months, in healthy participants and in subjects with NSCLBP, to assess for differences between groups. The study utilises measurement methods described in Chapter 4.

The independent variable for the study was patient classification: healthy or NSCLBP. The dependent variables are detailed in Table 10.

Table 10: Dependent variables

Patient reported measures (questionnaires) – Pain as measured by pain questionnaire (Numerical Rating Scale) – Disability as measured by Oswestry Disability Index questionnaire – Self-perceived change in pain and disability as measured by Patient Global Impression of Change questionnaire **Kinematics** – Single task dynamic trunk stability (Maximum Lyapunov Exponent) – Dual task dynamic trunk stability (Maximum Lyapunov Exponent) **Muscle morphology** – LMM thickness on left and right sides at the levels of L3 and L4

7.3.2 Subjects

7.3.2.1 Study population

The study population included people between 25 and 55 years of age who were either healthy or who had NSCLBP. A participant had to meet all the inclusion criteria and none of the exclusion criteria to be eligible for a study, as detailed in Table 3.

7.3.2.2 Sample size

Total number of recruited participants was 40: n = 20 in the healthy group; n = 20 in the NSCLBP group (all receiving medical management – pharmacological/ psychological therapies/physiotherapy). The sample size is in line with previous similar research in this field (Arampatzis *et al.*, 2017).

7.3.2.3 Recruitment

Potential NSCLBP participants were identified by members of the clinical care team within the pain management unit, or through the musculoskeletal (MSK) back pain physiotherapy clinic, both located in St Thomas' Hospital. With the patients' consent, the participant information sheet was sent out and they were contacted by the chief

investigator via telephone, email or face-to-face conversation with regards to taking part.

Healthy control subjects were recruited from within St Thomas' Hospital via presentations at audit meetings and word-of-mouth.

Figure 12 illustrates the process of recruitment and participating numbers through to completion.

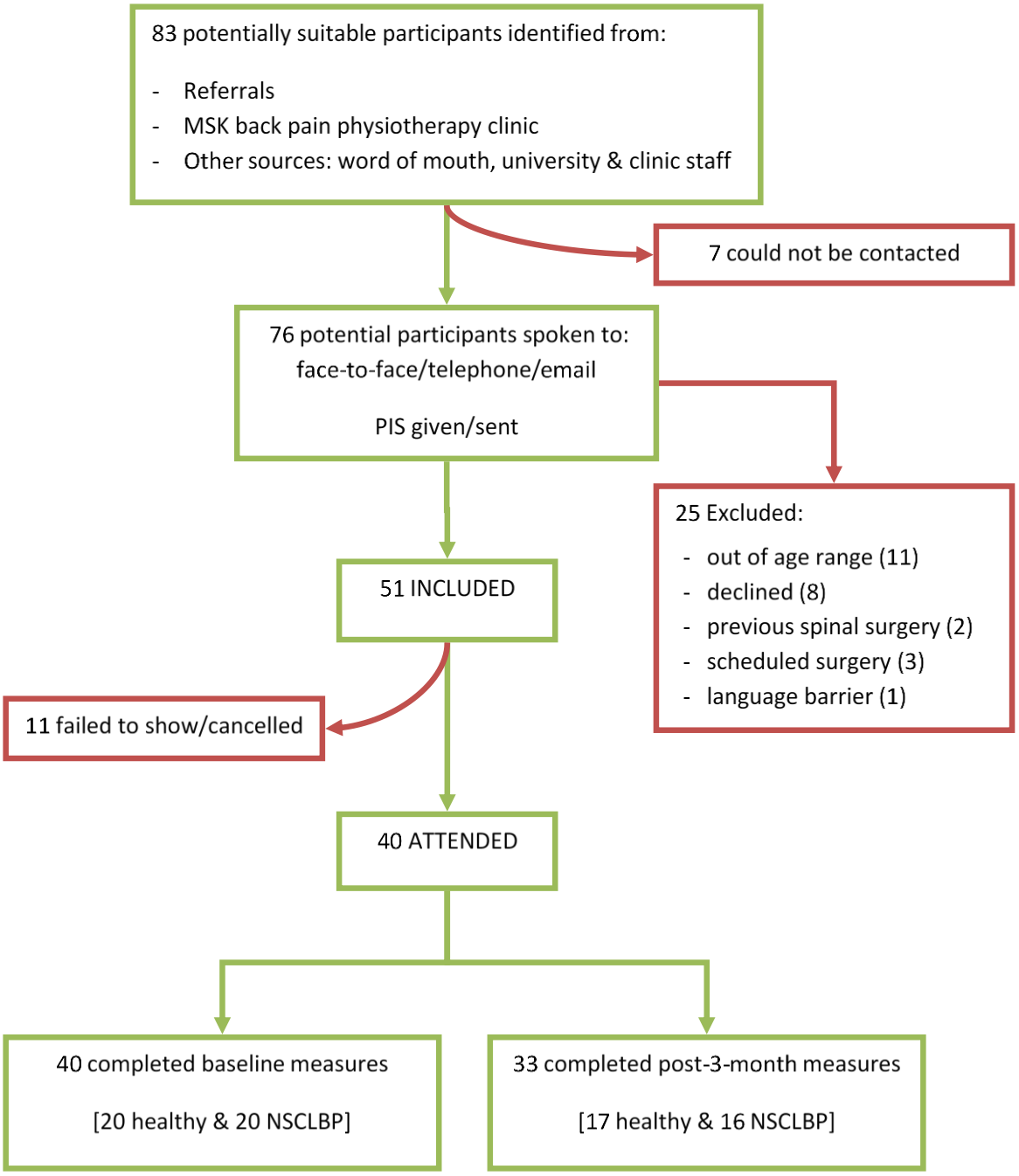


Figure 12: Flowchart of recruitment for NSCLBP and healthy participants

7.3.3 Study protocol

Various parameters were measured during each stage of the study. Collection of each outcome measure is detailed in Figure 13, which shows the study flow.

Every participant was asked to attend on two occasions – once for baseline measurements and again at least 3 months later for repeated measures. In addition, the NSCLBP group were contacted at 1-month and 2-months to discuss pain and PGIC (telephone questionnaire).

Each participant was expected to be involved in the study (from enrolment to completion) for around 3-4 months.

7.3.4 Procedure

Kinematic data was collected as described in section 4.7.1. Subjects completed a cyclical tap test under single and dual task conditions in order to calculate λ_{max} as a measure of local dynamic trunk stability; at baseline and at 3-months.

LMM thickness was measured bilaterally at L3 and L4 as described in section 4.7.2. Measurements were taken from all subjects at baseline and again at 3-months.

Questionnaires to record patient reported measures (pain, disability and global impression of change) were completed by the NSCLBP group during visits at baseline and 3-months.

Telephone questionnaires were devised to measure pain and global impression of change at 1-month and 2-months. These questionnaires were completed via verbal responses to reduce the time-burden of the study and minimise the number of visits required. The purpose of the telephone contact was twofold: firstly, to monitor patients' progress and pain levels, and secondly, to maintain contact with patients and ensure they remained interested in the study in an attempt to minimise attrition.

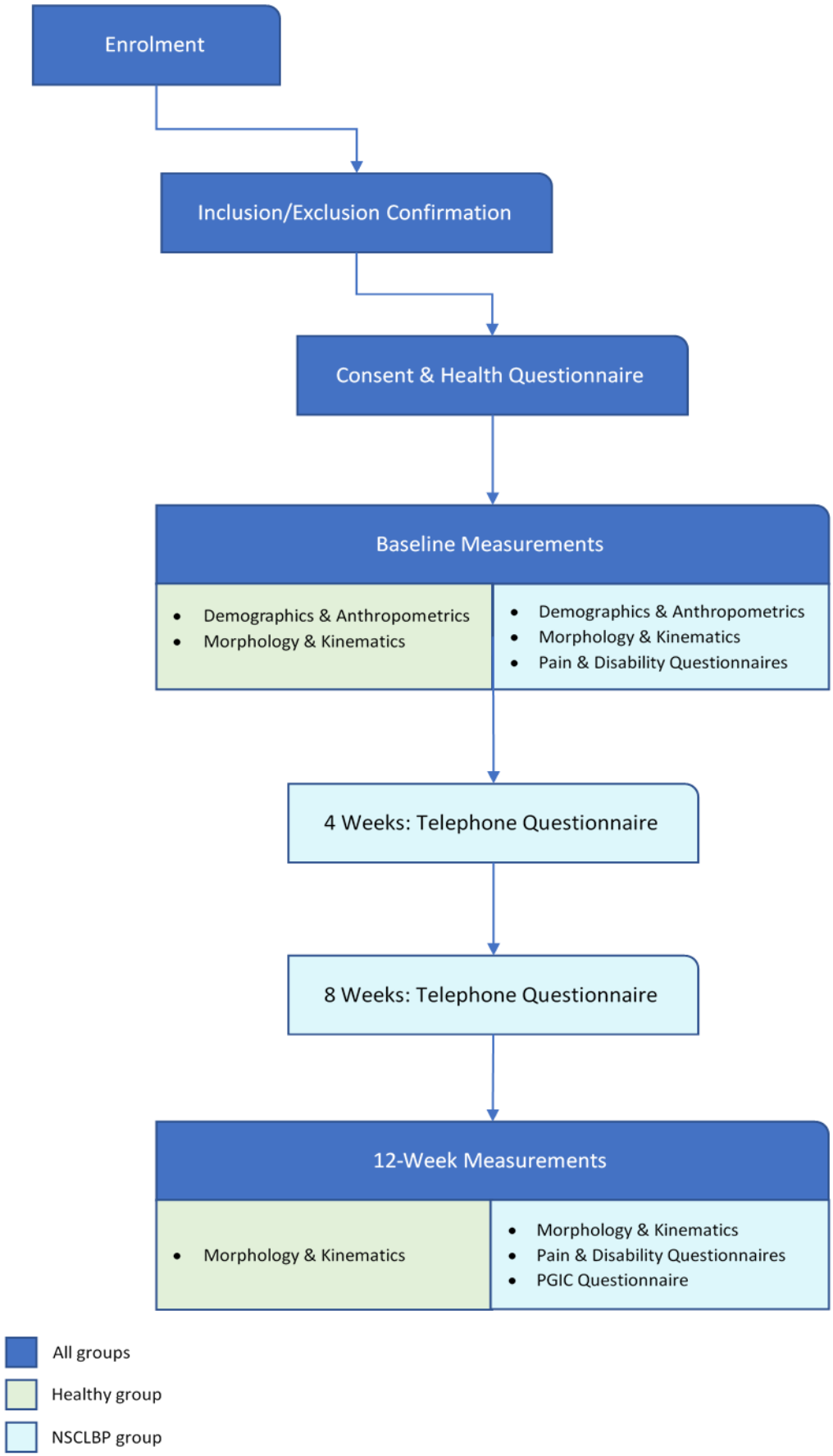
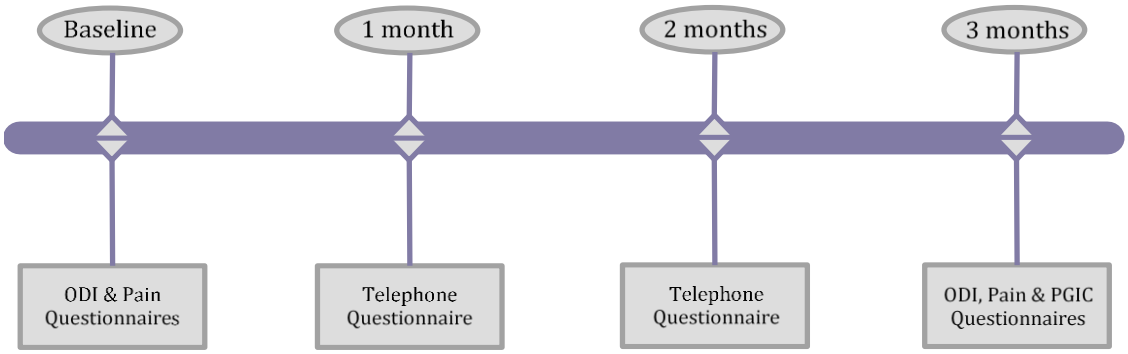


Figure 13: Flow diagram for study protocol

Figure 14 illustrates when questionnaires were used through the course of the study.



ODI: Oswestry Disability Index
PGIC: Patient Global Impression of Change

Figure 14: Use of questionnaire timeline

7.3.5 Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics 21 (SPSS Inc, Chicago, IL), with the significance level set at $\alpha = 0.05$.

For all data, normality was confirmed using the Shapiro-Wilk test and homogeneity of variance was confirmed using the Levene's test. Where a violation of sphericity was found in Mauchly's test, a Greenhouse-Geisser correction was applied. Post-hoc tests with Bonferroni correction were applied to significant main effects if applicable.

Anthropometric between-group data were subjected to independent samples *t* tests if normally distributed or else Mann-Whitney U tests if not normally distributed. Since gender comprises two categorical variables, Chi-square test was used to evaluate differences in gender between groups.

Local dynamic stability data was normally distributed so was subjected to a mixed repeated measures ANOVA with condition (single or dual task) and time (baseline and 3-months) as within-subject factors and group (healthy and NSCLBP) as between-subject factor.

Cognitive task outcomes utilised Chi-square test for between group differences and McNemar's test to examine outcomes within subjects. Cognitive answer error data was not normally distributed, so Mann-Whitney U tests were used for between-group differences and Wilcoxon signed-rank tests used for within-subject analysis.

LMM thickness was subjected to a one-way ANOVA with repeated measures on each level of LMM as well as mean LMM thickness.

Pearson product-moment correlation coefficients were used to assess relationships between local dynamic stability and LMM thickness, pain, disability and PGIC where appropriate.

Tests used for between-group analysis are summarised in Table 11.

Table 11: Test selection for between-group analysis

	Between group differences (Healthy control & NSCLBP)		
	Normally distributed	**Not normally distributed**	**Categorical variables**
Anthropometric data			
Outcomes	Mass	Age Height BMI	Gender
Test	Independent *t*-test	Mann-Whitney U test	Chi-square test
Experimental data			
Outcomes	Stability (single & dual task) LMM thickness	Cognitive task answer errors	Cognitive task pass/fail
Test	Independent *t*-test or Mixed repeated-measures ANOVA	Mann-Whitney U test	Chi-square test and McNemar test

7.4 Results

Eighty-three participants were identified as being potentially suitable for the study. Seventy-six were contacted and checked for eligibility, of whom 40 were eligible and agreed to participate in the study (Figure 12). Twenty were included in the NSCLBP group and 20 in the control group. 7 participants discontinued the study following baseline measures due to lack of time (4 NSCLBP and 3 control). Longitudinal data are reported, with 16 NSCLBP and 17 healthy control data sets included in analysis.

Anthropometric data for both groups is displayed in Table 12. Data between groups were compared using a *t* test for independent samples if normally distributed or a Mann-Whitney U test if not normally distributed. Gender was analysed using a Chi-square test. The significance of between group differences are displayed as *p* values, with the level of significance for all comparisons set at $\alpha=0.05$.

Table 12: Anthropometric characteristics

Parameter	**Healthy (n=17)**	**NSCLBP (n=16)**	***p* value**
Gender	7M:10F	8M:8F	0.611
Age (years)	35.0 ± 7.8	42.7 ± 9.9	0.019*
Body height (m)	1.69 ± 0.12	1.73 ± 0.10	0.438
Body mass (kg)	74.24 ± 19.66	80.46 ± 13.12	0.2550
BMI (kg/m^2)	25.467 ± 4.92	27.13 ± 4.25	0.349

All figures are mean values ± standard deviation

BMI: Body mass index

p value resembles significance of between group differences

*Statistically significant differences ($p<0.05$)

Body height, body mass and BMI did not show any significant differences ($p>0.05$) between groups. There were significant differences in age between the control and NSCLBP groups, with the mean age of NSCLBP participants being approximately 8 years higher.

Measures of stability – maximum Lyapunov exponents for single task ($\lambda_{max\text{-}S}$) and dual task ($\lambda_{max\text{-}DT}$), and cognitive task (CT) answers were collected, along with morphological measures - LMM thickness on left and right sides at the levels of L3 and L4. Pain scores (NRS), levels of disability (ODI) and global impression of change (PGIC) scores were also collected from the NSCLBP group. All measures were recorded at baseline and again 3-months later. Results are displayed in Table 13.

Table 13: Baseline and 3–month outcome measures (mean values ± standard deviation)

	Control group (n=17)		NSCLBP group (n=16)	
Parameter	Baseline	3-months	Baseline	3-months
$\lambda_{max\text{-}S}$	4.785 ± 0.755	4.911 ± 0.816	4.738 ± 0.665	4.641 ± 0.809
$\lambda_{max\text{-}DT}$	4.524 ± 0.749	4.502 ± 0.927	4.719 ± 0.697	4.594 ± 0.670
CT answer (DT)	38.2 ± 1.5	37.4 ± 2.1	36.0 ± 6.4	37.6 ± 2.4
CT error	0.76 ± 0.97	1.24 ± 1.60	3.88 ± 5.43	1.50 ± 1.90
CT pass rate	7 P : 10 F	7 P : 10 F	6 P : 10 F	7 P : 9 F
$L3_L$ thickness (cm)	3.12 ± 0.68	3.22 ± 0.76	3.08 ± 0.56	3.10 ± 0.47
$L4_L$ thickness (cm)	3.30 ± 0.53	3.50 ± 0.80	3.28 ± 0.50	3.46 ± 0.60
$L3_R$ thickness (cm)	3.12 ± 0.53	3.06 ± 0.66	3.16 ± 0.48	3.08 ± 0.48
$L4_R$ thickness (cm)	3.27 ± 0.49	3.38 ± 0.62	3.28 ± 0.40	3.40 ± 0.54
Mean thickness (cm)	3.19 ± 0.52	3.26 ± 0.69	3.20 ± 0.42	3.26 ± 0.49
Pain on day			4.25 ± 2.14	3.00 ± 2.31
Overall pain score			4.59 ± 1.70	3.48 ± 2.15
ODI			29.8 ± 17.2	24.6 ± 16.6
PGIC				3.3 ± 1.9

$\lambda_{max\text{-}S}$: maximum Lyapunov exponent single task

$\lambda_{max\text{-}DT}$: maximum Lyapunov exponent dual task

CT: Cognitive task, DT: Dual task, ST: Single task

P: Pass, F: Fail

ODI: Oswestry disability index

PGIC: patient global impression of change

7.4.1.1 Local dynamic stability

Local dynamic stability data ($\lambda_{max\text{-}S}$ and $\lambda_{max\text{-}DT}$) were submitted to a mixed repeated measures ANOVA with condition (single and dual task) and time (baseline and 3-months) as within-subject factors and group (healthy control or NSCLBP) as between-subjects factor. Results are shown in Figure 15.

Both groups showed little change in λ_{max} in either single or dual task conditions from baseline to 3-months. Findings (in terms of λ_{max} values) showed there was:

- no significant effect of time ($F(1,31)=.089$, $p=.768$, $\eta_p^2=.003$).
- no significant time*group interaction ($F(1,31)=.663$, $p=.422$, $\eta_p^2=.021$).
- **a significant main effect of condition on stability ($F(1,31)=7.066$, $p=.012$, $\eta_p^2=.186$).**
- **a significant condition*group interaction ($F(1,31)=4.761$, $p=.037$, $\eta_p^2=.133$).**
- no significant time*condition interaction ($F(1,31)=.995$, $p=.326$, $\eta_p^2=.031$).
- no significant time*condition*group interaction ($F(1,31)=.458$, $p=.504$, $\eta_p^2=.015$).
- no significant between-subjects effect, i.e. group effect ($F(1,31)=.001$, $p=.975$, $\eta_p^2=.000$).

Further *t*-tests showed significant differences in the healthy control group between conditions at both baseline ($p=.046$) and at 3-months ($p<.001$).

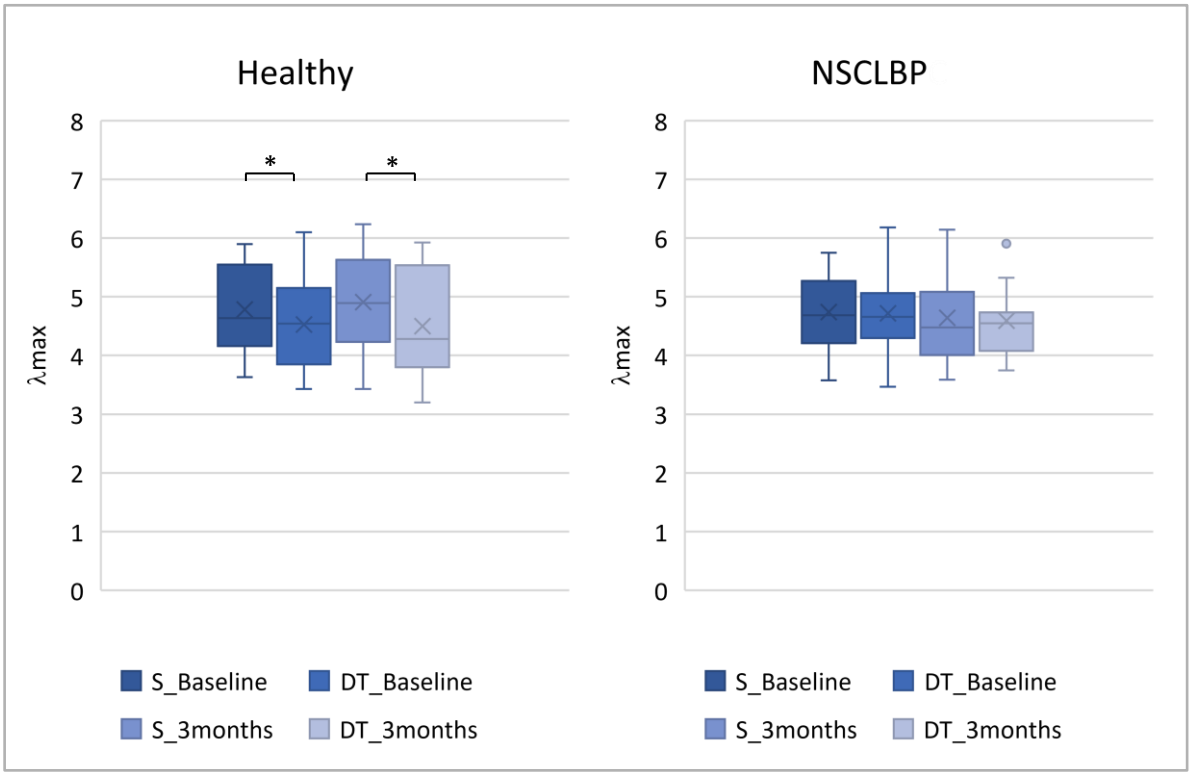


Figure 15: Local dynamic stability values (λ_{max}) during single task (S) and dual task (DT) conditions at baseline and at 3-months for healthy and NSCLBP groups. Mean values are indicated by X, median values are shown as a line in the box and the error bars represent standard deviations. *Statistically significant difference between conditions (p<0.05).

Changes in λ_{max} from baseline to 3-months were calculated for comparison against the standard error of measurement of 6.63% calculated in study 1 (Chapter 5), and changes in variation of λ_{max} in absolute terms were calculated using RMSE. Values are displayed in Table 14.

Table 14: Mean $\Delta\lambda_{max}$ and RMSE between baseline and 3-months

	Healthy	**NSCLBP**
Mean $\Delta\lambda_{max\_S}$	+0.126	-0.097
Mean $\Delta\lambda_{max\_DT}$	-0.022	-0.125
RMSE λ_{max_S}	0.503	0.893
RMSE λ_{max_DT}	0.437	0.542

7.4.1.2 Cognitive task

Pass rate of the cognitive task did not exceed 44% in either group, at any time point (Figure 16). Chi-square tests showed there to be no significant relation between group and likelihood of passing the cognitive task at baseline (X^2 (1, N=33) = .047, p=.829) or at 3 months (X^2 (1, N=33) = .022, p=.881). McNemar's test examined the repeated measures within subjects (baseline and 3-months). In the control group 9 out 17 subjects maintained their pass/fail status between timepoints, and 11 out of 16 subjects in the NSCLBP. In addition, there was an even split of subjects crossing over from a fail to a pass or pass to fail in both groups, suggesting no directional trend in change of status.

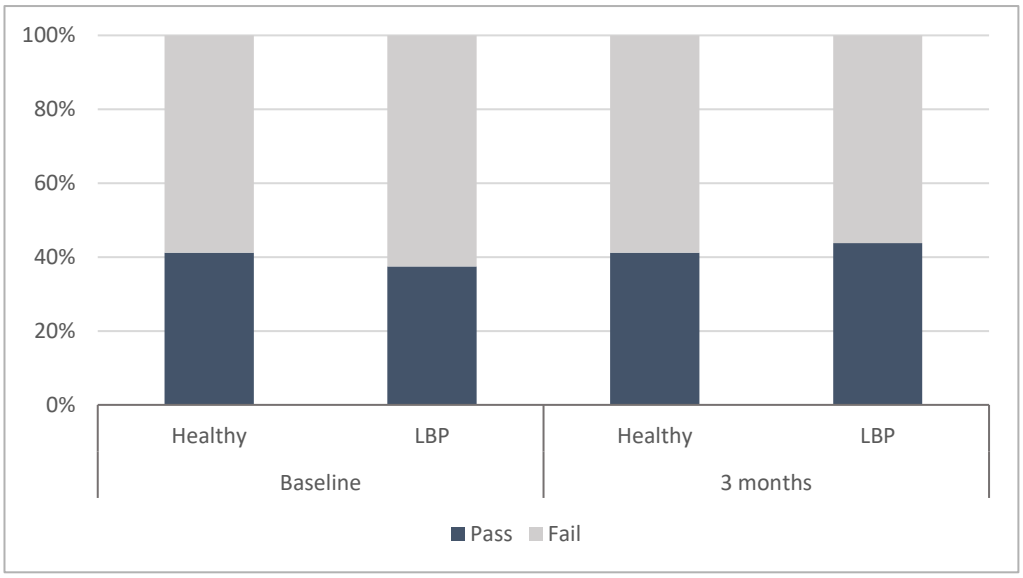


Figure 16: Percentage of subjects passing/failing the cognitive task during dual task conditions for healthy and NSCLBP groups at baseline and at 3-months.

Results for cognitive task answer error are shown in Figure 17. Single cognitive task answer errors were minimal (healthy M=0, SD=0.4, and NSCLBP, M=0, SD=0.7) with 88% of subjects passing the cognitive single test. Where there was an error with single task, dual task answer errors were normalised to this value. Between group differences were analysed using Mann-Whitney U tests, and within-subjects analysis with Wilcoxon signed-rank tests. Results showed:

- **Answer error in the NSCLBP group was significantly higher than in the healthy control group at baseline (*U*=75.500, *p*=.023).**
- Answer errors were not significantly different between the healthy control and NSCLBP groups at 3-months (*U*=124.000, *p*=.649).
- There was no significant difference in answer error between baseline and 3-months in the healthy control group (*Z*=-1.339, *p*=.180).
- **In the NSCLBP group, there was a significant difference in answer error between baseline and 3-months (*Z*=-2.059, *p*=.040).**

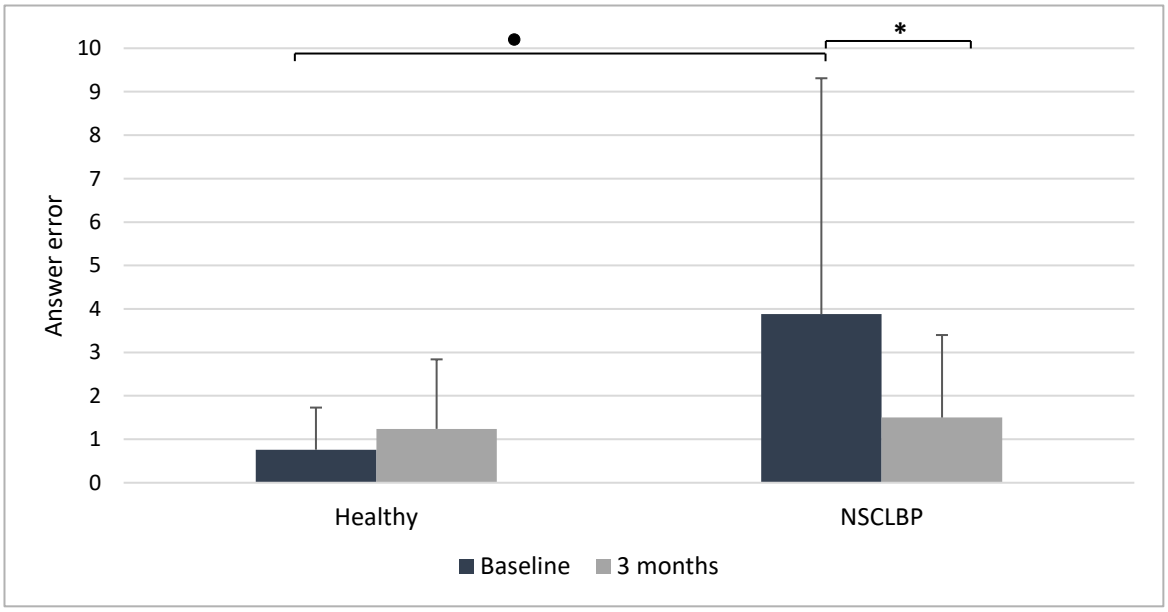


Figure 17: Answer errors in cognitive task during dual task conditions for healthy and NSCLBP groups at baseline and at 3-months.
All values are expressed as means with SD (error bars). •Statistically significant difference between healthy and NSCLBP groups at baseline ($p<0.05$). *Statistically significant difference between baseline and 3months in NSCLBP group ($p<0.05$).

7.4.1.3 Lumbar multifidus thickness

A mixed ANOVA was performed on each level of LMM thickness, as well as mean LMM thickness, with time as within-subject factor and group as between-subject factor. Interactions are illustrated in Figure 18. This revealed:

L3 Left LMM thickness

- No significant effect of time within-subjects, $F(1,31)=.553$, $p=.463$, $\eta_p^2=.018$.
- No significant interaction of time*group within subjects $F(1,31)=.285$, $p=.598$, $\eta_p^2=.009$.
- No significant effect between groups, $F(1,31)=.066$, $p=.799$, $\eta_p^2=.002$.

L4 Left LMM thickness

- **A significant effect of time within-subjects, $F(1,31)=4.401$, $p=.044$, $\eta_p^2=.124$.**
- No significant interaction of time*group within subjects $F(1,31)=.002$, $p=.963$, $\eta_p^2=.000$.
- No significant effect between groups, $F(1,31)=.014$, $p=.907$, $\eta_p^2=.000$.

L3 Right LMM thickness

- No significant effect of time within-subjects, $F(1,31)=1.792$, $p=.190$, $\eta_p^2=.055$.
- No significant interaction of time*group within subjects $F(1,31)=.009$, $p=.926$, $\eta_p^2=.000$.
- No significant effect between groups, $F(1,31)=.084$, $p=.774$, $\eta_p^2=.003$.

L4 Right LMM thickness

- No significant effect of time within-subjects, $F(1,31)=1.768$, $p=.193$, $\eta_p^2=.054$.
- No significant interaction of time*group within subjects $F(1,31)=.073$, $p=.789$, $\eta_p^2=.002$.
- No significant effect between groups, $F(1,31)=.053$, $p=.819$, $\eta_p^2=.002$.

Mean LMM thickness

- No significant effect of time within-subjects, $F(1,31)=1.449$, $p=.238$, $\eta_p^2=.066$.
- No significant interaction of time*group within subjects $F(1,31)=.013$, $p=.911$, $\eta_p^2=.001$.
- No significant effect between groups, $F(1,31)=.000$, $p=.987$, $\eta_p^2=.000$.

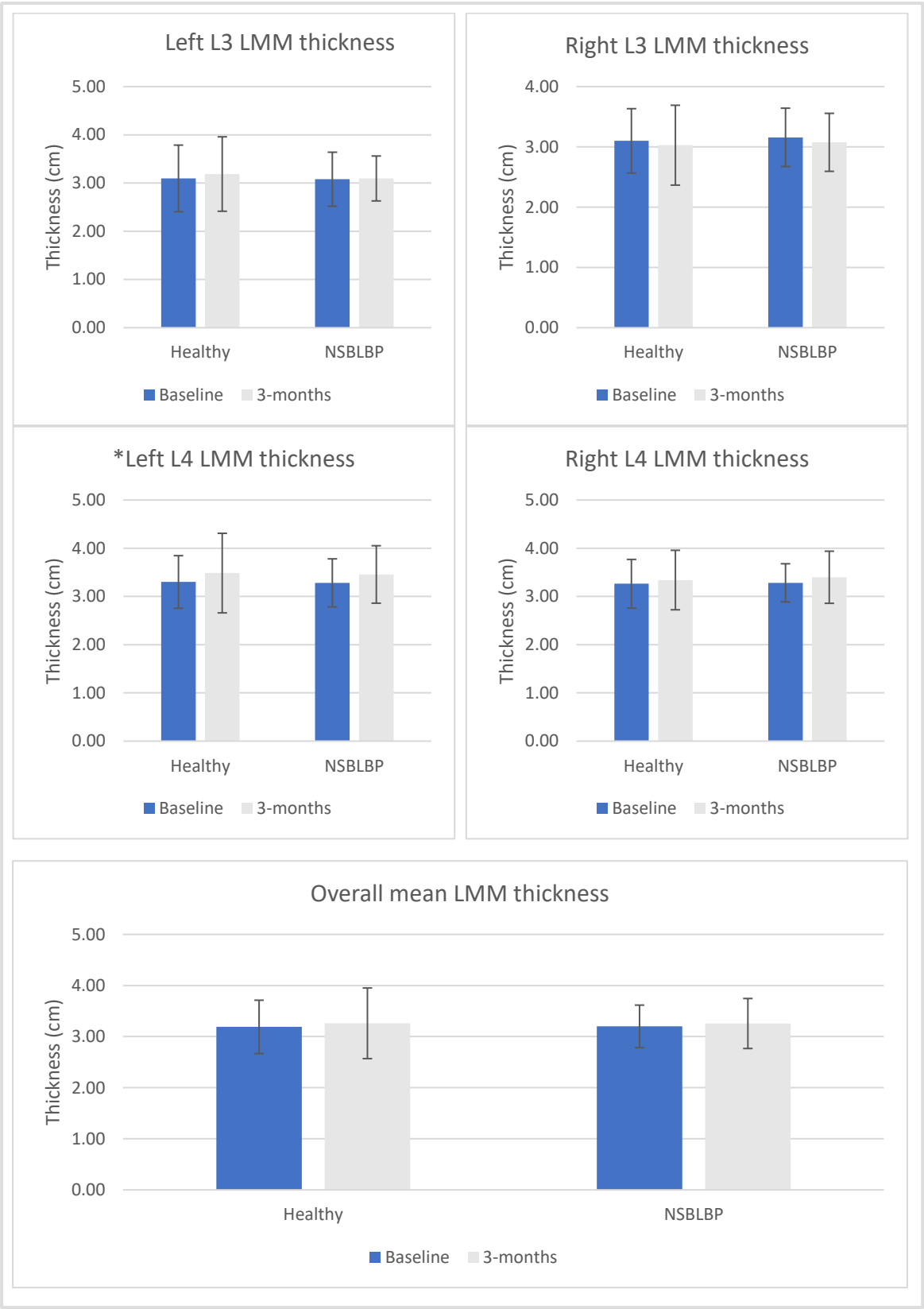


Figure 18: Mean LMM thicknesses at each spinal level and overall mean thickness for healthy and NSCLBP groups measured at baseline and 3-months.
*Statistically significant effect of time on within-subject change in Left L4 LMM thickness.

Pearson product-moment correlation coefficients were calculated to assess whether there was any relationship between LMM thickness and local dynamic stability under either condition. Results are displayed in Table 15. No significant correlations were found at any level of LMM, or during either condition of λ_{max} measurements.

Table 15: Correlation coefficient values for mean LMM thickness (at each spinal level and overall mean thickness) and λ_{max} in single and dual task conditions using all subjects at baseline and 3-months.

Relationship	***r***	**N**	***p***
L3 Left thickness vs. λ_{max_S} at baseline	.117	33	.516
L3 Left thickness vs. λ_{max_DT} at baseline	.158	33	.381
L4 Left thickness vs. λ_{max_S} at baseline	.162	33	.367
L4 Left thickness vs. λ_{max_DT} at baseline	.207	33	.248
L3 Right thickness vs. λ_{max_S} at baseline	.207	33	.247
L3 Right thickness vs. λ_{max_DT} at baseline	.261	33	.143
L4 Right thickness vs. λ_{max_S} at baseline	.208	33	.244
L4 Right thickness vs. λ_{max_DT} at baseline	.213	33	.235
Mean thickness vs. λ_{max_S} at baseline	.190	33	.291
Mean thickness vs. λ_{max_DT} at baseline	.232	33	.194
L3 Left thickness vs. λ_{max_S} at 3 months	.231	33	.197
L3 Left thickness vs. λ_{max_DT} at 3 months	.134	33	.456
L4 Left thickness vs. λ_{max_S} at 3 months	.214	33	.232
L4 Left thickness vs. λ_{max_DT} at 3 months	.133	33	.461
L3 Right thickness vs. λ_{max_S} at 3 months	.187	33	.299
L3 Right thickness vs. λ_{max_DT} at 3 months	.129	33	.475
L4 Right thickness vs. λ_{max_S} at 3 months	.209	33	.243
L4 Right thickness vs. λ_{max_DT} at 3 months	.168	33	.351
Mean thickness vs. λ_{max_S} at 3 months	.220	33	.218
Mean thickness vs. λ_{max_DT} at 3 months	.147	33	.415

7.4.1.4 Pain

Pain on the day of testing and overall pain is reported in Table 13. Paired *t* tests revealed a significant difference in pain scores on the day between baseline (Mean=4.25, SD=2.15) and 3-months (Mean=3.00, SD=2.31); $t(15)=2.331$, $p=.034$. There was also a significant difference in overall pain from baseline (Mean=4.59, SD=1.70) to 3-months (Mean=3.48, SD=2.15); $t(15)=2.364$, $p=.032$.

Pearson product-moment correlation coefficients were calculated to assess various relationships between pain and local dynamic stability. The correlation data is reported in Table 16, and displayed in scatterplots in Figure 19. There were no significant correlations between pain and local dynamic stability, during any condition or time point.

Table 16: Correlation coefficient data for pain (on day and overall) and local dynamic stability (λ_{max}) during single and dual task conditions, at baseline and at 3-months in the NSCLBP group.

Relationship	***r***	**N**	***p***
Pain on day vs. λ_{max_S} at baseline	-.010	16	.972
Pain on day vs. λ_{max_DT} at baseline	-.059	16	.828
Overall pain vs. λ_{max_S} at baseline	-.082	16	.762
Overall pain vs. λ_{max_DT} at baseline	-.142	16	.599
Pain on day vs. λ_{max_S} at 3 months	-.152	16	.573
Pain on day vs. λ_{max_DT} at 3 months	.285	16	.285
Overall pain vs. λ_{max_S} at 3 months	-.226	16	.401
Overall pain vs. λ_{max_DT} at 3 months	.160	16	.555

λ_{max_S}: maximum Lyapunov exponent during single task

λ_{max_DT}: maximum Lyapunov exponent during dual task

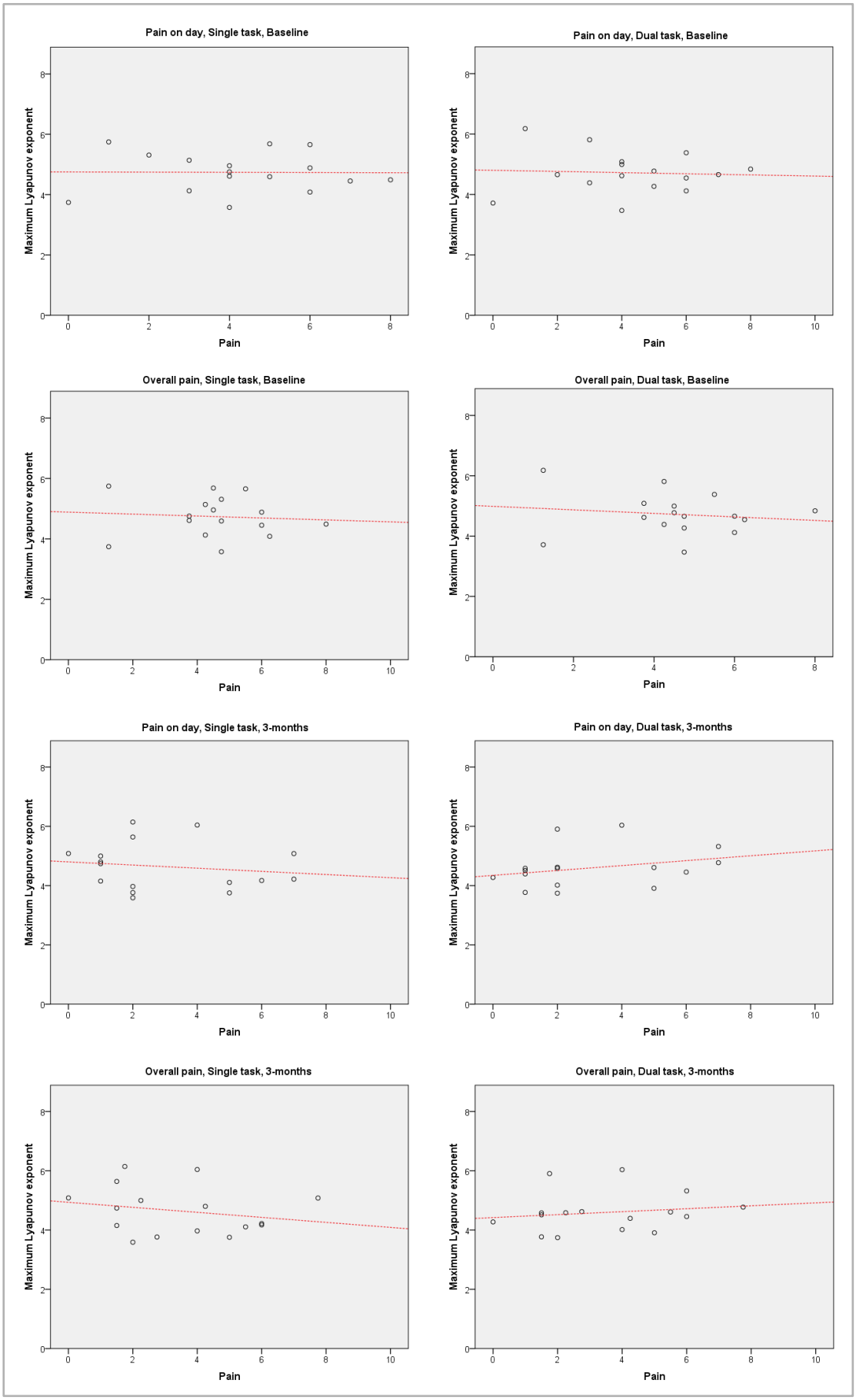


Figure 19: Correlations between pain (pain on day of testing and overall pain) and λ_{max} (single and dual task) in the NSCLBP group (n=16).
No significant correlations were found.

7.4.1.5 Disability

ODI data was collected at baseline and again at 3-months (Table 13). A paired *t*-test showed there was no significant difference between ODI scores at baseline (Mean=28.81, SD=17.22) and 3-months (Mean=24.63, SD=16.58); $t(15)=1.796$, $p=.093$.

Pearson product-moment correlation coefficients were calculated to assess relationships between ODI and local dynamic stability. The correlation data is reported in Table 17, and displayed in scatterplots (Figure 20). There were no significant correlations between ODI and local dynamic stability, during any condition or at any time point.

Table 17: Correlation coefficients for ODI and local dynamic stability (λ_{max}) during single and dual task conditions at baseline and 3–months in the NSCLBP group.

Relationship	***r***	**N**	***p***
ODI vs. λ_{max_S} at baseline	-.037	16	.892
ODI vs. λ_{max_DT} at baseline	-.066	16	.809
ODI vs. λ_{max_S} at 3 months	-.070	16	.798
ODI vs. λ_{max_DT} at 3 months	-.038	16	.889

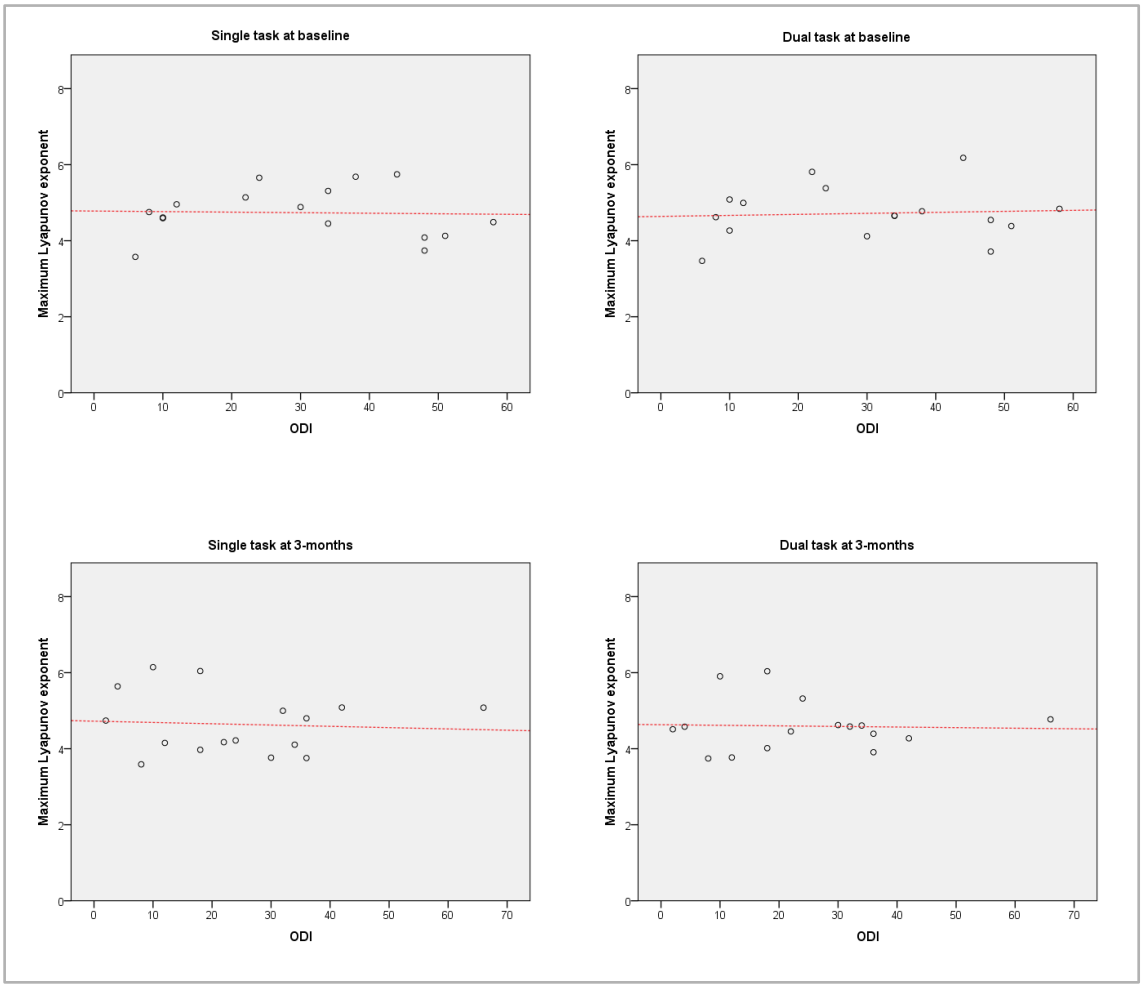


Figure 20: Correlation between ODI and local dynamic trunk stability (λ_{max}) during single and dual task conditions at baseline and 3-months in the NSCLBP group (n=16). There were no significant relationships.

7.4.1.6 PGIC

Mean PGIC was 3.31 ± 1.89 (SD), indicating that the average status of where patients perceived their condition to be after 3 months was 'a little better, but no noticeable change'.

A Pearson product-moment correlation coefficient was computed to assess the relationship between the change in stability, measured by λ_{max} and PGIC. There was no correlation between the two variables during single task, r=.038, n=16, p=.890, or during dual task, r=.039, n=16, p=.886. The results are shown in Figure 21, which

illustrates that patient global impression of change did not relate to the level of local dynamic stability under either condition.

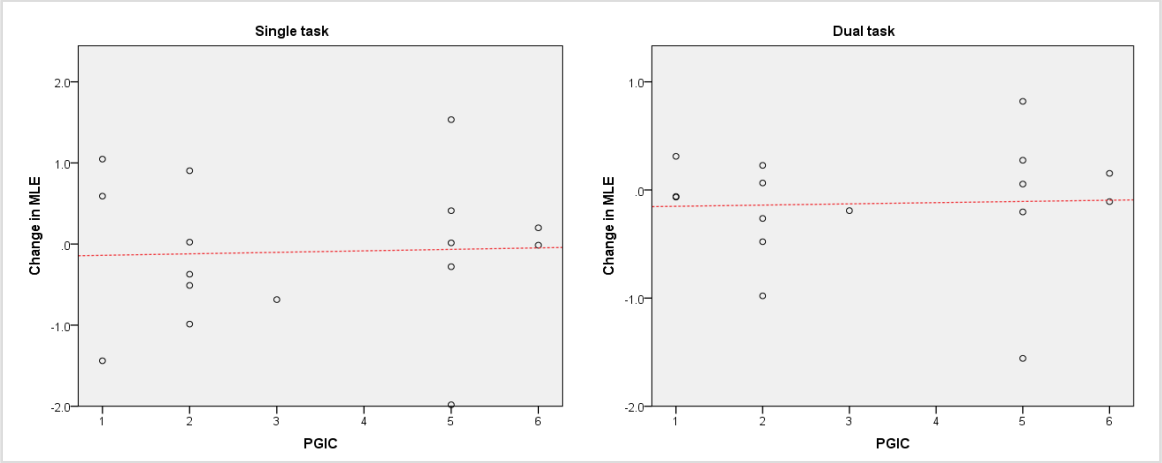


Figure 21: Correlation between PGIC and change in λ_{max_S} and λ_{max_DT} in the NSCLBP group (n=16).

7.5 Discussion

The primary aim of this study was to assess muscle morphology of LMM and local dynamic stability of trunk movements in patients with NSCLBP and age matched healthy controls during cyclical tap tests under two different conditions over a period of time. Contrary to the hypothesis that the NSCLBP group would be less stable than the healthy group, there was no significant difference between groups in the λ_{max} values under single task conditions at baseline or at 3-months. Dysfunction in the active, passive and neuromuscular systems is seen in those with LBP (Demoulin *et al.*, 2007), along with altered trunk muscle activation and reduced motor control (van Dieën *et al.*, 2003b), thus reduced stability in this group would seem most likely. This finding however is supported by previous studies that also reported no differences in λ_{max} between healthy and CLBP groups (Asgari *et al.*, 2015; Graham *et al.*, 2014; Moreno Catalá *et al.*, 2018). Graham *et al.* (2014) found that whilst there was no difference in

kinematic stability between healthy and LBP groups, there was reduced stability of muscle activations in the LBP group (as measured by EMG signals). Kinematics appear to be more tightly controlled than muscle activations (potentially due to inertial and damping properties of body segments), therefore it is possible that the activation dynamics actively try to maintain stability more so than the kinematics (Kang and Dingwell, 2009). They postulated that the lack of statistically significant differences in λ_{max} values between groups may be due to LBP participants increasing their antagonistic co-contraction in order to compensate for neuromuscular deficiencies, thus maintaining dynamic stability.

The current study explored the effects of a concurrent cognitive task on local dynamic stability (λ_{max}) in a sustained repetitive motor task involving trunk movement. The hypothesis that a dual task condition would reduce dynamic stability (increase λ_{max}) was rejected based on data collected in this study. The healthy control group became less unstable (lower λ_{max}) with the introduction of a secondary cognitive task, at both baseline and at 3-months. The NSCLBP showed no statistically significant difference in λ_{max} between single task and dual task conditions at either timepoint, although there was a trend towards a decrease in $\lambda_{max\text{-}DT}$ at 3-months. Neither group showed any reduction in stability with the introduction of the cognitive task as predicted. Despite the kinematic changes exhibited in the healthy group, and the relatively minimal changes in the NSCLBP group, neither group showed any more tendency towards passing or failing the cognitive task. However, the answer error in the NSCLBP group was significantly higher at baseline compared with the healthy control group; yet this was not the case at 3-months when there was no significant difference in answer error between the two groups. It is possible the significant reduction in pain between timepoints could have influenced performance, as well as other possible factors such as reduced level of kinesiophobia (familiarity of the testing procedure) or a learning effect.

Similar findings were reported by Santuz *et al.* (2020) who investigated how local stability of control signals is associated with robust motor output. They calculated short-term λ_{max} and Higuchi's fractal dimension of motor primitives (temporal components of muscle synergies) as measured by EMG during locomotion (walking and running) over ground and on a treadmill, with or without perturbations and in

aging. Their results indicated that less unstable and less complex motor primitives were associated with more challenging settings, whereas easier tasks allowed for more unstable and more complex control. They theorised that lower local instability and complexity of motor primitives might describe a strategy employed by the central nervous system to maintain acceptable levels of functionality when challenges are added globally to locomotion. Whilst their work supports the findings in this study, where healthy participants became less unstable with the introduction of a secondary cognitive task, drawing direct comparisons between the two studies should be done so with caution due to the different methodologies employed. Local dynamic stability has been shown to vary significantly and even give opposing results when using different methodological approaches (Dingwell and Kang, 2007).

Within motor control literature, the constrained action hypothesis has been used to describe how an internal focus of attention may interfere with the automaticity of the body's movements. It has yet to be shown to influence trunk motor control, but it is possible that this was a factor in the healthy control group. The introduction of physical tap points was suggested by Bourdon *et al.* (2018) as a means to help reduce the internal focus of attention. However, if the healthy control group found the motor task relatively easy, the introduction of the secondary cognitive task may have provided distraction and thus an improvement in stability. This theory has been suggested previously by Woollacott and Shumway-Cook (2002). Conversely, the NSCLBP group did not show this trend, suggesting that their focus with regards to the motor task remained constant throughout both single and dual task conditions; this was however at much more cost to the cognitive task.

Fraizer and Mitra (2008) asserted that physical performance improvement can be a selected strategy adopted to facilitate execution of a cognitive task. This could certainly have been the case in the healthy control group, where there were sufficient resources to improve stability whilst still able to complete the cognitive task with only modest errors. It is likely that healthy subjects have greater adaptability and are able to acquire different stable motor solutions that better suit the dual-task constraints (Longo *et al.*, 2018). Contrariwise, the NSCLBP group did not appear to have adequate resources to perform both tasks concurrently – their focus was on maintaining kinematic stability, but at the expense of the cognitive task which showed significantly higher errors. This group prioritised motor control over the cognitive task, and this

has been previously noted in groups with reduced sensorimotor control, as in NSCLBP, who may adopt the posture-first strategy (Sherafat *et al.*, 2014; Vuillerme and Nafati, 2007).

Another factor which should not be ignored is that slower psychomotor speed and impaired short-term memory has been observed in those with CLBP (Luoto *et al.*, 1996, 1999). This may have accounted for the higher answer error observed in the NSCLBP group, although measuring performance during the single cognitive task and normalising dual task errors to this value should have helped reduce confounding factors in this regard. The NSCLBP group shifted from large answer errors for the dual cognitive task at baseline towards error values at 3-months that were much more aligned with the healthy control group. Whilst not significant, at 3-months the NSCLBP group became less unstable during the dual task condition similar to the healthy group. This may have been noteworthy had the NSCLBP participants been receiving a targeted intervention or following a rehabilitation programme, however they weren't, and so it would be difficult to attribute a physiological reason behind this observation.

LMM thickness was not significantly different between the groups thus rejecting the hypothesis that differences in LMM thickness would exist between healthy and NSCLBP participants. In addition, there was little change overall (below the MDC of 5.15% determined in Chapter 6) from baseline to 3-months in both groups; although there was an increase in the thickness of the left L4 LMM just above the MDC observed in both groups. It is therefore unlikely LMM changes influenced stability. Further study would be required, with observations of significant changes in stability or LMM thickness to adequately prove/disprove the hypothesis that LMM thickness is related to local dynamic stability.

Minimal changes in λ_{max} were observed in both groups from baseline to 3-months under both conditions (Table 14), well below the set standard error of measurement of 6.63%; suggesting no measurable changes in local dynamic stability. Furthermore, RMSE values were similar across the three months and were in line with findings from study 1 (Chapter 5) suggesting the level of variation in absolute terms was fairly constant. That said, the NSCLBP group did show slightly wider deviation of measurements, the highest noted during the single motor task.

The lack of change in λ_{max} between baseline and 3-months in the NSCLBP (below the SEM of 6.63%), despite a significant reduction in pain between timepoints suggests a lack of direct association between pain and local dynamic stability, thus rejecting the hypothesis that LDS is related to pain. Arampatzis *et al.* (2017) similarly found that local dynamic trunk stability remained unchanged despite a significant reduction in LBP following an intervention. It would appear that the only studies that have reported changes in dynamic stability (measured by λ_{max}) related to pain are in those which simulated acute LBP through the introduction of a noxious stimulus (Ross *et al.*, 2015, 2017; Van Den Hoorn *et al.*, 2015). It is likely that the acute introduction of pain promotes different neuromuscular compensatory strategies to perturbations than those that may be seen in true CLBP patients. In the current study, it is possible that the lack of statistically significant differences in λ_{max} is due to the relatively low levels of pain exhibited by those subjects in the NSCLBP group (mean levels were low to lower-moderate) and relatively low mean levels of disability.

Another goal of this study was to investigate the feasibility of using the measuring instruments and test protocols described in Chapter 4 within the clinical setting with NSCLBP patients. The experimental setup had been designed to use small and minimal equipment; a standard sized clinical assessment room was used, and this provided enough space to conduct the kneeling tap-test as well as having enough room for the couch and ultrasound machine for measurement of LMM. The series of tests (questionnaires, stability tests and US measurement of LMM thickness) took between 20 and 30 minutes to complete. All recruited NSCLBP patients were able to perform and complete both physical movement tests. On occasion, a patient needed to have a slightly longer rest between single and dual task stability tests, but this did not cause deviation from the test protocol. Overall, the test procedure was easy to carry out in the available space, took a short amount of time using minimal resources, and was within the capabilities of patients to complete.

7.5.1 Limitations

Limitations of the present study include low subject numbers, the nature of the NSCLBP group, and possible design issues. The goal of the study was to provide proof-of-

principle, and therefore NSCLBP patients were recruited from the MSK physiotherapy clinics as well as from pain management. This meant that many of the participants only had low to low-moderate pain levels, and whilst they satisfied the inclusion criteria, some had only had LBP for less than a year. Findings may have been different in higher pain patients who had longer term LBP – the types of patients more likely to receive neuromodulatory intervention. Additionally, it is acknowledged that the age profile of the two groups was not optimally matched. The NSCLBP group had a higher mean age, and as older adults have been shown to display greater variability (Owings and Grabiner, 2004) this may have affected outcomes, although all subjects remained younger than 55 years.

This study used simple randomisation to order the performance of single and dual task movement tests. This type of randomisation can lead to imbalances (Clark and Westerberg, 2009) and learning effects may have come into play. For example, a learning effect may account for the reduced $\lambda_{max\text{-}DT}$ in the healthy group. Block randomisation may improve rigour for future studies.

7.5.2 Research implications

This study provides preliminary findings that demonstrate promise in using this testing procedure in patients with more severe NSCLBP who are suitable to receive neuromodulatory treatment. Further study of this population would be recommended, where larger differences may be observed. The motor task alone may be enough to detect differences between more heterogenous groups, however additional investigation of the effect of the dual task paradigm is implicated. In addition to challenging the human system beyond motor control alone, the cognitive element of the test adds a dimension that represents real-life scenarios more closely.

This testing regime has demonstrated good longitudinal reliability, providing a robust means to clinically assess patients over the long term.

7.6 Conclusion

In conclusion, this study showed there were significant differences between healthy and NSCLBP groups when comparing local dynamic stability using single and dual task conditions during movement tests. No significant associations were found between local dynamic stability measures and pain or LMM thickness. However, after 3-months when there had been a significant reduction in pain, NSCLBP subjects showed behaviour that was analogous to that of healthy subjects during dual task conditions. Future research should involve repeating these protocols in patients with higher levels of NSCLBP and a greater degree of disability with the intention of developing a valid clinical tool that can evaluate effectiveness of treatment interventions.

Chapter 8 : Feasibility of assessing local dynamic stability & lumbar multifidus muscle morphology in patients receiving a targeted intervention (Medial nerve stimulation): A case study

8.1 Chapter overview

This chapter reviews medial nerve stimulation as a neuromodulatory intervention aimed at rehabilitating LMM and restoring stability in NSCLBP patients, as well as reporting the feasibility of using the testing protocol described in previous chapters in a patient receiving this treatment.

8.2 Introduction

The effects of reconditioning programmes on paraspinal muscles in patients with CLBP have been investigated extensively. However, conflicting results have emerged regarding the observed changes in the targeted musculature. For example, several studies noted no change in paraspinal muscle cross sectional area following active rehabilitation programmes (Käser *et al.*, 2001; Mooney *et al.*, 1997), whereas in contrast other studies have shown that multifidus can significantly increase in size after several weeks of stabilization and dynamic-static resistance training (Danneels *et al.*, 2001). It has been postulated that active exercises to improve muscle structure and function can only be effective if performed accurately, and this cannot be achieved if the exercises themselves induce pain. As such, there has been an increase in the development and utilisation of alternative treatment protocols, including neuromodulatory techniques aimed at passively rehabilitating the key stabilising muscles of the spine, restoring stability and reducing pain and disability.

Neuromodulatory strategies for the treatment of CLBP may include Transcutaneous Electrical Nerve Stimulation (TENS) or Spinal Cord Stimulation (SCS) that focus on delivering low levels of electrical energy to nerve fibres which mask or interrupt pain signals before reaching the brain. These protocols are not without problem though. The neural stimulation may cause paraesthesia that the patient experiences as tingling and is often not tolerated well. SCS may only be indicated for the treatment of neuropathic pain and is not necessarily a viable treatment option for patients with predominant CLBP. Furthermore, these treatments are employed for pain management, and not as a long-term solution to the root cause of the pain.

8.3 Medial nerve stimulation

The inconsistent effects of rehabilitation programmes to improve spinal stability, pain and disability has opened the door to a new approach of overcoming motor control impairment. A form of neuromodulation, whereby an implanted device delivers electrical stimulation to the motor nerves responsible for contracting these stabilising muscles could potentially assist in rehabilitating lumbar multifidus muscles that have become deficient due to CLBP. The aim of this treatment intervention is to restore optimal muscle function and reduce the pain and disability associated with CLBP whilst minimising the recurrence of LBP.

8.3.1 The anatomy: the dorsal ramus

The dorsal ramus has attracted increasing clinical attention in both the diagnosis and treatment of low back pain (Saito *et al.*, 2006).

The anatomical course of the medial nerve of the dorsal ramus, with many twists and turns, implies that it is naturally predisposed to mechanical irritation or compression. The medial nerve gives rise to smaller branches which innervate the facet joints – one facet joint is supplied by the medial branches of two adjacent dorsal rami (Shuang *et al.*, 2015). The L1-4 medial nerves descend between one and three vertebrae, where they innervate the facet joints and multifidus.

Interestingly, it has been shown experimentally that dorsal ramus fibres sense pain (Sihvonen *et al.*, 1995). Bogduk (1980) in his study of lumbar dorsal ramus syndrome describes how irritation of the medial branch can cause referred pain in the lower extremities and spasm in myotomes of the same segment.

Pain management strategies commonly use facet joint blocks and neurotomies within the lumbar spine – the theory being that the medial nerve of the dorsal ramus supplies the zygapophyseal (facet) joint, hence, by blocking or anaesthetising the nerve, the pain will cease. However, these interventions tend to have mixed success rates, and effects are generally short-lived.

Whilst the prevalence and treatment of low back pain associated with the lumbar dorsal ramus continues to be investigated (Zhou *et al.*, 2012), there is now wider thinking of how the dorsal ramus may be implicated in the case of altered motor control of spinal muscles, and thus compromised functional dynamic stability.

8.3.2 The procedure

The procedure involves surgical implantation of the device with two leads being placed bilaterally near the medial branch of the dorsal ramus at the L3 vertebra. The leads are connected to the implanted pulse generator which supplies electrical pulses to the nerves, with the objective to activate the muscles supplied by these nerves (see Figure 22). Patients typically undergo 30-minute sessions of stimulation twice a day.

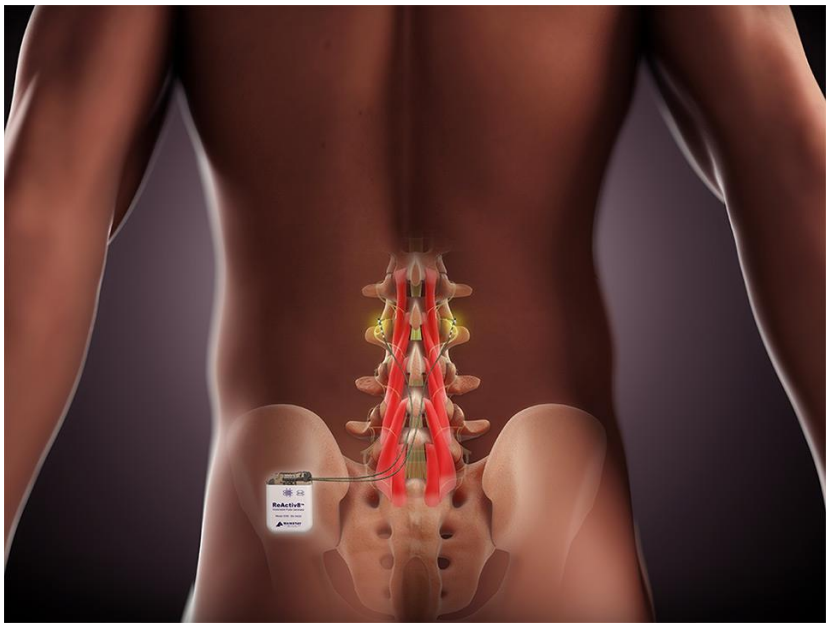


Figure 22: Illustration of the typical setup for medial nerve stimulation using the ReActiv8 product (Mainstay Medical, 2017).

The pain management team at St Thomas' Hospital are using this procedure in conjunction with spinal cord stimulation (wires delivering electrical stimulation are implanted in the spinal cord to block pain signals) as an alternative or adjunct treatment for CLBP patients. However, as this form of treatment is relatively new there is a dearth of evidence eluding to its efficacy. Furthermore, there seems to be only a weak hypothesis on how the intervention works, with no clinical evidence to support that it is effective in its claims.

Mainstay-Medical, the developers of a stimulating device named Reactiv8® have run an international, multi-centre, prospective single arm clinical trial. 47 subjects who had disabling CLBP despite a minimum of 90 days of medical management including at least physical therapy or drugs, no identifiable spine pathology, no prior spine surgery or SCS, were recruited and implanted at one of nine centres in Europe and Australia. Data were collected on pain (measured with a numeric rating scale), disability (using Oswestry Disability Index) and Quality of Life (EQ5D) at baseline, 90 days, 180 days and again at 1 year.

The results showed that there were statistically significant improvements across all three reported measures (p<0.001). The greatest improvement, both at 90 days and 1 year was seen in quality of life (EQ5D). The improvements seen in both pain and quality of life dropped between 3 months post implant and a year later, whereas

improvements in disability increased. Clearly, whilst the trial was both controlled and blinded, the fact that it has been commissioned by the manufacturers of the device under study may question potential bias of the results.

A feasibility study conducted by Deckers *et al.* (2015) aimed to test the hypothesis that, in patients with CLBP, electrical stimulation of the medial branch of the dorsal ramus nerve to contract multifidus can improve the severity of CLBP and its impact on disability and quality of life. They recruited 26 patients with continuing CLBP and implanted them with a stimulatory device as described in the study by Mainstay-Medical. Patients self-administered stimulation twice daily for 20 minutes. Low back pain (measured by Visual Analogue Scale), Oswestry Disability Index and Quality of Life (EQ5D) scores were collected at three and five months and compared to baseline. There were statistically significant and clinically important improvements, with the majority of patients experiencing a clinically important reduction in pain (73.7%) and disability (63.2%) as well as an improvement in quality of life (84.2%) at three months. Stimulation was withdrawn between months 4 and 5 to test durability of effect. Results showed that the majority of patients continued to experience a clinically significant reduction in pain (66.7%) and disability (52.6%) as well as improvement in quality of life (52.6%) at five months. Additionally, 5 of the 11 patients on disability benefit for CLBP resumed work by three months. The authors concluded that episodic stimulation to induce multifidus contraction can reduce CLBP and associated disability, improve quality of life and enable return to work.

Whilst the number of patients reaching or exceeding the minimally important change is encouraging, the statistics from this paper must be interpreted with some caution. In many cases there was an issue with the device. Lead migration caused numerous withdrawals which further reduced the already small sample size. This may have resulted in an overestimation of the overall effect if those subjects who withdrew had been experiencing less improvement. Compliance was self-reported and pain medications were not kept constant; both potentially impacting the results. This study only involved short-term follow up, and it is unknown whether any observed improvements may be sustained in the long-term. Finally, there was no control arm to the study. The placebo effect can therefore not be discounted. The authors claimed that the continuation of some improvement during the therapy-withdrawal phase suggested that the contribution of the placebo effect may have been limited.

Conversely, the paper discusses the reasons why most patients elected to resume regular use of their device after the 5-month visit: perceived prevention of recurrence, treatment of recurrences, to help them 'get going in the morning' and to create the pleasant sensation of having worked out the muscles; suggesting a likely psychological element to the improvements experienced. Furthermore, the study was funded by Mainstay-Medical.

This form of management pertains to the theoretical context that by overriding muscle control impairment caused by reflex inhibition, through electrical stimulation of the nerve, muscle function will be restored. There are no studies to date of objective morphological and functional changes occurring in the relevant musculature following stimulation of the medial branch of the dorsal ramus. As such, there is a lack of clarity over whether this device is directly affecting multifidus as intended, or whether its effect is more widespread.

8.4 Case study

This single case study details how a patient undergoing spinal cord and medial nerve stimulation handled the testing regime with the devised protocol described in Chapter 7, and reports measured outcomes.

8.4.1 The Subject

The patient was a 52-year-old male (referred to hereon in as Mr X) who had been deemed clinically suitable by his pain management consultant at St Thomas' hospital to receive spinal cord and medial nerve stimulation for ongoing NSCLBP. His job was largely sedentary, but he had been active with sport for leisure prior to the last couple of years.

Mr X consented to taking part in the study and to be written up as a case study. He was aware that he could withdraw his consent at any time without his hospital care being affected.

8.4.2 Relevant past medical history

Mr X had suffered with LBP on and off for the past 10 years, with episodes of pain and spasm becoming more severe and frequent over the past few years. Previous treatment had involved physiotherapy as well as invasive procedures, including a discectomy at L4/5, spinal injections and a facet joint denervation. He was of good health otherwise.

8.4.3 Current history

Recent clinical investigations revealed no specific pathology or anatomical cause for his CLBP, although some osteoarthritic changes had been noted in some lumbar spine facet joints. The muscle spasms associated with his LBP were becoming much more severe and almost completely debilitating. Furthermore, each spasmodic episode was lasting around 7 days, with episodes occurring every 10-14 days; more days than not in any given month were spent with severe disabling pain. Under the care of his pain management consultant, it was decided that Mr X would undergo a procedure to implant spinal cord and medial nerve stimulators. Following a successful trial period (where the device remains external to the body and effectiveness is monitored by measuring pain levels), surgical implantation of the device and wires took place.

8.4.4 Study

Mr X agreed to undergo the testing regime over the course of 3 months as detailed in Chapter 7. He attended the clinic at baseline and again at 3-months to perform the stability tests, have ultrasound scans of LMM and complete questionnaires. In addition, questionnaires were completed via telephone follow-up at 1-month and 2-months.

8.4.4.1 Baseline

Mr X attended having had his trial device and wires implanted nine days previously; the procedure had gone well with no complications. Only spinal cord stimulation had

been activated at that stage. Mr X was healing well, with good movement and a reported reduction in LBP.

Mr X completed all stability tests with no issues. He did however mention that he felt that the tests would have been a struggle if he had performed them pre-implant due to the pain and muscle spasms he was experiencing. He also said he would have felt fearful of the level of movement that was required.

USI for measurement of LMM thickness was complicated slightly by the presence of post-operative stitches and tape, along with the external device. Whilst it was still possible to locate the boundaries of the LMMs, accuracy may have been compromised. Additionally, there may potentially have been some swelling or associated changes of the muscle tissue due to the recent invasive intervention.

8.4.4.2 1-month follow-up

Telephone follow-up revealed that Mr X had had the full simulating device surgically implanted shortly after his baseline visit following a successful trial phase and had experienced no spasms since. Pain continued to be at a much lower level also. He felt that he was better overall, and the implant had made a real and worthwhile difference. At this point, only spinal cord stimulation had been activated, not medial nerve stimulation. No adverse events were reported, although he did mention that there had been a small amount of lead migration.

8.4.4.3 2-month follow-up

Another telephone conversation painted a similar picture to that at 1-month. Mr X continued to be experiencing much less pain, and movement was much better. He was able to do more and had started increasing his daily activity. He did report that he had had some transient mild right sided posterior leg pain, but otherwise no other adverse events were mentioned. At this point, medial nerve stimulation was still not in operation; spinal cord stimulation continued.

8.4.4.4 3-months

Mr X attended at 3-months post-baseline feeling well. Medial nerve stimulation had been activated a few weeks previously and the patient was complying with the prescribed schedule and experiencing no problems. Pain levels were still consistently low, and he felt a great deal better; there had been a considerable improvement in his condition.

8.4.4.5 Results

Outcome measures recorded from Mr X are displayed in Table 18. There should be cautious interpretation of these results in terms of generalisability, as single-subject measures have limited informative value in the context of this case study.

Table 18: Results for Mr X

	Baseline	1-month	2-months	3-months
Pain on the day	2			1
Worst pain during the last week	9			1
Lowest level of pain during the last week	4			1
Pain on average	5	2	2	1
PGIC		6	6	7
ODI	50%			24%
LMM thickness:				
L3 Left	4.14 cm			3.86 cm
L3 Right	4.04 cm			3.97 cm
L4 Left	3.74 cm			4.21 cm
L4 Right	4.14 cm			4.43 cm
Mean	4.02cm			4.12cm
λ_{max} (single task)	2.9918			3.2954
λ_{max} (dual task)	3.2141			3.0288
Dual task answer	38			38

PGIC: Patient general impression of change

ODI: Oswestry disability index

Overall pain reduced significantly from 5 at baseline to 1 at 3-months. Furthermore, the range and severity of pain Mr X was experiencing reduced considerably, with 9 being the highest pain score at baseline to 1 being the only level of pain experienced after 3 months. He also perceived a big improvement in his condition.

Disability measured by ODI decreased from 50% to 24%, which is considered as a clinically significant reduction. At baseline his disability was largely influenced by pain killers giving very little relief, pain preventing sitting at all, sex life being restricted by pain, pain restricting social life and not being able to go out as often, and only being able to lift very light weights. At the 3-month point, the impact of these factors had considerably reduced, with the exception of lifting weights.

λ_{max} was fairly consistent between time points, as was mean LMM thickness. However, L3 left, and L4 left and right thicknesses markedly changed from baseline to 3-months (-6.8%, +12.6% and +7% respectively).

8.4.5 Discussion

The purpose of this study was to determine the feasibility of using the devised testing protocol detailed in Chapter 7 with NSCLBP patients being treated with spinal cord and medial nerve stimulation. Whilst this is a single case study, various suppositions can be drawn.

Patients who have been selected for spinal cord and medial nerve stimulation inevitably have high levels of pain; a high score on VAS is a pre-requisite for eligibility. The initial intention was to conduct baseline measures pre-implant, however, due to the pain these patients are likely to be experiencing, the likelihood of them being able to perform the cyclical tap tests for stability is low. This was supported by the opinion of Mr X based on his experience. Conducting testing sessions post-implant would allow the capture of non-pain-mediated movement; although the results of the study detailed in Chapter 7 found no correlation between pain and λ_{max} calculated from the tap tests. It would therefore seem preferable to measure stability once the device has been implanted, spinal cord stimulation has been activated and pain levels have decreased.

[Patients would have only proceeded to full implantation following a successful trial phase with reduced pain levels.]

In this case study, LMM thickness was measured post-trial implant which posed some issues with artefact – stitches, tape on the skin, and external wires - all affecting accessibility as well as clarity of ultrasound image. Patients undergo pre-procedure screening and attend several clinic outpatient appointments prior to having the trial device implanted, thereby providing plenty of opportunity to scan the LMMs beforehand. Furthermore, the influence of the invasive procedure involved with implanting the device is unknown, so scanning the LMMs in advance of implantation would be preferable.

The variability of the values for mean LMM thickness and λ_{max} (single and dual task) over the three-month period remain in line with the findings of the study in Chapter 7; values remained fairly consistent. Change in LMM thickness above the pre-determined MDC of 5.15% was noted in LMM at three levels however (L3 left and L4 left and right). Despite the stimulator having been switched on two-weeks previous to final measurements, no morphological change would be expected after such a short length of time. It is possible that swelling and oedema from surgical implantation of the device confounded these measurements and is something that should be considered in future studies. Repeated measures over a longer period (in excess of 12 weeks, but ideally over the course of a year or more) would be required for the hypothesised changes to potentially be seen.

8.4.6 Conclusion

Overall, this case study demonstrates the practicability of using the devised testing protocol for measuring LMM thickness and local dynamic stability of the trunk in patients receiving spinal cord and medial nerve stimulation. The hypothetical pretext of this intervention is to rehabilitate LMM and improve stability of movement. These tests could provide a means to monitor and measure objective outcomes of this treatment option. Recommendations based on the findings generated by this case study, such as pre-scanning LMM and measuring baseline stability post-implant,

should be incorporated into future study designs. Further study is clearly implicated, with a larger sample size, to fully establish whether this is a suitable clinical tool for use with this population.

Chapter 9 : General Discussion

There is a clinical need to develop and utilise reliable objective tools that can be used to assess patients, measure progression and analyse efficacy and effectiveness of treatment interventions. The literature review identified gaps within the current body of knowledge regarding the reliability and practicality of using suitable measures of functional stability as an adjunct to the currently used subjective measures of assessing NSCLBP patients within a clinical setting.

This thesis details the exploratory work conducted to develop and scrutinise a potentially useful testing regime for such patients. The cyclical tap-test protocol used in the collection of kinematic data was adapted from procedures developed by the team in Berlin to improve suitability to this specific patient group and for use within the clinical setting. Furthermore, the implementation of the dual cognitive task was an addition designed to represent real-life when the demand on neuromotor control is challenged by the necessity to multi-task. The use of a dynamical systems theoretical approach to assess local dynamic stability through the calculation of Lyapunov exponent conceivably enhances the current medical assessment and interpretation of motor behaviour and performance.

9.1 Main findings

Results are reported in the relevant chapters for each study, therefore the following section details findings specific to each element under investigation.

9.1.1 Measures of local dynamic stability

Kinematic data collected during a 3-minute cyclical tap-test was utilised to calculate the Maximum Lyapunov exponent as an indicator of local dynamic trunk stability.

Study 1 (Chapter 5) evaluated the test-retest consistency of the protocol and found good-excellent reliability (ICC=0.760, Cronbach's α=0.883) when using fixed delays to

calculate λ_{max}. Standard error of measurement was determined to be 6.63%. Furthermore, the longitudinal data collected in study 3 (Chapter 7) supported these findings. An ICC of 0.777 was found among healthy subjects who were tested and retested 3 months apart. It was concluded that the local dynamic stability measure derived from kinematic 3-dimensional acceleration time series, from the 3-minute tap-test calculated with fixed delays, is reliable in its use for studies with a repeated measures design.

Study 3 (Chapter 7) assessed local dynamic stability of the trunk under two different conditions over a period of 3 months, comparing healthy subjects and those with NSCLBP. Contrary to the hypothesis that healthy participants would be less unstable than those with NSCLBP, it was found that there was no significant difference in λ_{max_S} between groups. Furthermore, the hypothesis that stability would become more unstable in the dual task condition was also rejected. There were however differences between the groups when comparing λ_{max} under different conditions. It was found that the healthy groups became less unstable in their motor task with the introduction of a simultaneous cognitive task (at baseline and at 3-months), whereas there were no significant differences between λ_{max_S} and λ_{max_DT} in the NSCLBP group at either timepoint. It was evident that the NSCLBP group prioritised the motor task with increased cost to the cognitive task. Their data showed little variation in λ_{max} compared to the healthy group, yet significantly larger answer errors were noted at baseline. It was concluded that there were significant differences between healthy and NSCLBP groups when comparing local dynamic stability using single and dual task conditions during movement tests. No significant associations were found between local dynamic stability measures and pain, disability or LMM thickness. However, after 3-months when there had been a significant reduction in pain, NSCLBP subjects did show behaviour that was analogous to that of healthy subjects during dual task conditions, with significantly lower cognitive errors recorded.

9.1.2 Measures of LMM thickness

Study 2 (Chapter 6) evaluated the test-retest reliability of using ultrasound imaging to measure LMM thickness and found it to be excellent, with an ICC value of 0.988. Minimal detectable change (with 95% confidence) was determined to be 5.15% based

on the calculated standard error of measurement. It was concluded that ultrasound imaging is a reliable method to use in measuring LMM thickness.

In study 3 (Chapter 7) the measurement of LMM thickness showed that there were no significant differences in thickness between healthy and NSCLBP participants and furthermore, there was no distinct change in LMM thickness from baseline to 3-month follow up in both groups.

9.1.3 Patient reported outcome measures

Study 3 (Chapter 7) utilised NRS, ODI and PGIC questionnaires to track levels of pain, disability and perception of change in the NSCLBP group. Whilst there were significant changes in these measures from baseline to 3-months, these did not correlate with levels of stability in either single or dual task conditions.

9.1.4 Feasibility and practicalities

Study 3 (Chapter 7) was conducted in a clinical setting without any major difficulties. The practicalities of setting up and conducting the testing protocol were straightforward. In addition, study 4 (Chapter 8) used a case study to evaluate the use of the protocol on a NSCLBP patient receiving spinal cord and medial nerve stimulation. The case study demonstrated the feasibility of using the devised testing procedures in patients receiving this type of medical intervention. Future study should involve the exploration of more suitable timings for measurements, and suitability within a larger sample size. Additionally, observations made throughout the studies revealed that the test regime could potentially preclude people who have pre-existing knee conditions who find the kneeling-down posture too uncomfortable to sustain for the duration of the test.

9.2 Limitations and Methodological considerations

Specific limitations for each study have been discussed within the relevant chapters, therefore this section will focus on general considerations for the methodologies employed within this thesis.

9.2.1 Participants

With regards to the reliability studies conducted, the relatively small subject numbers generally increased the width of the confidence intervals, and despite yielding good to excellent reliability correlation coefficients, these values should be interpreted with some caution. For the tap-test reliability in particular, more extensive test-retesting would need to be conducted for more reliable or precise estimates.

The longitudinal study recruited 40 subjects with 33 completing the study; an attrition rate of 17.5%. When comparing characteristics between two groups, the size of the study should reflect the magnitude of the expected effect size (Hackshaw, 2008). The use of an innovative protocol meant that there were no previous data with which power may be estimated. Group sizes were therefore determined according to similar studies in the field (Arampatzis *et al.*, 2017; Moreno Catalá *et al.*, 2018). Whilst significant results were found between conditions in the healthy group, no differences were found between groups in each condition. The relatively small study size may have made it harder to distinguish between a real effect and random variation. The boxplot in Figure 15 suggests this may be evident, where the boxes of the healthy group were generally much wider, suggesting greater variability. Furthermore, small studies have more tendency to produce false-positive results, or over-estimate magnitude of association (Hackshaw, 2008). As a feasibility or hypothesis-generating study, the study size and subsequent results are acceptable, but a larger confirmatory study would be needed to make definitive conclusions.

Interventions such as neuromodulation are not limited to 25-55year olds, so exploration in future studies should include a wider age-range of participants – it is known for example that older people can show greater variability which may in turn affect stability. Further considerations would be the inclusion of NSCLBP participants

with higher levels of pain and disability; this would provide additional information of whether the use of this test is feasible in those with more pain, as well as potentially finding significant differences between those with and without NSCLBP.

9.2.2 Confounding factors

Attempts were made to limit or control for potential confounding factors, however there were some possible influences that were not accounted for and should perhaps be considered in future studies.

Fear of movement and fear avoidance strategies are believed to be contributory factors in chronic pain and motor control dysfunction. It is also believed that fear of movement with fear avoidant behaviours occur independently of pain intensity (Vlaeyen *et al.*, 1995). These factors, along with cognitive influences could significantly affect measures of variability and stability, by essentially overruling natural movement patterns. Anxiety occupies attentional resources and may lead to decrements of motor control (Shanbehzadeh *et al.*, 2018) and therefore the introduction of the cognitive task during dual task conditions may reveal disparate changes between λ_{max_S} and λ_{max_DT} when cognitive demands are diverted elsewhere. The Tampa Scale of Kinesiophobia (TSK) is a Likert scaled questionnaire aimed to estimate the degree of pain-related fear of movement. Further study including the use of this tool alongside stability and pain measures may help identify if kinesiophobia is an influential factor.

9.2.3 Measures

The use of measures of dynamic stability is inherently problematic. As previously discussed, the human system is both deterministic and stochastic (Faisal *et al.*, 2008), and therefore measures of stability are likely to be influenced by not only the deterministic properties of the system, but also dynamical and measurement noise. The tap-test was devised to minimise potential variation and focus movement to the trunk. Previous studies have fixed the pelvis in order to restrict motion only to the trunk (Hodges *et al.*, 2013; Ross *et al.*, 2015, 2017), however these methods can impose constraints that may alter movement strategies. The pelvis was left unconstrained in

the tap-test protocol in order to observe natural movement patterns. A chair was placed behind the pelvis in order to limit anterior-posterior movement, and the kneeling down posture eliminated movement from the ankles, knees and hips. It is believed that movement during the test was trunk dominated, however this may be a potential source of inter-individual variation.

The results of these studies should be interpreted with caution, and only within the context of local dynamic stability. The literature review revealed that use of the word stability is a source of controversary, often with no distinction between local or global stability (Dingwell and Kang, 2007). Moreover, consideration of the measure of stability is of utmost importance. The use of alternative measures of stability such as Floquet multipliers can produce quite different, if not opposite results to λ_{max} (Dingwell and Kang, 2007), thus limiting comparability. This is of less importance in a clinical sense, where focus is of longitudinal tracking of patients receiving interventions, and outcome measures will be principally compared within-subject.

The Biometrics accelerometer and DataLog system used for kinematic data collection was a source of several potential issues. Firstly, it was subject to connectivity issues, which is problematic if using with patients in a clinical setting - it is not as easy to ask patients to return. Secondly, the use of a wired accelerometer presents issues regarding application (feeding wires around clothing and hair) and presentation of signal noise. Future study may investigate the use of a wireless accelerometer.

Whilst LMM is a key spinal stabiliser, it is not the only muscle group that contributes to spinal stability. The measurement of LMM only in these studies may appear to be reductionist in approach, however, in the context of the examined intervention - medial nerve stimulation, it is the key muscle group of interest. In future research there may be a case for examining other related muscles and their potential contribution within the context of the study.

9.3 Research Implications

Trunk control is dependent on adequate sensory feedback and muscular control (Crisco *et al.*, 1992), yet both may be compromised due to the morphological changes in key stabilising musculature and altered neural activity that is well documented in people with CLBP. It would therefore seem logical that those with NSCLBP would show more instability in their trunk movement when compared to those without LBP. However, this reasoning was not reflected in the findings of this study where no statistically significant difference in the measure of local dynamic stability between healthy and NSCLBP groups was noted. This has also been the finding of other studies utilising maximum Lyapunov exponent to measure local dynamic stability during a repetitive motor task (Arampatzis *et al.*, 2017; Catalá *et al.*, 2018; Graham *et al.*, 2014). It is feasible this approach is not sensitive enough to detect differences between heterogenous populations, or else that the lack of difference in LMM thickness between groups and the observed levels of pain and disability was not significant enough to contribute towards changes in stability. It is also viable that the movement task was not specific enough to sufficiently challenge the NSCLBP group and as such, differences in stability were not observed between groups. NSCLBP is known to be a multidimensional and complex issue, with many potential pain-inducing sources. The protocol utilised in this study specifically investigated the LMMs, both structurally and functionally, however differentiating between NSCLBP patients and varying the movement task accordingly to load other implicated structures or tissues may improve specificity and thus identification of differences. Moreover, it is well recognised that differentiation of NSCLBP groups according to aetiology can enhance treatment specificity and hence efficacy (Leboeuf-Yde *et al.*, 1997).

The human system may be described as being robust when it is able to withstand perturbations or uncertainty (Kitano, 2004), and the ability of the central nervous system to respond to changes in dynamic stability and altered sensory feedback to make necessary adjustments may be an indication of this. Performance of a secondary task increasing cognitive demand could challenge dynamic stability and thus existing neuromotor strategies. To date we have limited knowledge on how humans choose from available control strategies while moving and being cognitively challenged, particularly in those with musculoskeletal conditions. This study showed that the dual-tasking effect was different between NSCLBP and healthy groups. The findings were

contrary to the expectation that participants would become more unstable with the introduction of the cognitive task, with a greater change anticipated in the NSCLBP group. In fact, the healthy group became less unstable in the motor task, with minimal errors in the cognitive task, whilst little change was seen in stability in the NSCLBP group, yet cognitive errors were significantly higher.

From a dynamical systems perspective, a sufficient amount of variability is necessary for a system to adapt to postural perturbations (Van Emmerik and Van Wegen, 2002). Fear or anticipation of pain during the task may reduce the variability of movement and thus reduce flexibility in NSCLBP participants to respond to the increased demand of dual tasking. Where the healthy group seemed able to improve stability during dual task conditions, the NSCLBP group did not appear to have the capacity to improve motor control; whilst they were able to sustain the same level of stability seen during single task conditions, this was at significant cost to the cognitive task. These findings suggest that a degree of cognitive regulation is involved in the performance of movement tasks in those with NSCLBP. In contrast, the healthy group had the capacity and were perhaps able to draw on previous experience to create anticipatory muscle activation patterns (Santuz *et al.*, 2018) in order to improve dynamic stability, and at minimal cost to the cognitive task. This suggests that motor control in the healthy group was more robust and had greater adaptability, and they were able to employ different modes of operation to improve performance.

This research has explored the application of non-linear analysis of dynamic stability within a clinical setting for a population with NSCLBP. It has identified differences in functional stability between those with and without NSCLBP when cognitively challenged. The findings reported were not as expected, and whilst possible theoretical explanations can be sought, they highlight the need for further study. Furthermore, the lack of correlation between LMM thickness, pain and disability suggest that perhaps these parameters are more suited to within-individual measures for longitudinal analysis rather than for identifying between-group differences.

9.4 Implications for Clinical Practice

It was seen in this study that different strategies were adopted in order to perform stable movement when cognitively challenged in those with NSCLBP compared with healthy individuals, and at different costs. Integrity between sensorimotor and cognitive processes is critical in maintaining stability and coordination of movement, yet this may be challenged in those with NSCLBP. This suggests that dual task situations are risk factors for people with NSCLBP. In this study there was no consequence to failing one or both tasks; participants with NSCLBP were able to control stability at the cost of the cognitive task. However, in a scenario where the secondary task may have real consequences and there is inadequate opportunity to sustain stability, injury may result. This study demonstrates that those with NSCLBP are unable to dual task to the same level of performance as their healthy counterparts, and in real-life situations that have significant consequences they are more likely to fail. NSCLBP may therefore be classed as a risk factor in being able to perform concurrent motor and cognitive tasks successfully.

Patients with NSCLBP and a diagnosis of clinical instability are frequently enrolled on a rehabilitation programme to improve trunk muscle size and strength. However, the data generated in this study suggests there is no relationship between muscle size and dynamic trunk stability – it is suggestive that neural control of spinal stability is the most significant influencing factor. On this basis, increasing muscle size through focused muscle rehabilitation without consideration to restoring neuromuscular control would have little impact on improving spinal stability.

For a diagnosis of clinical instability in NSCLBP to be useful it should be based on the identification of the underlying mechanism(s) driving the disorder, in order to inform appropriate targeted interventions. Objective monitoring of such factors would also measure progression and in turn enable more accurate prognosis and prediction of outcomes. The research performed and reported in this thesis has shown that the novel series of tests used to measure local dynamic stability of the trunk and potential influencing factors has good reproducibility, has been shown to be practical for use in the clinical setting and is feasible for use in people with NSCLBP. This may provide a reliable method of quantifying kinematic parameters as an adjunct to existing subjective measures.

With further development and investigation, this combined set of biomechanical measures may provide a means to identify patients who are exhibiting functional instability and direct their treatment accordingly. Similarly, in patients receiving targeted intervention such as neuromodulation or physical rehabilitation, it provides a way to monitor progression and track the effectiveness of such interventions.

9.5 Future research

The reliability of an innovative and potentially useful clinical tool was established within study 1 (Chapter 5), and study 3 (Chapter 7) demonstrated the capability of the testing protocol to identify differences between healthy and NSCLBP groups. Furthermore, it was established (in Chapter 7 and Chapter 8) that the tests were practical to perform in a clinical setting, and feasibility was confirmed. However, as with any research, further questions were generated, and clarification is required from future studies.

Further development to streamline the testing protocol for easy use within the clinical setting would enhance the engagement and use by clinicians. One aspect to investigate further is the use of a wireless accelerometer that can be attached to the skin with ease and allow a swifter set up of the test as well as eliminating potential noise and error from a wired device. Wireless sensors tend to be larger in size and this could influence its suitability and should be studied in a comparative study analysing limits of agreement. In addition, a larger scale reliability study should be conducted with a larger sample size and multiple raters to further validate the reproducibility of measures. It has been shown that averaging multiple measures of λ_{max} can help improve reliability (Ekizos *et al.*, 2018; Reynard and Terrier, 2014) therefore the incorporation of multiple measures at each time point, within the constraints of clinic appointments should be explored.

Between-group differences were identified in movement stability when in conjunction with a cognitive task. Differences were distinct at baseline, but less so at 3-months. There was a decrease in the level of pain and disability in the NSCLBP group between baseline and 3-months even though participants were not undergoing any targeted

treatment intervention. Additionally, there were no changes in LMM thickness. Further investigation is warranted as to why at 3-months the NSCLBP group showed less unstable movement during the dual task conditions similar to that seen in the healthy group. This finding was not significant and may not be apparent in a larger scale study, equally there may be some significance to this finding in relation to the reduction of pain and disability. In addition, randomisation of the order of task performance (single vs dual) needs to be tightened in future studies to help eliminate any learning effect.

Within the biopsychosocial framework, NSCLBP is recognised as being a multi-faceted problem that can be influenced by a multitude of factors. The battery of tests used in these studies focused primarily on analysing the biomechanical aspects of the disorder, yet it has been mentioned before that numerous other factors could influence pain as well as the performance of both motor and cognitive tasks. Such factors could include, but are not limited to fear of movement, anxiety, confidence, pain in adjacent regions (especially the knees), fitness levels, weight, balance and coordination. The strict inclusion/exclusion criteria used in these studies eliminated significant factors that may have confounded the results, but these elements may also impact findings. Future study should develop and incorporate more in-depth criteria that is queried before the start of the study.

Finally, future work is required to investigate the use of the described testing protocol in the evaluation of NSCLBP patients undergoing targeted intervention. This would include a larger scale study with an increased sample size, multiple arms to the study and over a longer period. The aim of such studies would be to observe changes in neuromuscular control in those receiving an intervention compared to those who receive no treatment. Results may provide indications of efficacy of the targeted intervention.

Chapter 10 : Conclusion

The research contained within this thesis has developed and employed a set of clinical tests to measure local dynamic stability of the trunk, morphology of key spinal stabiliser LMM, pain and disability of NSCLBP patients, and examined the relationship between these measures.

The stability measures utilised maximum Lyapunov exponents to quantify how the system responded to small internal perturbations and thus providing indicators of neuromuscular control errors. Differences in movement stability and cognitive accuracy were seen between healthy and NSCLBP participants. The healthy participants became less unstable during dual motor and cognitive tasks and performed the cognitive task with a high level of accuracy, whereas the NSCLBP participants maintained a similar level of stability between single and dual task conditions but with significantly lower accuracy in the cognitive task. However, with the decrease of pain NSCLBP participants were able to maintain movement stability with significantly less cognitive errors. The research suggests that NSCLBP patients rely on cognition to maintain stability of movement and do not have adequate resources to accurately perform concurrent motor and cognitive tasks; this may be related to pain.

It is believed that this research is the first of its kind to examine local dynamic trunk stability with cognitive dual task in NSCLBP patients within a clinical environment. It has shown that the execution of the tests has proven practical and feasible, with good reliability, and the findings have broader theoretical and practical implications for future research in this field.

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Appendices

Appendix A

Participant Documentation

Participant Information Sheet

Informed Consent Form

Health Questionnaire

Pain Questionnaire

Disability Questionnaire

Patient Global Impression of Change Questionnaire

Telephone Questionnaire

Participant Information Sheet

IRAS ID: 236346

The effect of neuromodulation on muscle size, local trunk dynamic stability and chronic low back pain

You are being invited to participate in a research study. Before you decide whether or not to take part, 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 your doctor, the researcher and family if you wish.

Why have I been chosen?

You are being invited to participate in this study because you are between 25 and 55 years of age, have chronic low back pain, and with your current treatment plan, your doctor has identified you as being eligible to take part in the study.

What is the purpose of the study?

This study is looking at how the size of lower back muscles and stability of the lumbar spine may relate to low back pain.

Why have I been invited to participate?

You have expressed your interest in this study, and are eligible to participate because you are between 25 and 55 years of age, have chronic low back pain, and are receiving relevant treatment as recommended by your doctor.

Do I have to take part?

No. It is entirely up to you whether or not you wish to take part. This information sheet is provided to help you with your decision. After reading this, if you do wish to participate, you will be asked to sign and date a consent form. You will still be free to withdraw from the study at any time without giving a reason. A decision not to take part, or a decision to withdraw at a later date, will not affect the standard of care that you receive.

What will happen if I take part?

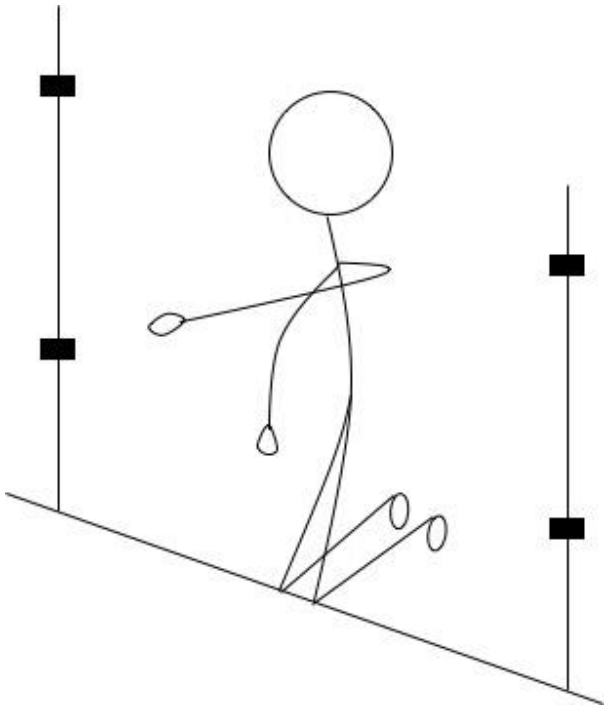
The table below shows what will happen if you decide to join the study compared to what will happen if you do not wish to participate.

Timepoint	Activity	Study	Standard care
Before study	Consent	If you decide to join the study, you will be asked to sign a consent form. You will keep a copy and a copy will be placed in your medical notes at the hospital and kept at the university. If you consent for your GP to be informed, we will send a letter to the practice.	You will not sign the study consent form. Your standard medical care will not be affected.
Start of study	Visit	This visit will coincide with your clinic appointment. It will involve measurements being taken and will take approximately an hour in addition to your usual appointment time. You will be asked to complete questionnaires, have an ultrasound scan of the muscles of your lower back and perform some movement tests.	You will attend your normal clinic visit, but not perform any additional tests.
4 weeks	Telephone follow-up	You will receive a phone call and asked a series of questions about your low back pain.	You will not receive this telephone follow-up.
8 weeks	Telephone follow-up	You will receive a phone call and asked a series of questions about your low back pain.	You will not receive this telephone follow-up.
12 weeks	Visit	This visit will coincide with your clinic appointment. It will involve measurements being taken and will take approximately an hour in addition to your usual appointment time. You will be asked to complete questionnaires, have an ultrasound scan of the muscles of your lower back and perform some movement tests.	You will attend your normal clinic visit, but not perform any additional tests.

There will be 4 occassions on which data will be collected, each being approximately 1 month apart.

Session 1 – will take approximately 1 hour and will coincide with your regular clinic appointment.

- You will be asked to complete questionnaires relating to your pain and how it affects your everyday life.
- An ultrasound scan of your lower back muscles will be carried out. You will need to lie on your tummy whilst this is done. Ultrasound gel will be applied to your skin and you will feel light movements over your skin whilst the scan is performed; it is not uncomfortable.
- Range of motion – this is to assess how your lumbar spine moves. Small sensors will be taped on to the skin of your back and you will be asked to bend forwards several times.
- Stability test – this is to look at how stable your spine is when it moves. A small sensor will be taped to the skin of your back and you will be asked to perform 3 minutes of movements. The diagram below shows the position you will be in during this test. You will kneel between two posts and reach across to tap each point with the opposite hand, alternating sides.



- Dual task stability test – this is to look how stable your spine is when there is an additional task to focus on. You will be asked to perform the stability test again whilst performing simple arithmetic and listening to a series of high and low pitched tones.

The researcher will explain and demonstrate what you need to do at each stage, and you may watch a video to help you understand what the test will entail.
If at any point you are uncomfortable or in pain, then you will be able to stop.

Session 2 – telephone follow-up call, lasting 5-10 minutes.

- The researcher will call you at a pre-arranged time, approximately 4 weeks after session 1 and ask you how you think your treatment is going and to rate your pain.

Session 3 – telephone follow-up call, lasting 5-10 minutes.

- The researcher will call you at a pre-arranged time, approximately 4 weeks after session 2 and ask you how you think your treatment is going and to rate your pain.

Session 4 - will take approximately 1 hour and will coincide with your regular clinic appointment.

- This will be a repeat of what you did in session 1.

Will my treatment be affected by the study?

You should have a treatment/management plan in place that you and your clinician have agreed on. This makes you eligible to take part in the study. However, taking part in this study does not prevent you from receiving best care, so if your clinician believes another form of treatment should be offered, then this will be discussed with you.

What are the possible benefits of taking part?

It is unlikely that you will gain any personal benefit from participating in this research. However, the information we collect from the study will contribute to the body of knowledge on chronic low back pain, including the treatment and management of the condition.

Will the data collected in this study be kept confidential?

All data collected will be handled in a confidential manner and stored in a locked filing cabinet and on a password protected computer in an environment locked when not occupied. All data will be stored in this manner at London South Bank University. Only the research team will have direct access to the information. Any contact details and identifiable data on the health questionnaire will be retained securely at the University. These details will be stored for 3-6 months following completion of the study, when they will be destroyed. Any research data collected in reference to you will be coded, and you will not be identifiable. All data will be held for 5 years after it is published, and will then be safely destroyed.

What should I do if I want to take part?

If you wish to participate please contact the researcher. You will be asked to sign a consent form at the start of the study. With your permission your GP will be notified of your participation in the study.

Changing your mind

You are free to withdraw from the study at any time without giving a reason and without any consequences. However, once the data has been analysed and incorporated into any research publication, you will no longer be able to withdraw. If you wish to discuss this further please contact the researcher directly.

What will happen to the results of the research study?

All data obtained during the experiment will be analysed individually, but the group results will be used in publications including reports and scientific articles and will be disseminated to key public, scientific and professional stakeholders via presentations. If you wish to receive a copy of the study results please let the researcher know at any point during the study, or via email if you decide after the study has ended.

Who is organising and funding the research?

This research is funded by London South Bank University and Guys and St Thomas' NHS Trust. It is conducted by a research team in the University's Applied Science department. The study data may be reviewed by the university sponsor for auditing/monitoring purposes.

Who has reviewed the study?

This study is being completed as part of a Doctoral Degree at London South Bank University. It has been reviewed and ethically approved by the London-Surrey research ethics committee (Health Research Authority).

Contact for Further Information

If you have any questions or concerns regarding this project, please contact the researcher. If you have any concerns about the way in which the study has been conducted, please contact the Academic Supervisor for this study in the first instance, or the Chair of the University Research Ethics Committee.

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University Research Ethics Committee:

Email: SASethics@lsbu.ac.uk

Thank you!

Thank you very much for taking the time to read this information sheet.

Consent Form

Full title of Project: The effect of neuromodulation on muscle size, local trunk dynamic stability and chronic low back pain

IRAS ID: 236346

Name, position and contact details of Researcher: Helen Lumbard, PhD student
lumbardh@lsbu.ac.uk
Tel: 020 7815 7937 / 07950868837

Participant Identification Number for this study:

Personal Details	
Name	
Date of Birth	
Address	
Telephone Numbers	
Email Address	
Gender	
Ethnic background	

Taking part	Initial
I confirm that I have read the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
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.	
I agree to take part in the above study.	

Use of my information	Initial
I understand that relevant sections of my medical notes and data collected during the study may be looked at by Helen Lumbard as well as clinical staff at Guy's & St Thomas' NHS Trust. I give permission for these individuals to have access to my records.	
I understand that the information collected about me may be used to support other research in the future, and may be shared anonymously with other researchers.	
I understand that the study data may be reviewed by the university sponsor for auditing/monitoring purposes.	
I agree to my General Practitioner being informed of my participation in the study.	

Name of Participant	Date	Signature
Name of Person taking consent	Date	Signature

When completed: 1 for participant; 1 for researcher site; 1 to be kept in medical notes. Version 3.2. 26/7/2018

London South Bank University
EST 1892

Guy's and St Thomas' NHS
NHS Foundation Trust

Health Questionnaire

Full title of Project: The effect of neuromodulation on muscle size, local trunk dynamic stability and chronic low back pain

IRAS ID: 236346

Name, position and contact details of Researcher: Helen Lumbard, PhD student
lumbardh@lsbu.ac.uk, Tel: 020 7815 7937

Participant Identification Number for this study:

Past Medical History (please tick the box that applies & provide more details where required)	Yes	No
I currently have low back pain and have done for the past 6 months or longer.	☐	☐
I have been following a training/rehabilitation programme for my low back muscles during the previous 3 months, or I intend to start doing so in the next 4 months.	☐	☐
I have had spinal surgery and/or a serious spinal injury. *If yes, please give details:*	☐	☐
I have been told that I have a spinal condition. *If yes, please give details:*	☐	☐
I have been diagnosed with other medical conditions. *If yes, please give details:*	☐	☐

I have a known plaster/tape allergy. *If yes, please give details:*	☐	☐
I have a known allergy to ultrasound gel. *If yes, please give details:*	☐	☐

Name of Participant	Date	Signature

Name of Researcher	Date	Signature

Version 3.1 1/7/18

London South Bank University

Guy's and St Thomas' NHS
NHS Foundation Trust

Pain Questionnaire

Full title of Project: The effect of neuromodulation on muscle size, local trunk dynamic stability and chronic low back pain

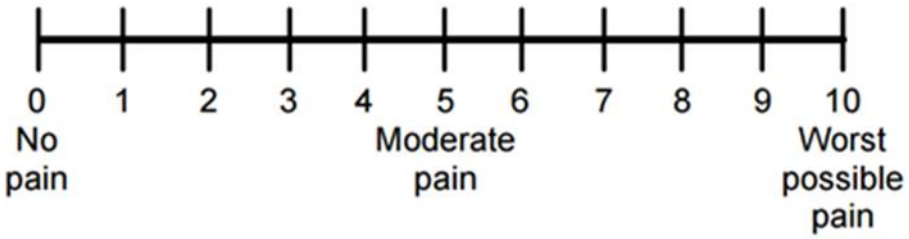
IRAS ID: 236346

Participant Identification Number:

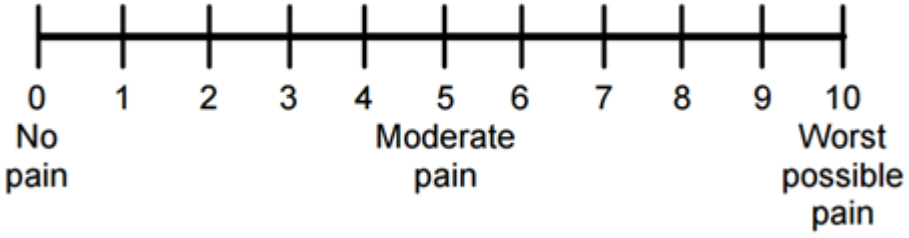
Date:

Circle the number on the scale that best represents the intensity of your pain.

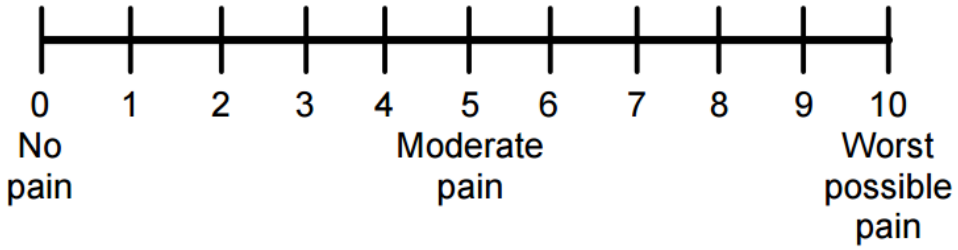
How would you rate your low back pain today?



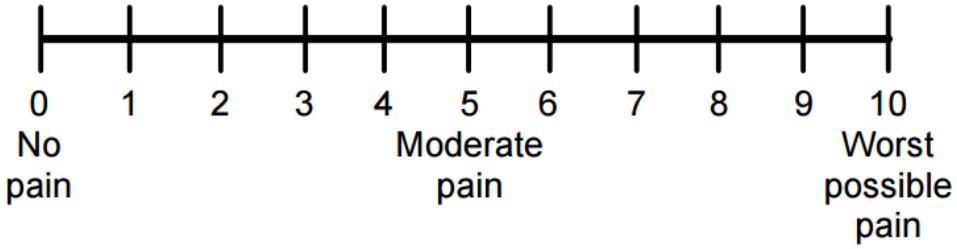
What is the worst your low back pain has been in the last week?



What is the lowest level of pain you have experienced in the last week (whilst awake)?



How would you rate your low back pain on average?



Oswestry Questionnaire

Full title of Project: The effect of neuromodulation on muscle size, local trunk dynamic stability and chronic low back pain

IRAS ID: 236346

Participant Identification Number:

Date:

Please read:

This questionnaire is interested in how your low back pain affects your ability to manage in everyday life. Please answer *every* section, and tick only *one* box in each section. You may consider that 2 statements in any 1 section relate to you, but please *just tick the box that most closely describes your situation.*

Section 1 - pain intensity

- ❑ I can tolerate the pain I have without having to use pain killers
- ❑ The pain is bad but I manage without taking pain killers
- ❑ Pain killers give complete relief from pain
- ❑ Pain killers give moderate relief from pain
- ❑ Pain killers give very little relief from pain
- ❑ Pain killers have no effect on the pain and I do not use them

Section 2 - personal care (washing, dressing, etc)

- ❑ I can look after myself normally without causing extra pain
- ❑ I can look after myself normally but it causes extra pain
- ❑ It is painful to look after myself and I am slow and careful
- ❑ I need some help but manage most of my personal care
- ❑ I need help every day in most aspects of self care
- ❑ I do not get dressed, wash with difficulty and stay in bed

Section 3 – lifting

- ❑ I can lift heavy weights without extra pain
- ❑ I can lift heavy weights but it gives extra pain
- ❑ Pain prevents me from lifting heavy weights off the floor, but I can manage if they are conveniently positioned, e.g. on a table
- ❑ Pain prevents me from lifting heavy weights but I can manage light to medium weights if they are conveniently positioned
- ❑ I can lift only very light weights
- ❑ I cannot lift or carry anything at all

Section 4 – walking

- ❑ Pain does not prevent me walking any distance
- ❑ Pain prevents me walking more than 1 mile
- ❑ Pain prevents me walking more than 1/2 mile
- ❑ Pain prevents me walking more than 1/4 mile
- ❑ I can only walk using a stick or crutches
- ❑ I am in bed most of the time and have to crawl to the toilet

Section 5 - sitting

- ❑ I can sit in any chair as long as i like
- ❑ I can only sit in my favourite chair as long as i like
- ❑ Pain prevents me from sitting more than 1 hour
- ❑ Pain prevents me from sitting more than 1/2 hour
- ❑ Pain prevents me from sitting more than 10 minutes
- ❑ Pain prevents me from sitting at all

Section 6 - standing

- ❑ I can stand as long as I want without extra pain
- ❑ I can stand as long as I want but it gives me extra pain
- ❑ Pain prevents me from standing for more than 1 hour
- ❑ Pain prevents me from standing for more than 1/2 hour
- ❑ Pain prevents me from standing for more than 10 minutes
- ❑ Pain prevents me from standing at all

Section 7 - sleeping

- ❑ Pain does not prevent me from sleeping well
- ❑ I can sleep well only by using tablets
- ❑ Even when I take tablets I have less than six hours sleep
- ❑ Even when I take tablets I have less than four hours sleep
- ❑ Even when I take tablets I have less than two hours sleep
- ❑ Pain prevents me from sleeping at all

Section 8 - sex life

- ❑ My sex life is normal and causes no extra pain
- ❑ My sex life is normal but causes some extra pain
- ❑ My sex life is nearly normal but is very painful
- ❑ My sex life is severely restricted by pain
- ❑ My sex life is nearly absent because of pain
- ❑ Pain prevents any sex life at all

Section 9 - social life

- ❑ My social life is normal and gives me no extra pain
- ❑ My social life is normal but increases the degree of pain
- ❑ Pain has no significant effect on my social life apart from limiting my more energetic interests, e.g. dancing, etc.
- ❑ Pain has restricted social life and I do not go out as often
- ❑ Pain has restricted my social life to my home
- ❑ I have no social life because of pain

Section 10 - travelling

- ❑ I can travel anywhere without extra pain
- ❑ I can travel anywhere but it gives me extra pain
- ❑ Pain is bad but I manage journeys over two hours
- ❑ Pain restricts me to journeys of less than one hour
- ❑ Pain restricts me to short necessary journeys of less than ½ hour
- ❑ Pain prevents me from travelling except to the doctor or hospital

Patient Global Impression of Change Questionnaire

Full title of Project: The effect of neuromodulation on muscle size, local trunk dynamic stability and chronic low back pain

IRAS ID: 236346

Participant Identification Number:

Date:

Since beginning this study, how would you describe the change (if any) in ACTIVITY LIMITATIONS, SYMPTOMS, EMOTIONS and OVERALL QUALITY OF LIFE related to your lower back pain? (tick ONE box)

No change (or condition has got worse)	☐	1
Almost the same, hardly any change at all	☐	2
A little better, but no noticeable change	☐	3
Somewhat better, but the change has not made any real difference	☐	4
Moderately better, and a slight but noticeable change	☐	5
Better, and a definite improvement that has made a real and worthwhile difference	☐	6
A great deal better, and a considerable improvement that has made all the difference	☐	7

Telephone Follow-Up Questionnaire

Full title of Project: The effect of neuromodulation on muscle size, local trunk dynamic stability and chronic low back pain

IRAS ID: 236346

Name, position and contact details of Researcher: Helen Lumbard, PhD student
lumbardh@lsbu.ac.uk, Tel: 020 7815 7937

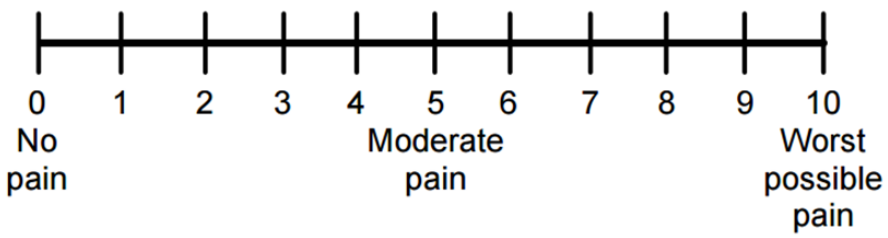
Participant Identification Number:

Date of contact:

Point of Contact	4	8
4 weeks or 8 weeks post-baseline	☐	☐

Compliance	Yes	No
Have you been complying with the treatment regime as prescribed by your health care professional?	☐	☐

NRS



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Since beginning this study, how would you describe the change (if any) in ACTIVITY LIMITATIONS, SYMPTOMS, EMOTIONS and OVERALL QUALITY OF LIFE related to your lower back pain? (tick ONE box)

No change (or condition has got worse)	☐	1
Almost the same, hardly any change at all	☐	2
A little better, but no noticeable change	☐	3
Somewhat better, but the change has not made any real difference	☐	4
Moderately better, and a slight but noticeable change	☐	5
Better, and a definite improvement that has made a real and worthwhile difference	☐	6
A great deal better, and a considerable improvement that has made all the difference	☐	7

Additional Notes

Completed by:

Date:

Appendix B

Raw data for repeated λ_{max} values (Chapter 5)

Subject	Gender	Age	Height (m)	Weight (kg)	BMI (kg/m^2)	λ_{max} 1 (FD)	λ_{max} 2 (FD)	λ_{max} 1 (ID)	λ_{max} 2 (ID)
1	F	29	1.83	77	22.99	5.448	4.874	5.481	4.860
2	F	40	1.75	59	19.27	4.751	4.024	4.904	4.018
3	F	25	1.73	65	21.72	5.550	5.606	5.754	5.683
4	M	27	1.93	92	24.70	4.767	4.615	4.753	4.485
5	M	36	1.73	86	28.73	5.455	5.132	5.495	5.173
6	F	53	1.63	53	19.95	6.724	6.015	6.777	5.897
7	F	25	1.60	56	21.88	4.981	5.011	5.075	5.088
8	M	27	1.75	74	24.16	4.244	4.352	4.376	4.400
9	F	26	1.74	65	21.47	4.413	4.049	4.708	4.255
10	M	30	1.86	85	24.57	5.496	4.885	5.478	4.759
11	M	28	1.58	62	24.84	4.652	5.364	4.640	5.224
12	M	48	1.73	82	27.40	4.546	4.471	4.720	4.581

Appendix C

Raw data for repeated LMM thickness measurements using USI (Chapter 6)

LMM thickness (cm) – L3 Left

Subject	D1M1	D1M2	D1M3	D1M4	D1M5	D1M6	D1M7	D1M8	D1M9	D1M10	D2M1	D2M2	D2M3	D2M4	D2M5	D2M6	D2M7	D2M8	D2M9	D2M10
1	3.35	3.31	3.33	3.39	3.37	3.37	3.37	3.31	3.41	3.39	3.44	3.41	3.43	3.34	3.39	3.50	3.46	3.48	3.46	3.46
2	3.00	3.05	2.91	3.00	3.03	3.02	3.07	3.10	3.12	3.05	3.14	3.12	3.07	3.12	3.19	3.19	3.19	3.21	3.19	3.12
3	3.02	3.03	2.98	3.00	3.00	2.98	2.98	2.96	2.98	2.98	2.89	2.95	2.84	2.93	2.91	2.88	2.88	2.88	2.86	2.91
4	1.98	2.00	1.91	2.05	2.02	1.98	1.97	2.02	2.05	1.97	2.03	2.01	2.07	2.02	2.05	2.01	2.05	2.03	2.07	2.03
5	2.47	2.50	2.50	2.50	2.54	2.50	2.52	2.54	2.59	2.54	2.50	2.40	2.58	2.54	2.49	2.50	2.59	2.36	2.45	2.43
6	3.25	3.16	3.09	3.25	3.09	3.26	3.09	3.17	3.21	3.21	3.12	3.14	3.15	3.14	3.12	3.12	3.14	3.15	3.15	3.14
7	2.80	2.86	2.85	2.87	2.81	2.79	2.85	2.87	2.95	2.85	2.72	2.79	2.75	2.79	2.80	2.80	2.79	2.84	2.79	2.77
8	2.77	2.79	2.75	2.67	2.75	2.71	2.73	2.71	2.71	2.73	2.73	2.71	2.76	2.70	2.77	2.70	2.73	2.74	2.76	2.74
9	2.04	2.02	2.02	2.13	2.11	1.95	1.97	1.97	2.04	1.97	1.99	2.03	1.98	1.92	2.01	2.00	1.97	1.92	1.97	2.05
10	2.75	2.79	2.70	2.68	2.75	2.61	2.66	2.70	2.73	2.84	2.75	2.75	2.77	2.79	2.73	2.68	2.66	2.72	2.77	2.75
11	2.63	2.73	2.70	2.71	2.74	2.74	2.73	2.71	2.67	2.56	2.70	2.73	2.70	2.62	2.73	2.68	2.68	2.65	2.62	2.68
12	2.49	2.53	2.58	2.65	2.64	2.65	2.64	2.68	2.59	2.67	2.58	2.59	2.59	2.71	2.62	2.61	2.62	2.61	2.64	2.65

LMM thickness (cm) – L3 Right

Subject	D1M1	D1M2	D1M3	D1M4	D1M5	D1M6	D1M7	D1M8	D1M9	D1M10	D2M1	D2M2	D2M3	D2M4	D2M5	D2M6	D2M7	D2M8	D2M9	D2M10
1	3.38	3.35	3.34	3.41	3.48	3.51	3.36	3.36	3.45	3.50	3.29	3.31	3.30	3.25	3.33	3.24	3.35	3.34	3.33	3.28
2	3.21	3.24	3.31	3.32	3.34	3.25	3.27	3.30	3.31	3.24	3.31	3.36	3.37	3.28	3.39	3.40	3.40	3.34	3.34	3.31
3	2.93	2.98	3.04	3.10	2.95	2.97	3.01	3.03	2.98	3.01	3.00	3.03	3.05	2.99	3.01	2.98	3.00	2.99	3.02	3.09
4	2.08	2.09	2.01	1.99	2.04	2.03	2.07	2.08	2.01	2.02	2.09	2.11	2.10	2.07	2.04	2.09	2.06	2.05	2.11	2.10
5	2.68	2.69	2.69	2.68	2.66	2.67	2.68	2.66	2.66	2.68	2.61	2.63	2.58	2.60	2.63	2.59	2.61	2.60	2.64	2.62
6	3.15	3.13	3.16	3.17	3.19	3.21	3.19	3.20	3.13	3.17	3.20	3.21	3.23	3.17	3.18	3.20	3.21	3.17	3.23	3.20
7	2.70	2.77	2.78	2.71	2.76	2.75	2.77	2.79	2.71	2.70	2.68	2.69	2.68	2.68	2.68	2.66	2.69	2.67	2.71	2.71
8	2.80	2.81	2.84	2.80	2.78	2.78	2.79	2.80	2.85	2.86	2.87	2.86	2.85	2.88	2.86	2.89	2.86	2.87	2.88	2.85
9	2.08	2.06	2.07	2.10	2.03	2.11	2.12	2.06	2.07	2.05	2.10	2.13	2.07	2.16	2.08	2.18	2.09	2.08	2.12	2.18
10	2.85	2.89	2.84	2.94	2.81	2.89	2.91	2.92	2.94	2.90	2.80	2.81	2.84	2.79	2.78	2.88	2.85	2.83	2.86	2.87
11	2.70	2.70	2.70	2.71	2.71	2.73	2.70	2.71	2.69	2.73	2.79	2.77	2.80	2.82	2.81	2.78	2.78	2.78	2.82	2.81
12	2.51	2.53	2.52	2.50	2.54	2.55	2.59	2.59	2.54	2.56	2.57	2.60	2.64	2.58	2.58	2.59	2.61	2.58	2.57	2.59

LMM thickness (cm) – L4 Left

Subject	D1M1	D1M2	D1M3	D1M4	D1M5	D1M6	D1M7	D1M8	D1M9	D1M10	D2M1	D2M2	D2M3	D2M4	D2M5	D2M6	D2M7	D2M8	D2M9	D2M10
1	3.64	3.60	3.59	3.66	3.64	3.63	3.61	3.67	3.62	3.65	3.70	3.68	3.71	3.69	3.68	3.68	3.71	3.67	3.69	3.70
2	3.28	3.30	3.27	3.36	3.33	3.33	3.34	3.29	3.27	3.30	3.33	3.28	3.27	3.33	3.34	3.36	3.30	3.27	3.31	3.33
3	3.40	3.42	3.36	3.39	3.40	3.41	3.41	3.38	3.39	3.38	3.36	3.33	3.38	3.36	3.40	3.41	3.36	3.34	3.39	3.36
4	2.28	2.28	2.28	2.27	2.29	2.28	2.26	2.28	2.29	2.30	2.26	2.38	2.37	2.28	2.29	2.30	2.34	2.33	2.29	2.38
5	2.68	2.69	2.70	2.66	2.67	2.72	2.71	2.68	2.66	2.66	2.73	2.76	2.80	2.75	2.81	2.77	2.80	2.76	2.77	2.73
6	3.53	3.55	3.55	3.53	3.57	3.56	3.60	3.63	3.62	3.64	3.64	3.67	3.68	3.70	3.68	3.73	3.71	3.72	3.68	3.68
7	3.07	3.08	3.09	3.08	3.07	3.11	3.06	3.05	3.10	3.07	3.05	3.04	3.06	3.10	3.11	3.03	3.04	3.05	3.10	3.09
8	3.05	3.06	3.05	3.03	3.04	3.06	3.07	3.05	3.09	3.00	2.99	2.97	2.99	2.97	2.97	2.99	3.02	3.04	2.99	2.98
9	2.21	2.27	2.26	2.26	2.28	2.24	2.23	2.30	2.28	2.29	2.17	2.20	2.22	2.18	2.20	2.21	2.16	2.18	2.20	2.21
10	3.10	3.09	3.07	3.08	3.11	3.13	3.09	3.13	3.06	3.11	3.20	3.18	3.17	3.21	3.23	3.15	3.21	3.23	3.18	3.18
11	2.99	3.03	3.00	3.01	2.98	2.97	3.04	3.02	2.96	3.04	2.96	2.90	2.88	2.89	2.90	2.90	2.93	2.91	2.93	2.95
12	2.81	2.84	2.88	2.91	2.79	2.77	2.85	2.79	2.88	2.90	2.91	2.98	2.95	2.99	2.89	2.90	2.94	2.90	2.89	2.91

LMM thickness (cm) – L4 Right

Subject	D1M1	D1M2	D1M3	D1M4	D1M5	D1M6	D1M7	D1M8	D1M9	D1M10	D2M1	D2M2	D2M3	D2M4	D2M5	D2M6	D2M7	D2M8	D2M9	D2M10
1	3.59	3.56	3.63	3.58	3.67	3.68	3.57	3.65	3.57	3.69	3.64	3.64	3.68	3.70	3.73	3.63	3.65	3.70	3.68	3.69
2	3.27	3.37	3.33	3.34	3.28	3.29	3.33	3.37	3.36	3.29	3.23	3.33	3.24	3.25	3.26	3.23	3.27	3.27	3.24	3.27
3	3.51	3.49	3.48	3.55	3.51	3.49	3.55	3.56	3.53	3.54	3.48	3.45	3.39	3.49	3.48	3.39	3.39	3.45	3.44	3.45
4	2.41	2.38	2.38	2.35	2.36	2.40	2.35	2.35	2.36	2.36	2.36	2.39	2.33	2.33	2.39	2.37	2.40	2.40	2.38	2.37
5	2.71	2.68	2.70	2.67	2.66	2.76	2.77	2.67	2.68	2.71	2.77	2.79	2.80	2.82	2.77	2.76	2.80	2.81	2.75	2.77
6	3.55	3.56	3.53	3.56	3.54	3.58	3.53	3.55	3.56	3.54	3.56	3.57	3.53	3.56	3.58	3.55	3.57	3.56	3.55	3.57
7	3.13	3.13	3.13	3.15	3.17	3.12	3.14	3.15	3.14	3.13	3.17	3.21	3.23	3.24	3.19	3.19	3.18	3.23	3.22	3.20
8	3.01	3.03	3.10	3.07	3.08	3.04	3.01	3.02	3.09	3.07	3.09	3.11	3.07	3.08	3.13	3.08	3.14	3.13	3.11	3.10
9	2.15	2.14	2.15	2.13	2.11	2.12	2.15	2.16	2.15	2.12	2.21	2.17	2.19	2.15	2.16	2.20	2.20	2.21	2.19	2.18
10	3.15	3.13	3.16	3.14	3.15	3.19	3.21	3.13	3.18	3.20	3.20	3.21	3.17	3.23	3.26	3.16	3.18	3.19	3.21	3.22
11	3.02	3.02	3.03	3.08	3.09	3.07	3.03	3.01	3.05	3.01	3.10	3.07	3.11	3.13	3.06	3.16	3.17	3.10	3.12	3.11
12	2.90	2.91	2.85	2.89	2.92	2.93	2.90	2.91	2.89	2.96	3.00	2.98	3.03	2.96	2.99	3.03	3.01	2.98	3.01	2.99

Appendix D

Raw data for longitudinal study (Chapter 7)

Healthy group data

					λ_{max}				Cognitive answer		
Subject	ID	Gender	Age	BMI	B_ST	B_DT	3M_ST	3M_DT	B_ST	B_DT	3M_DT
1	02M73HH	M	45	23.71	4.8302	4.7957	4.9123	4.3751	38	37	38
2	11R77CH	M	41	31.85	4.0183	3.6525	4.4921	3.7857	38	39	37
3	12E86CH	F	31	21.64	5.5772	4.7026	5.3615	4.2414	38	38	38
4	12M78KH	M	39	36.44	4.3719	4.7391	4.6016	4.2782	38	38	36
5	12B89DH	M	29	26.03	5.8279	6.1030	6.0394	5.8679	38	39	38
6	12S90WH	M	28	33.44	5.445	5.3450	5.5332	5.4104	38	39	41
7	12T63WH	F	55	31.93	3.9754	3.8947	3.9013	3.1992	38	39	38
8	01L85WH	M	33	20.59	5.8174	5.0221	6.0175	5.8602	38	38	39
9	01A87PH	F	31	23.88	4.3075	4.2566	4.5837	4.2806	38	38	37
10	01S79DH	F	39	24.39	4.6363	3.9558	4.1889	4.0681	39	40	39
11	01K90MH	F	29	22.94	4.42	5.2736	5.7285	5.6604	38	38	38
12	01S87HH	F	31	20.76	4.659	3.8057	4.157	3.3229	38	39	39
13	01K84BH	F	34	19.49	3.6304	3.7279	3.4295	3.4651	38	38	35
14	01S89GH	F	29	22.31	5.5122	4.5410	5.1346	4.8829	37	33	32
15	01E73CH	F	45	24.86	3.7979	3.4299	4.8934	4.0817	38	38	38
16	01S88DH	M	30	26.22	5.8942	5.453	6.235	5.9262	38	39	38
17	02R92AH	F	26	25.86	4.6240	4.2146	4.2709	3.8202	38	39	34

	Ultrasound measures (cm)							
Subject	B_L3L	B_L4L	B_L3R	B_L4R	3M - L3L	3M_L4L	3M_L3R	3M_L4R
1	2.7	3.05	2.83	2.84	2.8	2.95	2.83	2.94
2	4.06	3.49	4.05	3.58	4.14	3.89	4.13	3.67
3	2.72	3.14	2.75	3.18	2.63	3.67	2.75	3.84
4	3.37	4.72	3.44	4.22	4.78	5.42	4.48	4.7
5	3.49	3.92	3.59	3.98	3.64	4.36	3.48	4.21
6	4.67	3.74	4.1	3.82	4.71	4.96	3.98	4.1
7	3.05	3.11	2.74	3.14	3.33	3.69	2.52	3.02
8	2.84	3.15	2.94	3.35	2.64	2.91	2.58	2.96
9	3.1	3.42	3.02	3.11	2.52	2.83	2.66	2.83
10	2.71	2.74	2.76	2.79	2.72	2.88	2.77	2.9
11	2.59	2.98	2.5	2.83	2.58	2.93	2.42	2.66
12	1.8	2.91	2.44	3.18	2.87	2.92	2.46	3.11
13	2.45	2.59	2.56	2.62	2.35	2.44	2.43	2.76
14	3	2.95	3.04	2.99	2.54	2.9	2.51	2.94
15	3.63	3.49	3.47	3.41	2.92	3.51	2.92	3.28
16	3.86	3.96	3.77	3.95	3.86	3.98	3.7	4
17	2.59	2.75	2.7	2.48	3.15	2.99	2.86	2.86

NSCLBP group data

					λ_{max}				Cognitive answer		
Subject	ID	Gender	Age	BMI	B_ST	B_DT	3M_ST	3M_DT	B_ST	B_DT	3M_DT
18	04R77OM	F	41	20.08	3.7413	3.7151	4.1526	3.7699	38	38	38
19	11A65SM	M	53	31.77	4.0838	4.546	4.1074	4.6105	38	35	38
20	01B63MM	F	55	30.11	4.4519	4.6586	4.1723	4.4555	38	26	37
21	01D67MM	F	51	28.96	4.8852	4.1189	5.085	4.2726	38	34	37
22	01K87EM	F	31	28.2	4.4892	4.8393	5.08	4.7735	36	38	37
23	01J82VM	M	36	21	5.6829	4.7746	4.9975	4.5836	38	34	38
24	02A71PM	M	37	24.49	5.6568	5.3814	4.2177	5.3213	38	38	38
25	02V75AM	F	43	30.46	4.9576	4.9939	3.9709	4.0145	38	19	33
26	02P65WM	M	53	28.75	4.6108	5.0851	6.1445	5.9046	40	38	38
27	02J83KM	M	35	29.98	4.5933	4.2683	5.6406	4.5795	38	38	38
28	03A68LM	M	51	21.57	5.1393	5.811	6.0429	6.0382	38	49	44
29	03D87MM	M	32	29.86	4.7542	4.6201	4.7398	4.5125	38	36	39
30	03L92AM	F	26	23.53	5.7466	6.1802	3.7644	4.6228	38	37	36
31	03V69SM	F	49	26.35	5.3107	4.6573	4.8004	4.394	38	39	34
32	03A66BM	F	53	35	4.1274	4.3866	3.7548	3.9081	38	39	38
33	04D83JM	M	35	23.29	3.5752	3.4699	3.5896	3.7447	38	38	39

	Ultrasound measures (cm)							
Subject	B_L3L	B_L4L	B_L3R	B_L4R	3M_L3L	3M_L4L	3M_L3R	3M_L4R
18	2.22	2.81	2.4	3.05	2.88	2.93	2.43	2.95
19	2.96	2.64	3.11	3.12	2.99	2.8	3.14	3.12
20	2.99	3.21	3.09	3.43	2.97	3.25	3.08	3.23
21	3.61	3.86	3.35	3.71	3.74	4.03	3.51	3.69
22	2.58	2.83	2.64	2.74	2.64	2.81	2.6	2.62
23	2.27	2.88	2.51	2.94	2.28	2.94	2.72	2.96
24	3.05	3.64	3.34	3.66	3.05	3.49	3.12	3.44
25	3.94	2.51	3.9	2.57	3.53	4.52	3.8	4.45
26	3.42	3.78	3.51	3.71	3.42	3.89	3.28	3.84
27	3.47	3.74	3.13	3.59	3.43	3.76	3.36	3.64
28	3.25	3.49	3.78	3.2	3.13	3.13	2.78	3.23
29	4	4.16	3.85	3.99	4	4.16	3.83	4.08
30	2.25	2.76	2.5	2.89	2.4	2.83	2.08	2.94
31	3.27	3.47	3.47	3.31	3.22	3.35	3.28	2.99
32	3.25	3.55	3.11	3.48	3.15	4.42	3.39	4.26
33	2.75	3.16	2.84	3.12	2.69	2.99	2.81	2.93

	Pain										PGIC			ODI	
Subject	B_at test	B_min	B_max	B_average	1M	2M	3M_at test	3M_min	3M_max	3M_average	1M	2M	3M	B	3M
18	0	0	2	3	2	3	1	0	2	3	6	3	5	48	12
19	6	6	8	5	7	6	5	5	5	7	1	1	2	48	34
20	7	5	7	5	5	5	6	5	8	5	2	2	5	34	22
21	6	6	6	6	10	10	0	0	0	0	1	1	6	30	42
22	8	6	10	8	6	8	7	6	10	8	1	1	1	58	66
23	5	2	7	4	1	1	1	0	5	3	2	2	3	38	32
24	6	2	7	7	6	6	7	4	7	6	1	1	1	24	24
25	4	4	6	4	5	5	2	5	5	4	1	1	2	12	18
26	4	2	5	4	2	3	2	1	2	2	3	5	5	10	10
27	5	2	8	4	2	2	2	0	3	1	3	1	1	10	4
28	3	2	8	4	1	2	4	2	7	3	7	6	2	22	18
29	4	1	6	4	4	2	1	0	4	1	3	5	6	8	2
30	1	0	1	3	5	4	2	0	6	3	1	5	5	44	30
31	2	0	9	8	6	8	1	1	9	6	1	1	2	34	36
32	3	1	8	5	4	5	5	3	7	5	1	2	2	51	36
33	4	3	7	5	4	2	2	0	4	2	1	4	5	6	8

Appendix E

Raw data for case study (Chapter 8)

Anthropometrics

ID	Gender	Age	BMI
02M57CS	M	61	26.5

Local Dynamic Stability

λmax_S Baseline	λmax_DT Baseline	λmax_S 3months	λmax_DT 3months	Cognitive task answer Single	Cognitive task answer DT - Baseline	Cognitive task answer DT – 3months
2.9918	3.2141	3.2954	3.0288	38	38	38

LMM thickness (cm)

L3_L_Baseline	L3_R_Baseline	L4_L_Baseline	L4_R_Baseline	L3_L_3months	L3_R_3months	L4_L_3months	L4_R_3months
4.14	3.74	5.04	4.14	3.86	4.21	3.97	4.43

Pain

At test - B	Min. - B	Max. - B	Average - B	1 month	2months	At test - 3M	Min. - 3M	Max. - 3M	Average - 3M
2	4	9	5	2	2	1	1	1	1

PGIC

1month	2 months	3 months
6	6	7

ODI

Baseline	3 months
50	24