Straight Leg Raise treatment for individuals with spinally referred leg pain: exploring characteristics that influence outcome.

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This thesis is dedicated to Chris Mercer, whose unwavering support and belief in me made this all possible. And to Amelie and Louis, who will finally get to know their Mummy from underneath the cloud.
Abstract

The primary aim of this thesis was to assess the differences in response to a 3 x 1 minute SLR tensioner treatment between 3 sub-groups of individuals with spinally referred leg pain (somatic referred pain, radicular pain and radiculopathy). Preliminary studies of the 3 outcome measures were required prior to the main study. These were: validity of the method to measure nerve excursion using ultrasound imaging (UI) which was assessed in pig nerves; repeatability of sciatic nerve excursion during a side-lying modified SLR measured with UI in the posterior thigh, and repeatability of pressure pain thresholds (PPT) and vibration thresholds (VT). The 3 outcome measures were repeatable and the sciatic nerve excursion technique was valid. Sixty seven participants were placed into one of the 3 sub-groups and further assessed to identify the presence of central sensitisation (CS). Five questionnaires were completed by participants to assess disability and psychological characteristics. Sciatic nerve excursion, PPT and VT were measured prior to and after a 3 x 1 minute SLR tensioner technique.

No significant differences (p>0.05) were found for any of the 3 outcome measures between the 3 groups. Slight improvements in VT were seen in the radiculopathy group after treatment, which were not significant, but indicated that even in individuals with conduction loss, no detrimental changes to nerve conduction occurred after treatment. A varied response to nerve excursion was seen. Longitudinal nerve excursion at the posterior thigh decreased after treatment in individuals with pain below the knee; this location of pain being more common in the radiculopathy and radicular groups. The decrease in nerve excursion suggests regional changes to nerve compliance after treatment, which may have occurred at the nerve root. Since it was not possible to measure nerve root excursion, these findings are speculative.

Only 2 participants were identified with CS, suggesting a low prevalence of the condition in individuals with spinally referred leg pain. This may be due to individuals with CS choosing not to participate in the study, or a limitation of the method used to identify CS.

Disability and psychological factors were not significantly different at baseline between the 3 sub-groups, and were not correlated with the outcome measures.

A 3 x 1 minute SLR tensioner technique in individuals with spinally referred leg pain of greater than 3 months of duration is not effective in improving pain or nerve conduction. However, it is not harmful, even in individuals with loss of nerve conduction. Changes to nerve excursion after treatment may be related to individual differences in nerve compliance, and possibly restriction of the nerve root.
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Declaration

I declare that the research contained in this thesis, unless otherwise formally indicated within the text, is the original work of the author. The thesis has not been previously submitted to this or any other university for a degree, and does not incorporate any material already submitted for a degree.

Signed ________________________________

Dated ________________________________

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Chapter 1 Introduction

1.1 Motivation for the study

The researcher is a neuromusculoskeletal (NMS) physiotherapist who has been qualified for 22 years. For the last 12 years she has been a lecturer at the University of Brighton, teaching NMS physiotherapy to undergraduate and postgraduate students. The development internationally of the theory and understanding of neurodynamics has rapidly developed during the researcher’s career, with an initial over consideration of the biomechanics of nerve with minimal consideration for the neurophysiology, and later an over reliance on animal physiology studies. Hence in the early stages of her career, strong tensioner neural mobilisations were the mainstream of neurodynamic management, with a later denouncement of the benefits of these techniques and even suggestions of harm (Dilley et al., 2005; Hall and Elvey, 2004, pg 425). However such assertions were based on a few innovative, but limited animal studies in the absence of robust clinical trials, and the researcher undertook a preliminary study looking at the effects of a SLR treatment technique on vibration thresholds (VT) (a measure of conduction of the large diameter afferents) in asymptomatic participants, including a small cohort of runners (Ridehalgh et al., 2005). It was postulated that runners may be predisposed to a minor peripheral nerve injury because of the repeated nature of running, and high incidence of ankle sprains. The results of the study found no significant increases in VT in either the runners or non-runners, indicating no evidence for detrimental changes to nerve conduction after the technique.

More recently, evidence has emerged of the potential benefits of such treatments (see chapter 4), but little is known about immediate changes after neurodynamic treatment particularly in individuals with a condition where neurodynamics is an important treatment modality; spinally referred leg pain. Since the postulated effects include changes to the mechanics of the nerve, changes to pain, and potentially changes to conduction (either positively or negatively), a study was required which addressed how
a neurodynamic mobilisation affected these parameters in this sub-group of low back pain. However, since the presentation and underlying pathophysiology of individuals with spinally referred leg pain is varied, a system of sub-grouping was necessary to assess how such measures responded to a standard treatment in individuals with different causes of the condition. This introduction and subsequent introductory chapters provides the rationale for the study by exploring the current body of work on nerve treatment for individuals with spinally referred leg pain, and identifying the gaps in the literature.

1.2 Incidence and prognosis of Low back pain and spinally referred leg pain

Low back pain is a major problem in many Westernised countries. It constitutes over £12.3 billion in expenditure in the UK per year, with £1.6 billion attributable to health care, £1.6 billion to informal care and around £9.1 billion due to loss of economic productivity (Whitehurst et al., 2012). The aetiology of LBP is wide and varied; ranging from localised tissue damage to widespread diffuse areas of symptoms with no known cause (Billis et al., 2007; Dunn and Croft, 2005). Referred leg pain due to lumbar spine dysfunction can occur as a result of nerve root compression (radiculopathy), nerve root irritation (radicular pain), or somatic referred pain from non-neural structures (Bogduk, 2009; Feinstein, 1987; Kellgren, 1977; Schäfer et al., 2009). Individuals with spinally referred leg pain are considered to have poorer prognosis than individuals with LBP alone (Haugen et al., 2012; Hill et al., 2011; Kongsted et al., 2012). Reasons for the poorer prognosis for these individuals include higher levels of pain, disability, and certain psychological characteristics in this group (Hill et al., 2011; Jensen et al., 2010; Walsh and Hall, 2009a).

1.3 Pathophysiology and presentation of spinally referred leg pain

Individuals who have nerve root compression or irritation have a predominant neuropathic pain mechanism, where the pain emanates from the nervous tissues...
themselves (Berger et al., 2012). However, pain can be referred into the lower limb from non-neural structures of the spine, and is described as mechanical nociceptive pain, or somatically referred leg pain (Bogduk, 2009). With respect to the neuropathic pain causes of spinally referred leg pain, radiculopathy differs from radicular pain in that there is a loss of conduction to either the sensory or motor nerve fibres, or a combination of both in a radiculopathy, whereas conduction is preserved in radicular pain (Bogduk, 2009). The presence of a radiculopathy can be identified by the loss or absence of sensation within a dermatomal region, weakness in the muscles supplied by the corresponding nerve root or spinal nerve, and a reduction or absence of the tendon reflex of the corresponding segment (Bogduk, 2009). Individuals with radicular pain have normal neurological integrity tests (sensation, muscle strength and reflexes) but display sensitivity to palpation of the peripheral nerve trunks which extend from the nerve roots and to movements of these nerves, such as during a straight leg raise test (SLR) (Schäfer et al., 2009). Patients with somatic referred leg pain have normal neurological integrity tests and normal nerve motion and nerve palpation tests, but the individual’s pain is reproduced by movements to the lumbosacral spine (Petty, 2011a; Refshauge and Gass, 2004).

Some individuals with referred leg pain may develop a complex pain presentation called central sensitisation (Giesecke et al., 2004; Schmidt-Wilcke et al., 2006). According to the International Association for the Study of Pain (IASP), central sensitisation is “an enhanced responsiveness of nociceptive neurons in the CNS to their normal afferent input” (Sandkühler, 2007). It has been suggested that patients with central sensitisation can be identified using a number of subjective questions and physical tests, and these can be applied in the clinical setting without the need for expensive equipment (Jensen et al., 2010; Nijs et al., 2010).

1.4 Neurodynamic tests: SLR and slump tests

The SLR is a common nerve motion test used by physiotherapists to assess and treat patients with low back and leg pain (Butler, 2000; Shacklock, 1995; Shacklock, 2005a;
This and other tests such as the slump test are termed neurodynamic tests, and use sequences of joint movements which lengthen the nerve bed and result in nerve excursion through the nerve bed (Butler, 2000; Shacklock, 2005a). The SLR test consists of hip flexion, knee extension and dorsi or plantar flexion with inversion or eversion to emphasise a particular nerve (tibial, peroneal or sural), as it passes close to the ankle (Breig and Troup, 1979).

The motion that occurs during the SLR test has been analysed in animal and cadaveric studies (Boyd et al., 2005; Boyd et al., 2013; Breig and Marions, 1963; Breig and Troup, 1979; Coppieters et al., 2006; Fleming et al., 2003; Goddard and Reid, 1965) in the sciatic nerve and lumbosacral nerve roots, but limitations of these studies exist since they are not representative of humans in vivo.

Nerve motion has been difficult to measure in vivo in the past, due to the lack of sensitive equipment available to perform such measurements. Recently, longitudinal nerve motion has been measured in the upper and lower limb using ultrasound imaging which has been shown to be a reliable and valid measuring tool (Dilley et al., 2001; Ellis et al., 2008; 2012; Erel et al., 2003; Hough et al., 2000; 2007). However, none of these studies have investigated any changes to nerve excursion after a neurodynamic treatment technique.

### 1.5 Neurodynamic Treatment

The SLR or slump tests can be converted into neurodynamic treatment techniques by placing the limb in the test position and repeatedly oscillating one of the joint sequences. For example, a SLR treatment could consist of positioning the individuals in supine, with their hip flexed, ankle dorsiflexed (to influence the tibial nerve), and flexing and extending the knee joint. Such a treatment could be described as a tensioner technique as studies have found that adding a sequence of joint movements together which lengthen the nerve bed increase the strain, and tensile stress on the nerve (Coppieters and Butler,
An alternative approach is to use a slider technique, where joints at one end of the test manoeuvre increase nerve bed length, whilst the ones at the opposite end reduce the nerve bed length. It is thought that greater excursion and less strain occurs during a slider technique (Coppieters and Butler, 2008; Coppieters et al., 2009; Ellis et al., 2012). The theoretical benefits of such treatments are to remove inflammatory exudates and oedema, increase venous return, improve the nerve’s viscoelastic behaviour (Butler, 2000; Shacklock, 2005a), improve axoplasmic flow (Butler, 2000) and have an effect on segmental and descending pain inhibitory pathways (Katavic, 1999). There are limited clinical studies that have shown the effectiveness of such techniques; however all have used different treatment doses. Slump tensioner techniques (the slump test consists of the same leg movements as SLR but with the addition of cervical and thoracic flexion) or SLR alongside lumbar mobilisations and exercise was more effective than just lumbar mobilisations and exercise in patients with LBP and non-radicular leg pain (Adel, 2011; Cleland et al., 2006; Nagrale et al., 2012). It is not known if all patients with referred leg pain behave in the same way to neurodynamic treatments, although a recent study suggests that people with nerve root pain, may benefit more from neurodynamic treatment than individuals with other forms of referred leg pain (Schäfer et al., 2011). The method of group allocations and small numbers of patients recruited within the nerve root pain group (9), make the results less conclusive, warranting further research in this area.

Some authors have suggested that longitudinal nerve techniques, particularly tensioner techniques are not appropriate for patients with neuropathic pain as they may cause ectopic firing of nociceptors (Dilley et al., 2005), or reduce blood flow, and potentially nerve conduction (Boyd et al., 2005). Such events could contribute to central pain processes occurring (Dilley et al., 2005). The rationale for this is predominantly based on laboratory studies on animals, and it is not known if these effects occur in humans. One study suggests that this may not be the case in human subjects, as temporal summation was found to reduce in patients with carpal tunnel syndrome (CTS) treated with a tensioner technique compared to a sham movement treatment (Bialosky et al., 2009). Such improvements in temporal summation indicate that the excitability of the...
cells within the dorsal horn has been dampened down; and this may be important in preventing central pain processes from occurring (Rygh et al., 2005). It is important therefore, that studies which investigate the effects of neurodynamic treatment techniques, observe the effects of both pain and nerve conduction.

1.6 Measuring effectiveness of neurodynamic treatments

Monitoring the amount of nerve excursion in the sciatic nerve may help to provide some useful information about what happens to the nerve mechanically after a SLR. Ultrasound imaging is currently one of the most accessible methods of assessing nerve excursion, and has been shown to have considerable repeatability (Dilley et al., 2001; Ellis et al., 2008). However such measurements do not demonstrate any changes to the neurophysiology. Measuring nerve conduction through electrophysiological testing are often negative in neuropathic pain conditions where no major insult has affected the nerve (Atroshi et al., 2003; Finsen and Russworm, 2001; Greening and Lynn, 1998). VT have been advocated to detect minor nerve dysfunction such as upper limb work related disorder (Greening and Lynn, 1998), and lumbosacral radicular pain (Freynhagen et al. 2008). It is a valid and reliable measure of the activity of the large diameter afferent nerves, and this sensation has been shown to be an early sign of nerve dysfunction (Dellon, 1980; Phillips et al., 1987).

Measurements of pain are often the most important measure to the patient, but can be difficult to quantify and are subject to bias. Pressure pain thresholds (PPTs) are used to assess the pain perception of an individual to pressure over particular areas. Deterioration in an individual’s pain response would result in a lowering of their pain threshold, whereas an elevation in PPT would suggest an improvement in pain response (Antonaci et al., 1998). A number of studies have used PPT to analyse changes to pain after manual therapy (De-Le Llave-Ricon et al., 2012; Krouwel et al., 2010; Moss et al., 2007; Silva et al., 2013; Sterling et al., 2001; Willett et al., 2010). It has substantial repeatability (Antonaci et al., 1998; Kinser et al., 2009; Persson et al., 2004; Walton et al., 2011; Ylinen et al., 2007), and validity (Kinser et al., 2009).
1.7 Central Sensitisation

It has been demonstrated that patients with chronic low back pain have a lowering of PPT (Giesecke et al., 2004; Laursen et al., 2005; O'Neill et al., 2007) at the site of pain and in other regions around the body. Such widespread mechanical hyperalgesia is one of the features of a condition known as central sensitisation (Jensen et al., 2010; Woolf and Mannion, 1999). The prevalence of CS in individuals with spinally referred leg pain is not known. This condition is associated with higher levels of pain, disability and psychosocial factors (Meeus and Nijs, 2007), which may further augment CS processes.

1.8 Disability and psychosocial factors

Less favourable prognoses have been associated with higher levels of disability and certain psychological and social factors such as fear avoidance, depression, stress and anxiety (Haggman et al., 2004; Vlaeyen and Linton, 2000). In subjects with neuropathic pain; such as radicular pain or radiculopathy, catastrophising has been found to be high (Sullivan et al., 2005). Interestingly, even asymptomatic subjects who have greater responses to neurodynamic testing have been found to have higher scores on the pain catastrophising scale (PCS) (Beneciuk et al., 2010). For these reasons, several psychosocial scales are useful to assess if any of these characteristics have an interaction on the effects of treatment. Higher levels of disability may also play a role in how subjects behave to LBP treatments, and can be associated with poorer outcome (Grotle et al., 2004).

1.9 Overall Focus of the Study

There is a need to establish if individuals with different causes of their referred leg pain behave in the same way to neurodynamic treatment techniques, considering factors such as disability, presence of central sensitisation and other key psychosocial factors. The optimal treatment dose has not been established in the literature, but commonly 3 sets of mobilisation varying between 30 seconds to a minute have been advocated. The overall
focus of the study was to explore the difference in responses of individuals with spinally referred leg pain to a 3 x 1 minute SLR tensioner treatment.

1.10 Outline of the thesis

The thesis is divided into 9 chapters. In chapters 2-5, the justification for the study is provided by synthesising and evaluating the relevant literature of the most pertinent topics closely related to the subject matter. In chapter 2, the justification for the method of sub-grouping individuals into the 3 sub-groups chosen for the clinical study is discussed. In order for this to be achieved, a review of the literature around the pathobiological mechanisms for each sub-group is discussed, before a detailed analysis of methods of sub-grouping and justification of the sub-grouping system chosen is given. In addition, the processes which are thought to occur, giving rise to central sensitisation, and the method of identifying this presentation in individuals with spinally referred leg pain are critiqued. Finally, in chapter 2 the impact of psychosocial factors on prognosis in individuals with spinally referred leg pain is detailed.

In chapters 3 and 4 the principles behind neurodynamic assessment and treatment are explained. In chapter 3 the evidence behind the use of such tests, with particular reference to the SLR and slump test is critiqued. Chapter 4 includes the current evidence for the effects resulting from neurodynamic treatment and the effectiveness of such treatments, and a justification of the particular SLR technique used in the clinical study is given.

The choice, validity and reliability of potential outcome measures to assess the effects of a neurodynamic treatment are detailed in chapter 5. Chapter 6 presents the rationale for the study and the aims and objectives.

Chapter 7 consists of the preliminary studies to ensure valid and repeatable outcome measures were used in the study. It discusses the limitations and considerations of these outcome measures.
Chapter 8 forms the main clinical study. It presents the results of the study and discusses the results in light of other literature. Limitations of the work are addressed and put into context for extrapolation into clinical practice. Chapter 9 provides an overall summary of the study, main conclusions, original contribution to current knowledge and suggestions for future work.
Chapter 2 Spinally referred Leg Pain

Individuals with spinally referred leg pain do not all have the same aetiology for their pain. The cause of this type of pain, like all forms of low back pain is often multifaceted and links both physical or biological and psychosocial elements, and as such the approach taken to assessment and management should be biopsychosocial (Waddell, 2004). The neuromusculoskeletal structures responsible for this leg pain can be both neural (neuropathic pain) and non-neural (somatic referred pain) (Bogduk, 2009). Spinally referred leg pain that is neuropathic in origin can result from a number of causes, but is predominantly due to some irritation on either the nerve roots themselves, or the dorsal root ganglion (DRG) (Bogduk, 2009). If the nerve root is sufficiently compromised, a loss of nerve conduction may occur (Takahashi et al., 2003.; Yoshizawa et al., 1995). A common cause for nerve root and DRG compromise is a herniated intervertebral disc (Bogduk, 2009; Bono and Garfin, 2004).

The alteration of nerve conduction will only occur if there is sufficient disruption of the nerve signals, but in some cases there may be pain only, without alteration to nerve conduction. This is thought to be due to irritation of the dorsal nerve root or DRG since the protruded intervertebral disc material produces an inflammatory response (Bogduk, 2009; Chatani et al., 1995; Kawakami et al., 1994; McLain and Weinstein, 1994). The pain described due to irritation in the nerve root or DRG is called radicular or nerve root pain (Bogduk, 2009). When the nerve signals are disrupted, the condition is described as a radiculopathy (Bogduk, 2009).

The non-neural cause of spinally referred leg pain is termed somatic referred pain, emanating from the ligaments, capsules and muscles surrounding the spinal segments. The type of pain that these individuals experience is usually either a mechanical nociceptive pain or inflammatory nociceptive pain. Nociceptive pain is “Pain that arises

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1 A herniated intervertebral disc consists of the nucleus pulposus (the inner aspect of the disc) bulging or extruding from the annulus fibrosus (the outer layer of the disc). The traversing nerve root is more at risk from a herniated disc because it passes posterolateral to the disc before exiting through the intervertebral foramen of the level below.
from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors” (Merskey and Bogduk, 1994). In mechanical nociceptive pain, the activation of pain is related to the mechanical load on the tissue, and hence tends to be intermittent pain, related to specific activities (Loeser and Melzack, 1999; Petty, 2011a; van Griensven, 2005). With inflammatory nociceptive pain, the stimuli irritating the sensory nerve endings and causing pain are the inflammatory mediators released from the damaged soft tissue cells (Loeser and Melzack, 1999; Petty, 2011a; van Griensven, 2005).

Some patients with chronic LBP have been found to exhibit complex and abnormal processing of pain, sometimes referred to as central sensitisation (Jensen et al., 2010). This is thought to occur when the dorsal horn which normally acts to mediate pain either by amplifying it when needed (this may be appropriate at times of extreme danger where further movement could result in damage to structures) or diminishing it via descending pain mechanisms, acts in an over amplified way (van Griensven, 2005). The result of such amplification is sensitisation of neurones within the dorsal horn (Jensen et al., 2010) and long lasting enhancement (potentiation) of synapses within the anterior cingulate cortex (Arendt Nielsen and Henriksson, 2007; Li et al., 1999; Nijs, et al., 2010; Yunus, 2007). Certain manifestations of this pain are widespread allodynia (pain response to innocuous stimuli) and hyperalgesia (exaggerated pain on response to painful stimuli). It has been suggested that patients who have this condition may benefit less from manual based treatment than those without (Fernandez-de-las-Penas et al., 2010).

Individuals with different causes for their spinally referred leg pain may not only present differently, but are likely to behave differently to clinical interventions (Hill et al., 2011; Kongsted et al., 2013; Nee et al., 2013; Schäfer et al., 2009). It is crucial therefore to utilise a sub-classification system which is clinically viable, and able to discriminate between individuals with different causes of their leg pain. This chapter aims to evaluate the evidence for the aetiology and typical presentations of the sub-group categories of
spinally referred leg pain, and to identify the optimal clinical strategies for classifying individuals with referred leg pain.

2.1 Nerve root dysfunction

Nerve root compression alone does not appear to produce pain; compression or squeezing normal nerve roots with forceps is painless (Norlen, 1944; Rydevik et al., 1984), and therefore it is likely that the cause of pain is due to inflammatory mediators (Olmarker and Rydevik, 1991). Chemical substances involved in this process include phospholipase A2 and cytokines which are released from the nucleus pulposus (Kawakami et al., 1996; Omarker and Myers, 1998). An understanding of how pain and dysfunction due to nerve root compression and chemical irritation occur, is necessary to predict how individuals with these conditions can be identified, and establish the best methods for detecting radiculopathy and radicular pain.

2.1.1 Nerve root pathology

The two most common causes of nerve root dysfunction are compression or chemical irritation of the nerve root and/or DRG due to herniated disc material or central or lateral spinal canal stenosis (Sharma et al., 2012). Lateral canal stenosis occurs due to degenerative changes affecting the zygapophyseal joint, such as enlargement of these joints which directly compresses the DRG or nerve root. Central spinal canal stenosis is predominantly a degenerative condition which often results in bilateral leg pain and/or paraesthesia. Individuals with central canal stenosis are commonly over 60 years of age, have bilateral leg pain or pins and needles/numbness, have difficulty walking (particularly downhill) or prolonged standing, and their pain is relieved on lumbar flexion (Sengupta and Fischgrund, 2004). Such individuals would have pathology of the spinal canal commonly with progressive neurological loss due to narrowing of the spinal canal. In these cases, neurodynamic interventions (such as a SLR test) would not be a suitable intervention, since the optimal treatment techniques recommended for this condition include flexion exercises to open the spinal canal, and offload the neural
structures, and improve physical fitness and strength around the trunk and pelvis (Fritz et al., 1998; Overdevest et al., 2011).

Effects of Nerve root compression and chemical irritation on pain

Most methods exploring the pathophysiological mechanisms of how pain and dysfunction occur in nerve root disorders, consist of animal studies where controlled application of substances (Hashizumi et al., 1997; Hou et al., 2003; Kawakami et al., 1996; 2000; Obata et al., 2002, Omarker and Myers, 1998; Rothman and Winkelstein, 2007), or increasing amounts of compression, over increasing amounts of time (Hu and Xing, 1998; Hubbard and Winkelstein, 2008) are applied to the nerve root. However, whilst these studies are helpful in the understanding of animal models, they may not truly represent the mechanisms that occur in the human in vivo. For example it has been demonstrated that nerve root compression is often visible on myelography or MRI scans in the absence of pain or neurological deficit (Boden et al., 1990; Falconer et al., 1948; Rydevik et al., 1991; van Rijn et al., 2006), yet there is no mention of animals who display normal pain behaviours after experimental nerve root irritation. This indicates that the exact mechanisms of nerve root irritation cannot be entirely replicated in animal studies. However, since it is not possible to apply the same sorts of methods to humans, these are currently the most feasible options of assessing how nerve roots respond to simulated disc injury.

Radicular pain was previously believed to be related to the direct compression of nerve roots, but this has been refuted (Bogduk, 2009; Howe et al., 1977; Hu and Xing, 1998). Whilst it has been demonstrated that compression of the DRG leads to repetitive firing in a number of sensory nerves after mechanical stimulation, compression of the dorsal nerve root does not provoke such firing after mechanical stimulation (Howe et al., 1977). In addition, pain related behaviour (withdrawal of paws from painful stimuli) after a transient compression of the L5 dorsal nerve root was no different to a sham condition in rats (Hu and Xing, 1998). However, if the compression remains in situ, an
increase in pain related behaviours and sensory nerve firing occurs (Hou et al., 2003; Howe et al., 1977; Hu and Xing, 1998; Omarker and Myers, 1998). ²

Applying disc material to the nerve root (i.e. nucleus pulposus and annulus fibrosus) alone has an immediate and longer term effect on rat pain behaviours (Hou et al., 2003; Kawakami et al., 1996; 2000; Obata et al., 2002; Omarker and Myers, 1998). Increasing signs of pain behaviour seem to occur when compression is combined with the application of disc material to the nerve roots (Hou et al., 2003; Omarker and Myers, 1998), which might better reflect the pathological processes that occur in vivo. Heightened mechanical behavioural changes such as paw withdrawal to a mechanical stimulus, seem to occur more readily after placing nucleus pulposus material on dorsal nerve roots, but pain behaviour changes due to thermal stimuli seem to be more resilient, requiring a combination of mechanical compression with disc material (Hou et al., 2003; Kawakami et al., 1996; Kawakami et al., 2000; Omarker and Myers et al., 1998) (see figs 2.1 and 2.2 for schematic drawings of the location of where individual researchers have applied compression or chemical irritants to the nerve root complex). There are however, some exceptions to these studies. Hu and Xing (1998) found thermal hyperalgesia after an injection of carrageenan alone, and Chatani et al., (1995) found thermal hyperalgesia after circumferentially exposing the DRG and after loosely ligating the DRG with chromic gut suture. Both carrageenan and chromic gut suture impose mild inflammatory effects on tissues. There are two possible explanations for this; firstly the DRG was targeted rather than dorsal nerve root alone, which may have resulted in greater sensory changes, and secondly the substances used may have had different effects from nucleus pulposus material.

Whilst most studies have generally shown a hyperalgesic response to nerve root compression or irritation, some have shown an initial hypoalgesic response (Kawakami et al., 1996; Kawakami et al., 2000). These changes were found after placing the nucleus pulposus and annulus fibrosus onto the nerve root (Kawakami et al., 1996), and after the application of silk around the nerve root (Kawakami et al., 2000). This suggests that

² The details of these studies can be found in appendix 1.
pain may not always be an initial finding in radiculopathy, a finding which supports that of Howe et al., (1977), who found that only the acutely irritated DRG, not the nerve root, showed repetitive nociceptor firing to a light mechanical stimuli.

There are number of important issues to consider when extrapolating this animal data into human scenarios. In animal studies, the spinal canal was exposed and material was placed on the nerve root in a controlled manner, or compression applied, and this resulted in an event which is unlikely to occur in the same way as in human subjects with disc protrusion. The application of the disc material was very specifically applied to a small aspect of the nerve root or DRG, which is unlikely to be reflected in typical pathological herniated intervertebral disc protrusions. In addition, the pain response is assumed to accurately detect when a hyperalgesic response is occurring, but it is unknown if the same higher centre activation associated with pain (Wiech et al., 2008) occur to the same extent in rats, making it difficult to assess how well this relates to pain behaviour in humans.

Some studies obtained the disc material after excising the tail and using the coccygeal disc material (Hou et al., 2003; Kawakami et al., 2000; Obata et al., 2002), whereas others utilised other substances such as carrageenan or chromic gut suture (substances used to induce inflammation) (Hu and Xing, 1998; Rothman and Winkelstein, 2007), which may have had different effects on the nerve root. Whilst the effects of excising the tail might be expected to change the normal behaviour of rats, the studies compared the behaviours to rats who had the same initial excision of tail procedures (without the added nerve root compression/irritation) and their findings were not different to baseline measures (Hou et al., 2003; Kawakami et al., 2000; Obata et al., 2002). However, regardless of the procedure, the application of the substances into the canal is unlikely to best reflect situations in vivo, but it is the only option for assessing how separate events with regards to pain are likely to occur in humans at present.

The explanation for why such pain related behaviours occur in these animals after nerve root or DRG irritation has been debated by a number of authors. Some have suggested
that the deterioration in pain is related to structural changes (Hou et al., 2003) or endoneurial oedema (Chatani et al., 1995), whilst other have considered that it is related to expression of neurotrophic factors in the DRG (Obata et al., 2002), increased production of nitrous oxide (Hashizumi et al., 1997), or increase in PLA2 immunoreactivity (Kawakami et al. 1996). In addition microglial and astrocyte activity has been found to increase after application of chromic gut suture and compression to the C7 nerve root in rats (Rothman and Winkelstein, 2007). It is likely therefore, that the pain occurring in individuals with radicular pain is multifaceted and involves changes to nerve structure, as well as inflammatory and other immune system responses. The inflammatory and immune system changes will be discussed further in the next section.

**Fig 2.1 Transverse view of a spinal motion segment showing the relationship of cauda equina, traversing, exiting nerve roots and dorsal root ganglion. References shown demonstrate where on the nerve root the compression or irritation occurred, but not necessarily at this nerve root level**
Fig 2.2 Sagittal view of L3-L5 vertebral segments showing the relationship of the cauda equina, traversing and exiting nerve roots and their relationship with the intervertebral disc. References shown demonstrate where on the nerve root the compression or irritation occurred, but do not necessarily reflect the actual nerve root level.

Inflammation after nerve root compression and chemical irritation

Both direct contact of nucleus pulposus and compression to the nerve root have been shown to cause inflammation and resultant oedema within the endoneurial space. It has been established that animal models which mimic nerve compression result in inflammatory events that are greater than those caused by nerve transection (Hu et al., 2007), and evoke both local and remote immune-mediated inflammatory changes (Schmid et al., 2013). There are a number of methods that can be used to assess such changes including the observation of oedema in and around the nerve roots (Olmarker et al., 1993; Olmarker and Rydevik, 1989; Pedowitz et al., 1992; Rydevik et al., 1991), using protein tracers to identify oedema (Kobayashi et al., 1993; Kobayashi et al., 2004a; Kobayashi and Yoshizawa, 2002), and the identification of various immune system and inflammatory markers (Hubbard and Winkelstein, 2008; Kobayashi et al., 2004b; Obata et al., 2002; Rothman and Winkelstein, 2007).
Nucleus pulposus placed on the nerve roots in rats (Omarker and Myers, 1998) and pigs (Olmarker et al., 1993), was found to produce endoneurial oedema between 5-7 days post intervention (details of the studies can be found in appendix 2). A more severe effect on oedema and fibrosis was found with a combination of nerve root compression and nucleus pulposus (Omarker and Myers, 1998). However, the compression was created through medially displacing the nerve root in an attempt to reproduce the sort of compression that might occur during a herniated nucleus pulposus. It was not clear how much pressure was applied to the nerve root in this instant making it difficult to compare to comparable studies in both the periphery and within the vertebral canal. Both Rydevik et al., (1991) and Pedowitz et al., (1992) assessed the effect of specific amounts of compression applied to the nerve roots within the cauda equina. Oedema was found to occur with pressures over 50 mm Hg (Rydevik et al., 1991) with more severe changes at 200 mm Hg (Pedowitz et al., 1992). However in these, like the former mentioned studies, the presence of oedema was made from histological assessment which is an observational method, subject to bias.

Using a method of assessing oedema through the identification of protein tracers (Evans blue albumin (EBA) or horseradish peroxidase (HRP), studies have demonstrated that low levels of compression (50mm Hg) held for longer periods of time (>1 week), or higher pressures (>200 mmHg) held for short periods of time (1hour), are equally deleterious with regards to oedema proximal and distal to site of compression (Kobayashi et al., 1993; Kobayashi et al., 2004a). In addition, compression of the DRG itself shows similar changes (Kobayashi and Yoshizawa, 2002).

The presence of oedema suggests an inflammatory response, as it is one of the 5 cardinal signs of inflammation (DeLeo and Yezierski, 2001). A more direct way of assessing the immune system response is to look directly for the presence of cells which indicate that an inflammatory response has occurred. Such cells include glial cells, such as astrocytes, microglia and oligodendrocytes, which are the macrophages of the central nervous system (DeLeo and Yezierski, 2001). Macrophages produce a neurotrophic factor called nerve growth factor (NGF), and increases in retrograde transport of NGF lead to increase in production of substance P, calcitonin gene related peptides (CGRP), and
brain derived neurotrophic factor (BDNF) (Donnerer et al., 1992; Obata et al., 2002). In addition, glial cells synthesise proinflammatory cytokines, glutamate and nitrous oxide which act through N-methyl-D-Aspartate (NMDA) receptors (DeLeo and Yezierski, 2001). The opening of NMDA receptors are thought to enhance central sensitivity (Chen and Huang, 1992).

Increases in NGF and BDNF have been found in the DRG after nerve root irritation with nucleus pulposus and annulus fibrosus (Obata et al., 2002). Such changes may result in increased release of substance P and CGRP. However, Kobayashi et al., (2004b) found a decrease in substance P and CGRP after compression of the dorsal nerve root which was associated with chromatolysis of the axons within the DRG, suggesting a greater painful response after irritation rather than compression. Similar immune responses suggestive of chromatolysis were found to occur by Hubbard and Winkelstein, (2008) with the increased presence of macrophages as indicated by the increased presence of CD68. Another method of assessing the occurrence of macrophages is to evaluate staining for 2 proteins; Glial fibrillary acidic protein (GFAP) and CR3/CD11b, which indicate astrocyte and microglial activity respectively (Rothman and Winkelstein, 2007). Significant increases in GFAP were found in rats with compressed nerve roots and in rats with compressed nerve roots and application of chromic gut suture 1 and 7 days post nerve root injury, and in animals with chromic gut suture alone at 7 days. CR3/CD11b however, was only significantly different in the compressed and combined compressed and chromic gut suture groups, but not the chromic gut suture group alone. Such changes in glial cell activation with greater nerve root insult also resulted in greater pain responses from the rats, which seem to be in contrast to Kobayashi et al., (2004b). However, whilst substance P and CGRP reduced in the DRG (Kobayashi et al., 2004b), pain behaviours were not concurrently monitored, and therefore the direct link between reduction in the production of these neurotransmitters and changes to pain cannot be made. Generally small numbers of rats were used to analyse the immune system changes, for example Rothman and Winkelstein, (2007) used 4, 4 and 6 rats in each sub-group to assess for changes to glial cells. The subsequent use of statistical testing on such small numbers may have resulted in an inability to detect a significant change, so it is possible that for incidences where
statistical significance was not found (e.g. for chromic gut suture alone), that a false acceptance of the null hypothesis was made. In addition, such small numbers make it difficult to extrapolate the results to a greater population.

The inflammatory processes presented above coincide with the changes in pain behaviour discussed in the preceding section. Such changes to pain behaviour not only represent inflammatory responses but also possible changes to nerve structure and function. In animal studies, function of nerve fibres is typically measured using methods of assessing nerve conduction, whereas structural changes to the nerve are observed through histological analyses.

*Effects of Nerve root compression and irritation on nerve conduction and structure*

It has been postulated that the early behavioural changes previously described are related to aberrant firing of afferent nerves, but later are due to structural changes and immunoreactivity (Hubbard and Winkelstein, 2008). Detrimental changes can occur in the presence of disc material with or without compression, and this has been demonstrated by alteration in nerve conduction as well as by observing changes to nerve structure (Olmarker et al., 1993; Omarker and Myers, 1998; Takahashi et al. 2003). Olmarker et al., (1993) found that the application of nucleus pulposus alone to the nerve roots within the cauda equina was sufficient to cause an early (after 1 day), and prolonged (7 days) reduction in motor nerve conduction velocity compared to control animals who had fat applied to the nerve roots only. Takahashi et al., (2003) also found a marked reduction in cauda equina action potentials 1 week after application of nucleus pulposus to the sacrococcygeal nerve roots in dogs. However, greater changes to nerve conduction were demonstrated with a combination of compression and application of nucleus pulposus (Takahashi et al., 2003). Histological changes were also most severe in the combination group with greater nerve fibre injury (Takahashi et al., 2003), which was similarly demonstrated by Omarker and Myers, (1998) with evidence of axonal demyelination and Schwann cell hypertrophy in Sprague-Dawley rats (see appendix 2 for details of studies). These findings support the behavioural studies discussed in the
previous section, in that a combination of compression and chemical irritation affect pain behaviour greater than either compression or irritation alone. Some of the potential limitations with these studies relate to the way that a sham or control group was used as comparison. For example, in Olmarker et al.,’s (1993) study, control animals had the same procedure as the experimental animals, but fat was placed on the nerve roots instead of nucleus pulposus. However, there was no control group who had surgery without the application of any substances to the nerve roots. Whilst the NP group showed worsening nerve conduction compared to the fat group, it would be useful to see the contribution of the surgical procedure alone to ensure that this was not responsible for any of the changes found.

Whilst it is clear that both compression and chemical irritation together are more provocative than either alone, it is also useful to assess what magnitude of compression is needed to cause negative changes to structure and function. Lower levels of compression (<75 mm Hg) applied for short periods of time (4 hours or less), did not cause a change to nerve conduction or nerve structure (Pedowitz et al., 1992; Rydevik et al., 1991). Increasingly larger amounts of compression caused cumulative deterioration in nerve conduction and structural changes. Sensory nerve conduction appeared to be more greatly affected than motor conduction and recovery was slower in the sensory nerves (Pedowitz et al., 1992; Rydevik et al., 1991). Pedowitz et al., (1992) demonstrated only 1 out of 5 animals showed any sign of sensory compound nerve action potential recovery 1.5 hours after 200mm Hg compression was applied, compared to all animals showing partial recovery of motor function (Pedowitz et al., 1992).

Normally, pressure exerted from a prolapsed intervertebral disc occurs ventrally on the exiting or traversing nerve roots (Maus, 2002), however in Pedowitz et al.’s (1992) study, the pressure was exerted dorsally which may not produce the same effects as in vivo. Pedowitz et al., (1992) and Rydevik et al., (1991) compressed the nerve roots in the cauda equina which do not contain the same amount of connective tissue as the exiting or traversing nerve roots (Rydevik et al., 1991). This may mean that greater pressures are required outside of the cauda equina to cause the same changes.
Whilst lower pressures did not result in detrimental changes in the 2 studies described above, the length of time that the compression remains in situ is critical in determining the effect on nerve structure. Compression of the 7th spinal nerve root in dogs at low levels (7.5gf, equivalent to 50 mm Hg) for 1 week, caused Wallerian degeneration in the dorsal nerve root proximal to the compression site and distal to the compression site in the ventral nerve root (Kobayashi et al., 2004a). By 3 weeks, the myelin sheaths were depleted of axons, and on electron microscopy, breakdown of the blood-nerve barrier was seen. In addition, a further study by Kobayashi et al., (2004b) demonstrated chromatolysis occurring in the DRG 1 week after compression of 7th lumbar dorsal nerve root with 7.5gf. Chromatolysis is often a precursor to apoptosis (cell death) (Stoica and Faden, 2010). As mentioned in the previous section, support for these structural changes on light microscopy was shown by the reduction in neurotransmitters such as CGRP, substance P and somatostatin. It has been previously shown that chromatolysis inhibits the production of these neurotransmitters (Wells and Vaidya, 1989), but facilitates the production of structural proteins responsible for axonal regeneration, such as cytoskeleton and nerve growth factor. Consequently it appears that 1 week after sustained compression at low levels, degenerative and regenerative processes occur at sites distal to the compression.

Relating these figures to humans with disc pathology is important to understand the relevance of such pressures. Takahashi et al., (1999) looked at the nerve root pressures in 34 individuals diagnosed with lumbar disc herniation by myelogram. The pressures were taken with a pressure transducer inserted between the nerve root and the disc herniation (after laminectomy). An extensive range in pressures was found from between 7-256 mmHg (mean 53.2). No studies have looked at such low pressures as 7 mmHg, but the mean value of 53.2mm Hg is around the lowest level that researchers have looked at. Since most individuals with disc herniation will have a more chronic involvement of herniated disc material than the week or less in some of the short term studies, such low levels of pressure may be of sufficient magnitude to cause detrimental changes.
Deterioration in axonal fibres as described above may not be the same for large and small diameter nerves. Changes to the constitution of small compared to large nerve fibres have been found in a number of studies. Chatani et al., (1995) found exposure of the DRG, or the application of chromic gut suture to the L4 and L5 DRG of rats for 6 weeks, resulted in marked deterioration in the large diameter fibres, with increase in the small diameter fibres. In agreement, a dramatic increase in small fibres, and decrease in large fibres in the DRG and dorsal nerve root were found 2 and 12 weeks after loose ligatures of chromic gut suture and silk were applied to the nerve roots (Kawakami et al., 1994). Relating these findings to in vivo, Freynhagen et al., (2008) found that patients with radicular pain had greater changes to vibration thresholds (VT), a measure of the large diameter afferents (Greening and Lynn, 1998; Greening et al., 2003) than thermal testing.

In summary, animal studies have demonstrated the complex changes that occur in structure and conduction in nerve roots exposed to irritants or compression. It is possible that nerve conduction may be affected by the chemical irritation of the nerve root, although much greater changes occur with the added component of compression. Larger pressures, or low pressures prolonged over time, or the combination of pressure and the application of nucleus pulposus, are most deleterious to nerve structure and function. Limitations of the studies mean that whilst a similar model may occur in humans, the mechanism of the nerve root irritation is likely to be substantially different since the disc material or compression is not applied in an experimental situation. In addition, human beings may behave differently to animals when they have pain due to such factors as previous experience and thoughts and beliefs about pain. Caution must therefore be taken when extrapolating the type and level of dysfunction after nerve root irritation in vivo.

2.1.2 Summary of nerve root pathology studies and relevance

In animals, a combination of the compression and chemical irritation from either nucleus pulposus, annulus fibrosus or other irritants such as carrageen or chromic gut suture have been shown to cause greater deleterious effects on pain behaviours,
inflammation, large diameter nerve fibre loss and deterioration in both sensory and motor nerve conduction, but with more prolonged and less reversible changes to sensory nerve conduction. Such changes may coincide with the development of large diameter fibre loss and mechanical hyperalgesia.

Clinically, patients may present with a neuropathic referred leg pain which is due to nerve root irritation. Deterioration in nerve conduction as measured by reflexes, myotomes and dermatome testing may help to distinguish between those with a neurological compromise and those without. Therefore, for the purposes of this study those identified with a neurological compromise will be termed radiculopathy and those without will be termed radicular pain. In individuals with radiculopathy, measurements of nerve conduction of the sensory large diameter afferents such as through the use of VT is particularly useful (Freynhagen et al., 2008). In addition, since heightened mechanical hyperalgesia occurs after damage to the nerve root, measures of pressure pain threshold may be useful.

This section has identified the structural, conduction and behavioural changes that occur within the nerve root and DRG after a pathological event. However spinally referred leg pain may also occur in the absence of any pathology associated with the nerve root; known as somatic referred pain.

### 2.2 Somatic Referred Leg pain

Individuals with spinally referred leg pain that is not due to irritation or compression of the nervous tissue can be described as having somatic referred pain (Bogduk et al., 2009; Robinson, 2003). This form of referred pain is due to stimulation of nociceptors in somatic tissues such as muscle, disc, or zygapophyseal joint structures (Jung et al., 2007; Laplante et al., 2012; O’Neill et al., 2002; Robinson, 2003; Seaman and Cleveland, 1999), and is also known as nociceptive pain (Robinson, 2003; Seaman and Cleveland, 1999). Therefore somatic referred leg pain may occur due to dysfunction in the spinal joints (zygapophyseal, interbody, sacroiliac joints) or myogenic structures
(Robinson, 2003; Seaman and Cleveland, 1999). However the aetiology, pathology and clinical presentations are varied.

The mechanisms for somatic referred pain are not well understood, but are thought to be due to convergence of primary afferent nerves on second order neurones in the dorsal horn (Robinson, 2003). Somatosensory neurones respond to stimulus of local lumbar tissues, hip and proximal thigh tissues in the same way. If a lumbar structure such as zygapophyseal joint is injured, these neurones are activated, the information is projected to the contralateral somatosensory cortex, but the cortex cannot differentiate the injured tissue, and the individual feels the pain in the back and leg (Gillette et al., 1993). This has been demonstrated in studies that have injected hypertonic saline into spinal joints and followed the distribution of symptoms into the leg (McCall et al., 1979; Mooney and Robertson, 1976). A number of studies have looked at pain referral patterns which result from stimulating somatic structures with a range of stimuli (e.g. mechanical and chemical) (Feinstein et al., 1954; Fukui et al., 1997; Hockaday and Whitty, 1967; Inman and Saunders, 1944; Jung et al., 2007; Kellgren 1939; Laplante et al., 2012; Mooney and Robertson, 1976; O’Neill et al., 2002; Ohnmeiss et al., 1997). Whilst the distribution patterns have shown substantial variability between subjects and between studies, a consistent finding is that without exception the deep, non-neural tissues in the lumbar spine refer pain into the leg, which is felt as deep and often not well localised.

Some studies show pain referring as far as the foot (Inman and Saunders, 1944; Kellgren, 1939; Mooney and Robertson, 1976; Ohnmeiss et al., 1997; O’Neil et al., 2002) to calf without foot (Bernard and Kirkaldy-Willis, 1987; Feinstein et al., 1954; Jung et al., 2007) and distal referral to the thigh only (Fukui et al., 1997). Such differences might be related to the differences in methods of inducing or relieving pain and subjects used (symptomatic v asymptomatic). Such variation on methods include injections of noxious substances into the paraspinal muscles (Feinstein et al., 1954; Inman and Saunders, 1944; Kellgren, 1938), zygapophyseal joints (Kellgren, 1939; Mooney and Robertson, 1976), ligaments (Inman and Saunders, 1944; Kellgren, 1939), or scratching/ drilling the periosteum with a needle/wire (Inman and Saunders, 1944;
Kellgren, 1939). Both sclerotomal and non-segmental distributions have been found in different studies. Sclerotomes, like dermatomes and myotomes, reflect the embryonic formation of the musculoskeletal system. A sclerotome is the ventromedial portion of the somite that will give rise to the vertebrae and ribs, whereas the remainder of the somite is the dermomyotome, which later form the skin and muscular tissue (Palastanga and Soames, 2012). Inman and Saunders, (1944) found a sclerotome distribution of referred symptoms on 160 observations on 26 participants. However, spreading of saline outside of the stimulated structures could have occurred, resulting in irritation of the sensory nerves and a more segmental pattern of referral. In contrast, Feinstein et al., (1954) carefully controlled the amount of injected saline to avoid leakage and found that whilst a segmental distribution was found, it was neither dermatomal or sclerotomal in distribution. There were large areas of overlap between levels, suggesting that there is not a distinct referral pattern for each level. In agreement, using a more accurate method of fluoroscopy and arthrographic guidance of the needle, Mooney and Robertson, (1976) found a non-segmental distribution of symptoms.

Later studies (Fukui et al., 1997; Jung et al., 2007; Laplante et al., 2012; Ohnmeiss et al., 1997; O’Neill et al., 2002), were more robust in their methods, attempting to ensure that a clear diagnosis was made, that injections were accurately placed by using methods such as fluoroscopy, providing exact numbers of patients and fully reporting the results (see appendix 3 for further details of the studies). The exact location and distribution varied between these studies, and the patterns were predominantly neither dermatomal or sclerotomal in distribution, meaning that it would not be possible to identify symptomatic level from a pain distribution alone.

To summarise, somatic structures within the spine are capable of referring pain into the leg, in a non-uniform distribution. Such variety in the location and distribution of symptoms means that it is not possible to diagnose the structure responsible or even if the structure responsible is somatic or neurogenic from distribution alone. Further assessment is required, and section 2.4 discusses the way in which sub-grouping individuals in to radicular, radiculopathy and somatic can be achieved. However, individuals with spinally referred leg pain may not only have a neurogenic or somatic
presentation to their pain, but may also have an abnormal processing of pain which predominates; central sensitisation (Schäfer et al., 2011; Smart et al., 2012)

2.3 Central Sensitisation

Individuals with chronic pain may develop a condition called central sensitisation (CS), a condition where pain messages are abnormally processed, resulting in excessive pain, which may become less localised to the site of original dysfunction. There are a number of mechanisms thought to be responsible for central sensitisation, including altered processing of sensory information in the brain, disturbance in the normal descending inhibitory pain systems with concurrent increase in facilitatory ascending pain mechanisms, wind up of spinal cord neurones from repetitive stimulation of the primary afferent nerve fibres and long lasting enhancement (potentiation) of synapses within the anterior cingulate cortex (Arendt Nielsen and Henriksson, 2007; Li et al., 1999; Nijs, et al., 2010; Yunus, 2007). These mechanisms result in a variety of symptoms for patients including widespread hyperalgesia (heightened response to mechanical and warmth/cold) and allodynia (a pain response to non-noxious stimuli). However, heightened sensitivity to other sensory stimuli such as light, sound and smell has also been reported (Nijs et al., 2010).

CS has been reported in individuals with chronic LBP (Giesbrecht and Battie, 2005; Giesecke et al., 2004; Jensen et al., 2010; Schmidt-Wilcke et al., 2006), although there is limited evidence as to the proportion of individuals with chronic LBP who have this condition. Smart et al., (2012) found a prevalence of central sensitisation in 23% of 551 patients with low back (+/- leg) pain. The presence of CS was based on the results of a Delphi study of the opinions of 103 clinical experts (Smart et al., 2010a). As such, it is clear that an absolute diagnosis of CS cannot be made, but the likely presence of the condition can be ascertained.

With respect to the presence of leg pain, one study demonstrated that leg pain did not appear to increase the presence of central sensitisation and evidence of nerve root
irritation was often not associated with CS (Jensen et al., 2010). This suggests that neuropathic pain may not necessarily be more likely to lead to CS than somatic pain. This however, was in contrast to O’Neill et al., (2007) who found that 12 patients with referred leg pain and a diagnosis of radiculopathy demonstrated significantly increased sensitivity to pressure algometry over tibialis anterior (but not infraspinatus) compared to 12 controls. However, this could be a segmental increase in pain which may not be related to central sensitisation. In addition, O’Neill’s (2007) study only used 12 patients compared to the 326 (111 who had confirmed nerve root irritation) in Jensen et al.’s (2010) study.

Individuals with CS are considered to have higher levels of distress and depression (Apkarian et al., 2004; Arendt Nielsen and Henriksson, 2007), poorer general health-related quality of life (Smart et al., 2012) and poorer prognosis than those without this condition (Giesecke et al., 2004; Jensen et al., 2010; Thomas, 1999). It is thought that individuals with CS may not gain benefit from manual based treatments, since the normal mechanism of pain relief through the pain gate or descending pain inhibition are disrupted in this condition (Nijs et al., 2010; Zusman, 2008).

2.4 Clinical Identification of sub-groups of referred leg pain

As discussed, the 2 main types of spinally referred leg pain can be classified as mechanical nociceptive pain (somatic referred pain) or neuropathic (radicular and radiculopathy). In addition the presence of CS may be the predominating pain mechanism in some individuals with referred leg pain. Some authors have attempted to identify these patients by measures to identify the pain mechanism rather than the structures at fault (Beith et al., 2011; Smart et al., 2010a; 2010b; 2011; 2012; Schäfer et al., 2009).

Beith et al., (2011) utilised the painDETECT questionnaire to identify neural from non-neural cases of back and leg pain. This screening tool has been validated for the use in individuals with low back pain (Freynhagen et al., 2006). However the tool does not aim to identify those with and without a neural compromise (i.e. loss of nerve conduction),
and therefore individuals with both radicular pain and a lumbar radiculopathy would be grouped together. Since radiculopathy indicates a worsening neurological state than radicular pain, as deterioration in nerve function is seen with radiculopathy (Bogduk, 2009), this may be an important differentiation to make. In addition, the use of the pain DETECT in identifying neuropathic pain may be inaccurate in individuals with central sensitisation (Gauffin et al., 2013). Since CS is considered to be prevalent in individuals with chronic LBP (Jenson et al., 2010), it is possible that the use of this screening tool may not provide an accurate means of assessing neuropathic pain in these participants.

Smart et al., (2010a; b; 2011; 2012), found that a collection of signs and symptoms indicating either nociceptive, peripheral neuropathic pain and CS was reliable and had discriminative validity in identifying these 3 separate pain mechanisms in individuals with low back +/- referred leg pain. Such factors include the specific descriptors of pain used, or the location of symptoms. For example, individuals whose pain was located in large areas outside normally recognised referral patterns, and whose pain was evoked on every movement were considered to have central sensitisation. However, this method did not aim to distinguish between individuals with neuropathic pain with or without neural compromise. In addition, since many participants did not have leg pain (283/464) (Smart et al., 2012), there may have been more cues to a nociceptive (but non-somatic) cause of their LBP, regardless of other factors.

Schäfer et al., (2009) used a system to identify the cause of radicular pain, in addition to somatic pain and CS. The neuropathic pain questionnaire; the LANSS scale was used in association with other signs and symptoms to sub-group 40 individuals with back related leg pain. Good reliability of the system was found using 6 Physiotherapists (Kappa =0.71). Schäfer et al., (2009) suggested that a value >12 indicated the presence of CS, rather than neuropathic pain. Whilst the authors of the scale (Bennett, 2001) proposed that a score > 12 suggests neuropathic pain, and that in their original study some of the patients used had central pain, there was no discussion about the use of the scale for CS alone. The authors also supported their classification system with additional components in addition to the LANSS scale. These consisted of a number of test
procedures to identify any neural compromise (neurological integrity testing), or suggest mechanosensitivity of the nerve root. However, it was not clear how therapists decided that the leg pain was a somatic referral. It appeared that this decision was made as a result of negative findings on the other tests. It was not clear if the therapist attempted to reproduce the referred leg pain symptoms by stressing the lumbosacral spine. It is possible that the leg pain may have been caused by other non-spinal structures such as the hip joint, or even possibly non-musculoskeletal structures.

To be of relevance to the clinician, any sub-classification system should fit within current practice of identifying these types of patients. The remainder of this chapter provides support for a clinical assessment to identify the different sub-groups of individuals with spinally referred leg pain.

2.4.1. Identifying individuals with Radiculopathy

*Neurological Integrity Tests*

Clinicians have attempted to identify lumbosacral radiculopathy for many years using neurological integrity tests consisting of sensory testing of the lower limbs (light touch), isometric muscle testing and reflex testing. These tests have been advocated to show not only that a lumbosacral radiculopathy exists, but to identify the level of the nerve root compromise (Bono and Garfin, 2004; De Luigi and Fitzpatrick, 2011; Petty, 2011a). Clinicians must complete a full neurological integrity test for any individual who has either neurological symptoms or has spinally referred leg pain, not only to identify the presence of a nerve root involvement, but importantly to rule out serious spinal pathology such as cauda equina dysfunction (Bono and Garfin, 2004; Humphreys and Eck, 1999; Petty, 2011a; Refshauge and Gass, 2004).
Dermatomes

Sensory testing of the lower limb, normally using cotton wool, is commonly the first stage of testing for neurological compromise, since it is often thought that the large diameter sensory fibres are the first to show changes after a neuropathic incident (Freynhagen et al., 2008; Greening and Lynn, 1998). This is supported by animal studies on the lumbar spine which have shown that deterioration of the large diameter afferents and increase in the small sensory nerve fibres results after ligation of the nerve roots and DRG (Chatani et al., 1995; Kawakami et al., 1994). Reduction or absence of sensation is mapped out further to attempt to identify a pattern of sensory loss (Petty, 2011a; Refshauge and Gass, 2004). The distribution of altered sensation that appears to be related to loss of conduction of the nerve root is described as dermatomal (Foerster, 1933; Greenberg, 2003; Keegan and Garrett, 1948; Lee et al., 2008; McLachlan, 1990).

Historically dermatomal charts were devised from a number of different methods of establishing the sensory distribution of each nerve root (Foerster, 1933; Head and Campbell, 1900; Keegan and Garrett, 1948; Sherrington, 1894), and resulting in charts (see figs 2.3 and 2.4) which were not consistent between studies (see appendix 4). One criticism of older papers such as Head and Campbell, (1900) and Foerster, (1933) is that the methods were not always accurately detailed. However, repetition with methods used previously could not be done today due to ethical considerations. Later studies which attempted to study dermatomes by looking at the sensation in the skin of individuals with diagnosed herniated intervertebral discs also received criticism, since there is variability in how and where the nerve root is compromised, resulting in marked variability in dermatomal charts between individuals with seemingly the same nerve root involvement.

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3 it was not clear what benefit to patients sectioning nerve roots above and below one nerve root level would give, and indeed today it is well known that sectioning of nerve roots in individuals can result in irreversible pain states and considerable loss of function.
Nitta et al., (1993) also found much variability in distribution after nerve root block in individuals with a diagnosed herniated intervertebral disc. It is possible however that spread of anaesthetic may have resulted in more than one nerve root being anaesthetised. More recently, Lee et al., (2008) amalgamated a number of dermatomal charts to try to establish a more accurate chart (fig 2.5). There are no autonomous zones drawn due to overlap between levels, the exception being the midline, where there is minimal overlap. The blank areas represent considerable variation and overlap, such that no consistency regarding level could be drawn. Such variability makes being accurate about the nerve root level difficult based on dermatomal pattern alone, however simply identifying if a sensory loss has occurred in the leg for the lumbosacral nerve roots may be appropriate. Absence or reduction of sensation in the posterior leg/foot or anterior lower leg/foot in the absence of the presence of evidence of a more peripheral nerve lesion (e.g. sensory loss post leg trauma, or pathologies of the peripheral nervous system e.g. diabetes), would support a diagnosis of lumbosacral radiculopathy.

The validity of dermatomal testing will be examined alongside the other neurological tests. Prior to this an overview of myotomal and reflex testing will be presented.
Myotomes

Myotomes represent the motor supply from a single nerve root. Weakened groups of muscles supplied by a single nerve root are considered to be indicative of a radiculopathy (Refshauge and Gass, 2004; Petty, 2011a). Table 2.1 shows commonly used myotomes, but as with dermatomal charts it is known that there is considerable overlap in such myotomes. Early work by Sherrington, (1892) demonstrated by electrically stimulating the nerve roots in monkeys, cats, dogs and frogs that a number of nerve roots contributed to a number of muscles. How these directly relate to humans is not clear, as in animals the lumbar levels do not quite correspond to the same levels in humans (e.g. dogs have 7 lumbar vertebrae and 3 sacral vertebrae). Young et al., (1983) and Tsao et al., (2003) investigated the anatomical pattern of innervation of muscles by the lumbosacral nerve roots in patients with radiculopathy (identified either surgically or radiologically). Motor and sensory nerve conduction studies were performed by Tsao et al., (2003) but only EMG by Young et al. (1983). The findings suggested that L5 preferentially innervated extensor hallucis longus and tibialis anterior (Tsao et al., 2003; Young et al., 1983) and peroneus longus (Tsao et al., 2003) and for S1 gastrocnemius (Tsao et al., 2003; Young et al., 1983) and hamstrings (Tsao et al., 2003). It must be
noted that 16% of patients were incorrectly identified by the EMG findings compared to surgical findings (Young et al., 1983), which may lessen the strength of findings.

<table>
<thead>
<tr>
<th>Nerve Root Level</th>
<th>Muscle Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1/2/L3</td>
<td>Iliopsoas</td>
</tr>
<tr>
<td>L2/L3/L4</td>
<td>Quadriceps</td>
</tr>
<tr>
<td>L4/L5</td>
<td>Tibialis Anterior</td>
</tr>
<tr>
<td>L5/S1</td>
<td>Extensor Hallucis Longus</td>
</tr>
<tr>
<td>L5/S1</td>
<td>Peronei</td>
</tr>
<tr>
<td>L5/S1/S2</td>
<td>Gastrocnemius/gluteals/hamstrings</td>
</tr>
</tbody>
</table>

Table 2.1 Myotomes (Modified from Butler, 2000, Drake et al., 2005 and Iversen et al., 2013)

Myotomes and dermatome testing make up 2 of the 3 tests used clinically to identify a nerve root dysfunction; the third is reflex testing which will be discussed below, followed by a critical look at the use of these tests in clinical practice.

Reflex Testing

In the lower limb, the most common tendon reflexes that are tested are the patella reflex and the ankle jerk reflex. These are considered to test the L3 or L4 nerve root and S1 or S2 nerve roots respectively (Jönsson and Strömqvist, 1996; Butler, 1991; Petty, 2011a). This stretch reflex is thought to be decreased or absent in the presence of a dysfunction of the peripheral nerve pathways (either afferent or efferent), and increased in the presence of a central nervous system dysfunction. However, one study has demonstrated a reduction in reflexes following injection of hypertonic saline into the zygapophyseal joints (Mooney and Robertson, 1976), and thus the presence of a reduced reflex alone may not best reflect a nerve root dysfunction. There is some debate in the literature about the value of reflexes in the diagnosis of nerve root compression, and this alongside the validity of the other 2 tests discussed will be considered in the section below.
Validity of Neurological Integrity Testing
The majority of literature on this topic suggests that the tests described are not sufficiently accurate to diagnose a nerve root compression (van der Windt et al., 2011; Iversen et al., 2013). However, these systematic reviews have attempted to cluster a series of heterogeneous studies with varying robustness of methodology. In addition, most of the studies included in these reviews have not attempted to incorporate the amalgamation of both physical and subjective findings into the final decision making of the clinician; a factor thought to improve the accuracy of neurological testing (Mercer and Smith, 2007). In this study (Mercer and Smith, 2007), 5 extended scope physiotherapy practitioners examined 123 patients who were subsequently referred for MRI scans over a 9 month period. The results showed a sensitivity of 100%, specificity of 98%, and accuracy of 100% for a disc prolapse at the L3/4 level, a sensitivity of 89%, specificity 96% and accuracy of 94% for L4/5, and sensitivity 93%, specificity 85%, accuracy 89% for L5/S1. This study demonstrated that for experienced, highly trained physiotherapists, a full clinical examination including neurological integrity was an excellent indicator of intervertebral disc herniation. However, these were all patients referred to specialist clinics with a higher likelihood of nerve root involvement and may not reflect the population attending a standard Physiotherapy clinic. In addition all Physiotherapists were highly trained and used to seeing patients of this nature on a daily basis in their practice.

Such high sensitivity and specificity values have not been found in most other studies (Iversen et al., 2013; Lauder et al., 2000; van der Windt et al., 2011). Lauder et al., (2000) found sensitivity/specificity of myotomal testing to be 69/53% respectively, reflex testing sensitivity around 50% and specificity to be around 90%, and sensory testing 50% sensitive and 62% specific. If the findings were combined, specificity improved to 99% and the positive predictive value was 75%. Another interesting finding from Lauder et al.’s (2000) study was that 90% of individuals with a diagnosis of lumbosacral radiculopathy had one positive neurological integrity finding. However, the gold standard used was electrodiagnosis which has been reported to only have a diagnostic accuracy of 54% (van Damme et al., 1979), which reduces the conviction of
the results. Van der Windt et al.’s 2011 systematic review demonstrated poor validity for the tests with sensitivity of muscle weakness as a finding from 0.27 to 0.62 and specificity from 0.47 to 0.93. Reflex testing ranged from 0.14 to 0.89 for sensitivity and 0.6 to 0.93 for specificity, whilst sensation testing ranged from 0.14 to 0.61 and 0.6 to 0.93 (sensitivity and specificity respectively).

Such wide variation and generally overall poor validity do not support the use of these tests, however there were many limitations of both the systematic review (van der Windt et al., 2011) and original studies which question the credibility of this result. Firstly, the methodology of each study was so variable both in the gold standard used to identify the specific level (mainly MRI or surgery; surgery may be more valid), and in establishing if the gold standard was testing nerve root compression or disc herniation. Other important heterogeneous factors were the way in which tests were performed; some studies omitting details, others detailing techniques which are not normally used in practice. Examples include isotonic muscle testing rather than isometric (Kerr et al., 1988), range of movement compared to the other side as a measure of strength (Vucetic, 1996), and only testing one or two muscles for weakness. Perhaps most variance occurred in the sensory tests in that some tested pain, others tested light touch on both legs at the same time (potentially confusing the CNS with bilateral sensory input), and others looked at distribution of pins and needles or tingling. All of these factors make the conclusions of van der Windt et al., (2011) less convincing. Whilst there are limitations in the studies that were included in the van der Windt et al., (2011) study, a more recent study (Iversen et al., 2013), supports the conclusions made by van der Windt et al., (2011).

One hundred and sixteen patients were assessed by both a Physiotherapist and a medical practitioner and results compared to findings on MRI or CT scan (Iversen et al., 2013). Both the consideration of each individual test and allowing for the clinicians’ overall diagnosis of level at fault did not provide sufficient evidence for the clinical value of these tests (likelihood ratios for clinicians’ diagnosis 1.74 (+ve) and 0.73 for L5 and
1.29 (+ve) and 0.61 for S1⁴). However, the decision by the clinicians was based on a very directed examination and consideration of findings which are not all well supported in the literature. For example to diagnose an L4 radiculopathy the sensory loss within the L4 dermatome could be either a loss to light touch or pin prick, but it is unclear if a loss in both sensory modalities was needed to be considered positive. In addition weakness of ankle dorsiflexion was considered to be indicative of a motor loss of L4, which according to Young et al., (1983) best represents L5. In addition, a positive SLR alone was considered to be indicative of a radiculopathy, which has questionable validity for specific nerve root levels. Such clinical decision making may not best reflect current clinical practice, and may have resulted in an inaccurate diagnosis of nerve root involvement.

In support of the use of neurological integrity tests for assessing the presence of a radiculopathy, Takahashi et al., (1999) found a statistically significant greater nerve root pressure (59.8 (+/- 50.3) mmHg compared to 15 (+/- 5.3) mm Hg) in individuals with diagnosed disc herniation from MRI and positive neurological integrity, compared to those with negative neurological integrity. Whilst some changes to the nerve root pressure may have been induced by measuring pressure after a laminotomy, these changes would have been representative of all participants. The importance of this study is that all individuals were diagnosed with disc herniation from an MRI scan, yet not all had positive neurological integrity tests. It is possible therefore that the poor sensitivity values found in the aforementioned studies could reflect the differences in individuals with a visually identified herniated disc, i.e. not all individuals with herniated discs have sufficient neurological compromise to cause changes to neurological integrity, whilst others do. Hence, further studies are required to support these findings.

To summarise, the literature is generally not supportive for a single test for identification of nerve root level, but is more supportive of the combined use of the tests and the clinical presentation of the patients. Despite many papers suggesting poor validity

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⁴ Positive likelihood ratio considered to influence post-test probability and suggest robust clinical decision >5.0 and negative likelihood ratio <0.2 (Jaeschke et al., 1994)
measures for these tests, these remain the advised tests of choice for assessment of neurological integrity in clinical practice (Bono and Garfin, 2004; Humphreys and Eck, 1999; Petty, 2011a; Refshauge and Gass, 2004). In addition, the limitations of many of these studies may mean that the findings are not conclusive. The positive findings of clinical judgement alongside these tests from Mercer and Smith (2007), and improved diagnostic accuracy found by combination of tests by Lauder et al. (2000) suggests that there may still be justification for the use of these tests in clinical practice. Moreover, the lack of alternative tests for the diagnosis of nerve root involvement means that these tests continue to be routinely used in practice.

*Straight Leg Raise Test for diagnosis of radiculopathy*

The straight leg raise test has also been proposed as a test which accurately detects the presence of a radiculopathy (Kobayashi et al., 2003). The leg is lifted with the individual in supine and the knee extended. The test is known to influence the lumbosacral nerve roots; causing excursion and strain to occur (Gilbert et al., 2007 a and b, Goddard and Reid, 1965). The principle behind the positive test for radiculopathy is that the nerve root becomes pulled against the herniated disc leading to greater amounts of pain or neurological deficit (Rabin et al., 2007).

Indeed, Kobayashi et al., (2003) found a restriction in movement of the nerve root adjacent to the disc herniation during the SLR in 12 individuals with lumbosacral disc herniation, which significantly increased after removal of the disc herniation. In addition, blood flow measured using a laser Doppler flow meter, was markedly decreased at the angle that the individuals had complained of pain during the SLR and significantly increased after discectomy. The restriction and subsequent improvement in nerve root excursion during the SLR was supported by another study by the same authors 7 years later in a larger cohort of 32 participants (Kobayashi et al., 2010). However, despite this compelling evidence in support of SLR for radiculopathy, studies have not convincingly supported the use of SLR for diagnosing radiculopathy.
Predominantly sensitivity is good to excellent (Lauder et al., 2002; Poiraudeau et al., 2001; Rabin et al., 2007), but specificity varies from poor to good (Lauder, 2002; Poiraudeau et al., 2001; Vroomen, 2002). Some of the differences in the results of the studies may be related to the way in which the SLR test was performed, some specifically look for referral of pain below the knee (Rabin et al., 2007) whereas others lacked clarity in the description (Vroomen et al., 2002). It must be noted that the SLR is a neurodynamic test which aims to assess dysfunction in any of the neurological structures from the nerve root down to the continuation into the sciatic nerve and its distal connections (Butler, 1991; Butler, 2000; Shacklock, 2005a). Hence, its lack of specificity for radiculopathy is logical, since the test cannot identify lumbar disc herniations alone. Individuals with radicular pain and radiculopathy would be expected to have a positive SLR; therefore the test lacks the ability to discriminate between the 2 conditions. However, as explained in the section below, it is critical in differentiating between radicular and somatic referred pain.

In summary, the decision of sub-grouping individuals into radiculopathy should be decided based upon the clinical picture (e.g. history of the condition, location of symptoms into the leg which are aggravated by spinal movements) and the presence of positive neurological integrity tests. The use of the SLR will be discussed in greater detail in the section below, and further in chapter 3.

2.4.2. Identifying individuals with Radicular pain

Nerves that are sensitised will be painful when they are moved (Hall and Elvey, 2004; Walsh and Hall, 2009b). One way of testing lumbosacral nerve root sensitivity is with the use of neurodynamic tests, including SLR or slump tests (chapter 3 includes a discussion of the clinical use of the SLR and slump tests). These neurodynamic tests represent the ability of the nervous system to cope with movements which cause them to slide through their interfacing tissues, and at times become compressed or lengthened as a result (Boyd et al., 2005; Shacklock, 1995; Shacklock, 2005a). Nerves not only adapt to large changes in nerve bed length mechanically but also physiologically, because
throughout such movements they must continue to function (Butler, 2000; Shacklock, 2005a). In cases where the nerve becomes sensitised to movement, this suggests a degree of compromise in its ability to cope either mechanically or physiologically (Boyd et al., 2005; Gallant, 1998).

The SLR and slump tests are two neurodynamic tests which influence the lumbosacral nerve roots, lumbosacral plexus and continuations into the sciatic nerve and its divisions. The slump test additionally stresses the more proximal portions of the neuraxis by causing further excursion of the spinal cord and brain stem (Butler, 2000; Shacklock, 2005a). One study has shown substantial agreement between SLR and slump tests ($\kappa = 0.69$) and good reliability of both tests in individuals with spinally referred leg pain ($r = 0.64$) (Walsh and Hall, 2009c).

Beith et al., (2011) found a statistically significant reduction in range of SLR in patients with neuropathic back and leg pain compared to those with nociceptive back and leg pain. An important aspect of neurodynamic testing to determine the presence of a mechansensitive nerve is structural differentiation, since SLR alone moves many structures such as the lumbar spine, hip, knee and ankle joints and the surrounding myofascial structures. Structural differentiation consists of movements of the joints furthest away from the area of symptoms, such that a change in symptoms is unlikely to be attributable to the local non-neural structures, since they will not have been moved. An example would be a reproduction of symptoms in the buttock during SLR, which increase with the addition of ankle dorsiflexion. Since the proximal structures have not been moved, the increase in buttock symptoms is more likely to be due to changes in the nerve since dorsiflexion increases the strain in the tibial nerve (Alshami et al., 2007; Boyd et al., 2013; Coppieters et al., 2006) and sciatic nerve (Boyd et al., 2005; 2013; Coppieters et al., 2006).

It can therefore be concluded that SLR or slump test would identify pain referred from a nerve root dysfunction. In addition, it has been demonstrated that sensitised nerves do not just display sensitivity to movement, but also to touch, and this sensitivity is
commonly felt often along the course of the nerve trunk (Asbury and Fields, 1984; Walsh and Hall, 2009c). In the case of lower lumbar spinal nerve roots or DRG, the tenderness to palpation is likely to be felt along the course of the sciatic nerve (Dyck, 1987; Walsh and Hall, 2009c). This may be due to neurogenic inflammation mediated by the nervi nervorum (Hall and Elvey, 2004). The nerve trunk acts as a sensitised nociceptor, producing pain on even minor mechanical stimuli (Devor and Rappaport, 1990). As a result of this, palpation along the nerve trunk has been advocated (Schäfer et al., 2009, 2011; Walsh and Hall, 2009c). The validity of palpation as compared to slump tests or SLR was high (sensitivity 0.83, specificity 0.73) if 2 or more palpation sites were positive (Walsh and Hall, 2009c). Whilst a limitation of Walsh and Hall, (2009c) is around the issue of SLR and slump test as a gold standard for nerve dysfunction in this study, the aim was to see if the 2 tests related to each other in the presence of leg pain.

To summarise, the presence of radicular pain may be identified by a positive SLR or slump test and the presence of 2 or more tender points on nerve palpation at the sciatic (at the buttock), tibial (behind the knee) and common peroneal (around the fibular head) nerves. However, since the sensitivity and specificity of nerve palpation as compared to the SLR or slump test was not 100%, it is possible that a negative nerve palpation test could be found in the presence of a positive SLR or slump test and vice versa. Since there is a stronger body of evidence for the use of neurodynamic tests in identifying neuropathic pain (see chapter 3) than nerve palpation alone, a final decision on sub-group should be made on the findings of the SLR or slump test.

Neurological integrity tests are required to distinguish between radicular pain and radiculopathy. Individuals with negative neurological integrity, neurodynamic tests or nerve palpation may be considered to have somatic referred leg pain, however further examination is required to ensure that the pain is neuromusculoskeletal in origin and related to the spine, not other local structures such as the hip joint.
2.4.3. Identifying individuals with Somatic Referred leg pain

Somatic referred leg pain may arise from dysfunction of a number of different structures (muscles, joint structures, ligaments etc). For the purposes of the present study, the precise location of the source of somatic referred leg pain is not the critical concern. The main focus is on whether there is a neural or non-neural cause of spinally referred leg pain. The location of leg pain cannot be used to identify neural versus non-neural structures. Individuals with solely a somatic referred leg pain have no neurological signs and symptoms (Bogduk, 2009; Fukui et al., 1997; O’Neill et al., 2002), therefore, neurological integrity tests, which assess changes to nerve conduction (light touch, reflex testing and muscle strength), will be normal. Furthermore, neurodynamic tests using structural differentiation (Coppieters et al., 2005; Nee et al., 2012a) would also be negative, since the nerve is not irritated in these individuals (Bogduk, 2009; Fukui et al., 1997; O’Neill et al., 2002). In addition to negative findings in the tests described, individuals with somatic referred pain can be identified by reproducing their pain with movements which load the local soft tissues around the lumbar spine such as active range of movement (AROM) and passive accessory intervertebral movements (PAIVMS) of the lumbar spine, or manual testing of the muscles around the spine (Petty, 2011a; Refshauge and Gass, 2004).

Patients with pain emanating from their somatic spinal structures have pain on movements of their spine because the spinal structures are sensitised either chemically or mechanically. In addition, exclusion of pain from peripheral joints is essential to support the diagnosis. Hence, somatic referred pain may be identified if an individual has their symptoms reproduced by at least one physical test procedure of a spinal non-neural structure (and have negative neurological integrity and neurodynamic tests).

The proportion of patients who have somatic referred leg pain is thought to be higher than the other 2 sub-groups identified for this thesis (Beith et al., 2011). Fifty six percent of 343 patients referred for Physiotherapy for their low back and referred leg pain in the South East region of the UK were identified as having somatic referred pain. A similar finding was found by Smart et al., (2012). Fifty five percent of individuals
with back (+/- leg) pain in the UK and Ireland were thought to have a nociceptive cause for their pain.

In addition to identifying appropriate sub-grouping of individuals with spinally referred leg pain, it is important to ascertain if individuals have CS. The way in which CS may be identified is described in the section below.

**2.4.4. Determining Central Sensitisation Clinically**

There is no definitive diagnosis for CS, however a collection of symptoms and signs (pain for longer than 6 months (O'Neill et al., 2007), widespread areas of pain (Jensen et al., 2010; Smart et al., 2010a), hypersensitivity to warmth or cold (Berglund et al., 2002), and hypersensitivity to touch (Jensen et al., 2010; O'Neill et al., 2007; Smart et al., 2010a), may give an indication of such a condition.

Fibromyalgia is a condition in which CS is considered to be an important characteristic (Arendt Nielsen and Henriksson, 2007; Meeus and Nijs, 2007; Nijs et al., 2010; Yunus, 2007; Woolf, 2011). The use of tender point assessment has been used to diagnose fibromyalgia (Woolf, 2011; Jensen et al., 2010), since one of the key findings of CS is widespread mechanical hyperalgesia. It has been postulated that CS may be prevalent in some individuals with low back pain (O’Neill et al., 2007; Nijs et al., 2010; Schmidt-Wilcke et al., 2006), and found that a lowering of pressure pain thresholds occurs in individuals with chronic low back pain (Giesecke et al., 2004; Laursen et al., 2005; O’Neill et al., 2007). Jensen et al., (2010) assessed the presence and use of the same tender point assessment that is used to diagnose fibromyalgia in individuals with chronic low back pain. Three hundred and twenty six patients (111 with diagnosed radiculopathy) filled in a common mental disorders questionnaire which incorporated aspects of distress, anxiety and depression before a tender point assessment was completed (see appendix 27). The presence of greater than 8 tender points was associated with widespread pain (odds ratio 3.67). In addition patients with greater than 8 tender points had a longer duration of low back pain, and had positive associations with greater distress. Interestingly there was no association with the presence of nerve
root pathology and tender points; indeed there was a negative association between these
two variables.

It has been found that individuals with chronic low back pain have worse pain after
exercise (Hoffman et al., 2005), a finding also present in individuals with chronic
fatigue syndrome (another condition where CS has been demonstrated) (Whiteside et al.,
2004). This is in contrast to an improvement in pain in asymptomatic individuals and is
thought to be related to the abolition of descending inhibitory pathways found in CS.
However Meeus et al., (2010) found that whilst PPT decreased in individuals with
chronic fatigue syndrome after submaximal exercise on a static bike, it increased in both
asymptomatic individuals and patients with chronic low back pain. Therefore, this
method may not be useful in identifying CS in individual with chronic LBP. Thermal
hyperalgesia and wind up of spinal cord neurones from repetitive stimulation of the
primary afferent nerve fibres, have also been found to be prevalent in individuals with
CS (Desmeules et al., 2003; Li et al., 1999; Staud and Price, 2001). However the
protocol for testing thermal pain thresholds and wind up requires the use of expensive
time consuming quantitative sensory testing equipment, which are not practical for
physiotherapists to use during a standardised assessment. Testing of painful points can
be done using a hand held algometer, which is cost effective and time efficient. In
addition, there is no evidence that thermal hyperalgesia is any more valid for identifying
CS than mechanical hyperalgesia.

Therefore, if greater than 2 of the symptoms of CS are present as described above, and
greater than 8 painful points are revealed on physical assessment, an individual may be
identified as having a centrally sensitised pain mechanism. People with spinally referred
leg pain and CS may present with increased levels of disability. In addition, it has been
found that individuals with different causes of their leg pain may have different
contributions from non-physical factors such as psychological and social influences
(Smart et al., 2012). The next section discusses the relevance of such factors in
prognosis in individuals with low back and referred leg pain, and explains the rationale
for the choice of disability and psychosocial questionnaires that are frequently used in clinical studies.

2.5 The Impact of psychosocial characteristics on outcome of spinally referred leg pain

Low back pain, like all forms of pain is a complex process, affected by both physical and psychosocial factors (Haggman et al., 2004; Hill and Fritz, 2011; Jensen et al., 2010; Vlaeyen and Linton, 2000). Poorer prognosis has been associated with higher psychosocial factors such as fear avoidance (Vlaeyen and Linton, 2000; Wessels et al., 2006; Woby et al., 2004), depression and anxiety (Bergbom et al., 2011; Haggman et al., 2004;), kinesiophobia (Picavet et al., 2002; Thomas et al., 2010), and catastrophising (Bergbom et al., 2011; Picavet et al., 2002; Sullivan et al., 2005; Wessels et al., 2006). In addition high levels of disability are considered to be a poor prognostic indicator (Hayden et al., 2010; Heymans et al., 2010; Hill et al., 2011), and levels of disability have been demonstrated to relate well to psychosocial characteristics (Thomas et al., 2010; van Wilgen et al., 2010; Waddell et al., 1993).

It is therefore plausible that higher levels of disability and psychosocial factors could detrimentally affect the outcome of treatment intervention in individuals with spinally referred leg pain. It is therefore important to analyse any interactions in clinical studies assessing the effects of treatment interventions, since these factors could mask any positive effects that occur. It has been proposed that individuals with neuropathic causes of leg pain may have a poorer prognosis due to a number of factors, including psychosocial elements (Haugen et al., 2012; Hill et al., 2011; Kongsted et al., 2012). Assessing the differences between the 3 sub-groups in relation to psychosocial factors may add to the current body of evidence regarding specific psychosocial factors in sub-groups of individuals with spinally referred leg pain. This section gives an overview of the potential implications of higher levels of disability and psychosocial factors, and provides justification for the use of such questionnaires in clinical studies.
2.5.1 Psychosocial Factors and Prognosis

The prognosis for individuals with chronic low back pain is complex and affected by many variables (Hayden et al., 2010; Heymans et al., 2010). However, it is well recognised within the literature that high levels of a number of psychosocial factors can negatively affect prognosis (Bergbom et al., 2011; Haggman et al., 2004, Picavet et al., 2002; Sullivan et al., 2005; Vlaeyen and Linton, 2000; Wessels et al., 2006; Woby et al., 2004) and that these factors are high in individuals with spinally referred leg pain (Hill et al., 2011), particularly neuropathic leg pain (Haugen et al., 2012; Kongsted et al., 2012). Poorer prognosis has been linked to increased levels of certain psychosocial characteristics in individuals with chronic LBP. Chronic LBP varies in its definition, but most texts consider it to be LBP that has been present for between 3 to 6 months in duration (Freburger et al., 2009; Giesecke et al., 2004). The most common characteristics involving abnormal beliefs about the pain or about movement or work (Bergbom et al., 2011; Picavet et al., 2002; Sullivan et al., 2005; Thomas et al., 2010; Vlaeyen and Linton, 2000; Wessels et al., 2006; Woby et al., 2004) or high levels of depression, stress or anxiety (Bergbom et al., 2011; Haggman et al., 2004; Hill and Fritz, 2011). Appendix 5 details some of the studies which have looked into prognostic factors and the presence of psychosocial factors in low back pain. Chronicity and even development of LBP have been closely linked to pain catastrophising and kinesiophobia (Picavet et al., 2002), whilst recurrence and chronicity have also been linked with fear avoidance beliefs and depression (Burton et al., 2004). These psychosocial factors are defined and detailed in section 2.5.3. Burton et al., (2004) also found that the presence of leg pain was a factor associated with recurrence.

One study demonstrated that leg pain with neurological signs had poorer prognosis when associated with higher levels of kinesiophobia (Haugen et al., 2012), but Kongsted et al., (2013) showed that despite an increase in psychosocial factors in individuals with referred leg pain and neurological signs (Kongsted et al., 2012; ), prognosis was not affected (Kongsted et al., 2013). However, Kongsted et al., (2013) did not reveal what, if any intervention participants may have been having in the one year time frame that
participants were involved in the study, which could have resulted in heterogeneous factors explaining the results.

In contrast to Kongsted et al., (2013), Jensen et al., (2010) found that predictors of poorer prognosis were higher levels of fear avoidance, worrying and health anxiety, although these were no worse compared to individuals with low back and leg pain without neurological signs. These results appear to contradict Haugen et al., (2012) since Jensen et al., (2010) found no difference between the prognostic indicators for neurological versus non-neurological referred leg pain. However, Haugen et al., (2012), only looked at individuals who they considered to have a nerve root irritation resulting from a disc herniation, hence it is not known what differences in prognostic factors would have been found if individuals with and without neurogenic leg pain had been compared.

Limitations of all three studies were the way in which they concluded that patients had neurological cause for their leg pain. Kongsted et al., (2013) included participants with either a positive SLR (less than 60°) or any one positive neurological integrity test. Haugen et al., (2012) included individuals with pain or symptoms below the knee and a positive disc herniation on MRI or CT scan. Jensen et al., (2010) classified individuals with radiculopathy from positive MRI findings plus a positive SLR and loss of sensation or reflex. Jensen et al., (2010) attempted to improve the accuracy of the classification, by only permitting individuals into the group with a positive MRI scan, but this may have negated those with an inflammatory (but not visible compressive neuropathy) cause of radicular pain. This may have explained the lack of difference between the 2 groups. Similarly Haugen et al.’s (2012) classification did not include a neurological examination and hence individuals may not have had a neurological cause of leg pain despite the positive MRI or CT scan, since it is known that MRI scans often show pathological findings even in asymptomatic patients (Boden et al., 1990; Falconer et al., 1948; Rydevik et al., 1991; van Rijn et al., 2006). Likewise, Kongsted et al., (2013) may have grouped individuals with the radicular or radiculopathy together by allowing SLR to be the one positive test which categorised individuals in this way.
Whilst it is unclear if there is a difference in prognostic factors specifically between individuals with radiculopathy or radicular pain, Walsh and Hall, (2009a) found a greater level of disability and fear avoidance in a group of individuals with radicular pain than those with radiculopathy, somatic pain or greater neuropathic signs and symptoms. However, of interest, all sub-groups had borderline abnormalities for anxiety and moderately high fear avoidance, suggesting the presence of leg pain alone, regardless of the cause, may result in high levels of certain psychological sub-straits. Schäfer et al., (2011), using the same sub-grouping system, found a significantly greater level of anxiety in the individuals with CS, compared to the radicular and radiculopathy groups. Interestingly, there was no significant difference between the somatic referred leg pain group and the centrally sensitised group. In addition, no significant effect of any of the psychosocial factors (fear avoidance beliefs, anxiety and depression) was found on improvement in outcome of a neurodynamic treatment between the 4 sub-groups. Hence, despite the suggestion that prognosis may be poorer in individuals with neurogenic causes of leg pain, and that higher levels of psychological factors are a cause for this worse prognosis, there is limited evidence that has demonstrated this for individuals with referred leg pain.

Low numbers of participants in each group (minimum of 7 and maximum of 15, Walsh and Hall, 2009a; minimum of 9, maximum of 29, Schäfer et al., 2011), and the method of sub-grouping which were discussed in section 2.4 mean that further investigation of these psychosocial factors in individuals with referred leg pain are essential to ascertain their significance.

2.5.2 Association of disability and psychosocial factors

Whilst LBP has been recorded throughout history (Allan and Waddell, 1989), the associated disability has only been recorded in relatively more recent times (Waddell, 1987). This has been suggested to reflect a sociological phenomenon, related to the progression in medicine (Waddell et al., 1993). Whilst pain is linked to disability, it has

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5 the classification system used was that of Schäfer et al., (2009), details can be found in chapter 2.4
been demonstrated that this relationship is weak (Slater et al., 1991; Waddell et al., 1993). However, Grotle et al., (2004) found that pain was associated with disability, measured by the Oswestry disability Index (ODI). This difference in findings compared to those of Waddell et al., (1993) and Slater et al., (1991) may be because questions about pain are integrated into the ODI. Regardless of the exact relationship between pain and disability, there is a growing body of evidence which links high levels of disability with high levels of psychological factors. Fear avoidance factors have been linked closely with higher levels of disability (Crombez et al., 1999; Grotle et al., 2004; Waddell et al., 1993). Waddell et al., (1993) found that higher levels of fear avoidance beliefs about work correlated highly with higher levels of disability, but not pain. Fear avoidance beliefs about physical activity were significantly associated with high scores on the ODI (Grotle et al., 2004) in individuals with both acute and chronic low back pain. Crombez et al., (1999) found that fear avoidance beliefs were strongly correlated with disability in individuals with chronic low back pain.

Pain catastrophising and kinesiophobia have also been found to be important predictors of disability in patients with neuropathic pain (French et al., 2007; Sullivan et al., 2005) and chronic low back pain (Crombez et al., 1999; Picavet et al., 2002). In addition, pain related fear was found to be a strong predictor of chronic disability, 1 year after the first incidence of low back pain (Klenerman et al., 1995). Depression has been demonstrated to be linked with disability (Epping-Jordan et al., 1998). However, in a systematic review emotional distress (including anxiety, depression and stress) did not seem to be a predictor in chronic disability (Truchon and Fillion, 2000), although its presence may impact on disability through a vicious circle of distress, leading to inactivity and disability, which further induces emotional distress (Gatchel and Gardea, 1999). This is supported by Crombez et al., (1999) (not included in Truchon and Fillion’s 2000 systematic review) who found anxiety be less predictive of disability than fear avoidance or kinesiophobia. However in contrast, Wand et al., (2010) found that depression made a significant contribution to the prediction of disability as measured with the Roland and Morris disability questionnaire, whilst Grotle et al., (2004) found that distress was strongly related to disability in individuals with chronic LBP.
Since the factors discussed appear to be related to outcome in individuals with low back and spinally referred leg pain, these factors should be incorporated into clinical studies to assess if they have an impact on the effect of any treatment. A number of scales exist, and the following section describes and critiques each scale.

### 2.5.3 Choice of Disability and Psychological Questionnaires

A wide array of questionnaires for measuring a plethora of different psychological traits and identifying levels of disability can be found in the literature. As discussed in the previous section, the most pertinent psychosocial factors which have been related to poor outcome in individuals with low back and spinally referred leg pain have been emotional distress (Burton et al., 2004, Jensen et al., 2010; Kongsted et al., 2012; 2013; Schäfer et al., 2011; Smart et al., 2012), fear avoidance beliefs (Burton et al., 2004; Jensen et al., 2010; Kongsted et al., 2012, 2013; Schäfer et al., 2011; Walsh and Hall, 2009a; Woby et al., 2004) catastrophising (Picavet et al., 2002; Woby et al., 2004) and kinesiophobia (Haugen et al., 2012; Picavet et al., 2002). Even within these specific traits, a number of possible measurement tools are available in the literature. The choice of specific questionnaires should be based on the appropriateness of their use for the cohort in question, and acceptable validity and reliability. Each of the questionnaires is discussed below.

#### Oswestry Disability Scale (Appendix 6)

This is a self-reporting questionnaire which has been designed to assess the functional impairments of individuals with low back pain (Fairbank et al., 1980). It consists of 10 items covering levels of pain, personal care, and various functional activities such as lifting and social life. The total score is turned into a percentage score of sections completed. This allows for individuals to miss sections that may not be applicable (for example questions related to sex life, found to be omitted in 24% of cases by Fisher and Johnson, 1997). The classification system of severity recommended by the original authors (Fairbank et al., 1980) is as follows:

- **0-20%**: Minimal back pain
- **21-40%**: Moderate back pain
- **41-60%**: Severe back pain
- **61-80%**: Very severe back pain
- **81-100%**: Severe back pain with disability
0-20% minimal disability
20-40% moderate disability
40-60% severe disability
60-80% crippled\(^6\)
80-100% bed bound

Fisher and Johnson, (1997) assessed the content validity of the ODI in 190 patients undergoing rehabilitation for LBP. Specific tests were performed to assess the validity of 3 of the sub-sections of the ODI: sitting, lifting and walking (time of sitting was measured with a stop watch, walking distance was calculated until they needed to stop, and individuals were asked to hold greater amounts of weight by adding bags of flour to a carrier bag). There was significant correlation with the distance walked and specific section on walking (section 4), with high sensitivity and specificity calculated for this section (sensitivity 76%, specificity 96%). Statistical correlation was also found for sitting duration and section 5 of the ODI (sitting) with sensitivity and specificity 72 and 69% respectively. Lifting was better correlated with the weight lifted than the time of holding the weight, with sensitivity and specificity being 81% and 52% respectively. However, such low specificity could be linked to the fact that individuals may not lift in the way that they were tested in the study; a static hold of flour in a carrier bag may be easier to sustain than lifting a child from the floor for example. ODI has been found to correlate highly with other outcome measures for individuals with LBP (Roland Morris disability questionnaire (Stratford et al., 1994), and McGill Pain Questionnaire (Beurskens et al., 1995), but less well with measures of pain or physical examination (Beurskens et al., 1995). Internal consistency (a measure of how each construct within a questionnaire correlates with the other constructs) of the ODI is good, with Cronbach’s \(\alpha\) from 0.76 (Fisher and Johnson, 1997) to 0.87 (Kopec et al., 1996).

Repeatability of the ODI has been found to be excellent with ICC of 0.88 (Joshi et al., 2013) to 0.91(Kopec et al., 1996).

\(^6\) Unfortunately a revised classification system using a more appropriate term appears not to have been considered.
Fear Avoidance Beliefs Questionnaire (FABQ) (Appendix 7)

Fear of pain, and the attempt to avoid pain is an innate response in human beings (Waddell et al., 1993). However, it has been demonstrated that fear avoidance behaviours may impact on the level of disability in individuals with low back pain (Waddell et al., 1993; Walsh and Hall, 2009a). The FABQ was developed by Waddell et al. in 1993. It consists of 2 scales; the first related to fear avoidance beliefs about physical activity, and the second to fear avoidance beliefs about work. A score of 0 to 6 is used with 0 denoting completely disagree and 6 completely agree. There are 5 items in the first scale and 11 for the second scale. The total score is added after removing one item on the first sub-scale (physical activity) and 4 items on the second subscale (work). A higher score suggests higher fear avoidance beliefs, however a guide to what constitutes a more abnormal or concerning score has not been suggested by the authors (Waddell et al. 1993). Crombez et al., (1999) suggested that a physical activity score of greater than 15 may be used as a cut off score, and Fritz and George, (2002) have suggested a score of greater than 34 for the work scale, but both acknowledge that further work is required to demonstrate the validity of such scores.

The 2 sub-scales (physical activity and work) have been found to significantly correlate with each other (Crombez et al., 1999). This study also demonstrated excellent internal consistency for work (Cronbach’s α =0.84), but lower consistency for physical activity (0.57), this was accounted for by the lower number of items included in the scale (after removal of instructed items; 4, compared to 7 for work). However, Jacob et al., (2001), found a higher internal consistency of 0.7 for physical activity and Grotle et al., (2006) found higher values for both scales; 0.90 and 0.79 for work and physical activity respectively. It must be noted that in both studies the questionnaire was translated into other languages (Hebrew in the former and Norwegian in the latter), is it not known therefore if these higher values are reflective of differences in language or culture, and so it may be that the internal consistency found by Crombez et al., (1999) is more relevant to participants completing the FABQ in English. Crombez et al., (1999) also
demonstrated construct validity as assessed against the Tampa scale of kinesiophobia (TSK).

The FABQ has been shown to have good to excellent repeatability (Grotle et al., 2006; Waddell et al., 1993). Waddell et al., (1993) found an average kappa value of 0.74, and Pearson’s correlation of 0.95 and 0.88 (for work and physical sub-scales accordingly). Grotle et al., (2006) found a slightly lower re-test repeatability using the Norwegian version of 0.82 and 0.66 (for work and physical sub-scales). These studies support the use of this tool as a robust measure of fear avoidance.

**Tampa Scale of Kinesiophobia (TSK) (Appendix 8)**

Kinesiophobia is a condition where an individual develops an excessive and incapacitating fear of movement, which is beyond that which would be expected in “normal” painful situations (Kori et al., 1990; Lundberg et al., 2004), and is related to fear of re-injury. It shares some similarities with the physical activity sub-scale of the FABQ.

This questionnaire was initially developed by Kori et al., (1990). It consists of 17 items, scored using a 4 point Likert scale of 1= strongly disagree to 4= strongly agree. Items 4, 8, 12 and 16 require their score to be reversed because of the positive nature of the statement. A high score indicates a high level of kinesiophobia (French et al., 2007), although no specific score has been suggested as indicative of abnormality. The internal consistency of the Tampa scale is high (Cronbach’s $\alpha =0.68$, Crombez et al., (1999), 0.81, Lundberg et al., (2004), 0.84, French et al., (2007)). Construct validity has been demonstrated against the fear avoidance beliefs questionnaire (Crombez et al., 1999; French et al., 2007). In addition a high correlation exists between the Tampa scale and pain catastrophising and depression (French et al., 2007). Retest reliability of the Tampa scale has been found to be excellent (ICC, 0.91, Pearson’s correlation coefficient, 0.91, Lundberg et al., (2004)), however this was for the Swedish translation of the scale.
Pain Catastrophizing Scale (PCS) (Appendix 9)

Catastrophising is defined as “an exaggerated negative mental set brought to bear during actual or anticipated painful experience” (Sullivan et al., 2001 pg 53). This 13 item scale was originally developed by Sullivan et al., (1995). A 5 point score exists for the degree to which the individual has feelings and thoughts about each statement, ranging from 0 (not at all) to 4 (all of the time). The scale has been demonstrated to have high internal consistency (Cronbach’s $\alpha =0.87$) by the developers of the PCS (Sullivan et al., 1995), but further supported by Osman et al. (1997) ($\alpha =0.93$). Three subscale scores are produced by the PCS which assess rumination, magnification and helplessness. Its association with disability has been found in a number of studies (Picavet et al., 2002; Sullivan et al., 1998), with rumination being more greatly associated with disability (Sullivan et al., 1998). In addition, pain catastrophising has been demonstrated to be associated with intensity of pain and pain-related outcomes in individuals with neuropathic pain (Haythornthwaite and Benrud-Larson, 2000; Sullivan et al., 2005).

A clinically relevant level of catastrophising is a total score of $>30$ (Sullivan et al., 1995). Hence, whilst it might be useful to separate the scale into its 3 sub-sections, overall a score is required which determines whether an individual is catastrophising. In order to establish which, if any of the factors of pain catastrophising may have an impact on outcomes, both a total score and separate scores are important.

Concurrent validity has been demonstrated against Negative Thoughts in Response to Pain Questionnaire and anxiety symptoms on the Mood and Anxiety Symptom Questionnaire (Osman et al., 1997).

Retest reliability has been found to be 0.7 when re-administered after 8 to 12 weeks (Sullivan et al., 1995).
Short form -Depression Anxiety and Stress Scale (DASS 21) (Appendix 10)

Emotional distress has been related to disability in chronic low back pain (Jensen et al., 2010). Such distress has been separated into 3 sub-straits of distress: depression, stress and anxiety (Lovibond and Lovibond, 1995). The original DASS questionnaire scale is a 42 item scale which aims to assess the degree of depression, anxiety and stress (Lovibond and Lovibond, 1995). However, a short form (DASS 21) has also been developed (Lovibond and Lovibond, 1995). The DASS 21 has 7 items for each of the 3 sub-scales, and a 4 point likert scale, from “0 did not apply to me at all, to 3 applied to me very much, or most of the time”. Scores above 20, 14 and 25 on the depression, anxiety and stress subscales respectively are indicative of severe levels (original DASS).

Lovibond and Lovibond, (1995) suggest halving the values for each sub-scale to gain the same levels for DASS 21, which was supported by Henry and Crawford, (2005). Hence scores above 10, 7 and 12.5 would be indicative of severity for depression, anxiety and stress respectively.

Internal consistency of both DASS and DASS 21 has been found to be high (DASS anxiety $\alpha = 0.89$, depression $\alpha = 0.96$ and stress $\alpha = 0.94$, DASS 21 anxiety $\alpha = 0.81$, depression $\alpha = 0.92$ and stress $\alpha = 0.88$) (Clara et al., 2001). Similar internal consistencies for DASS 21 were found by Henry and Crawford, (2005) (0.88 depression, 0.82 stress and 0.9 anxiety). Both Antony et al. (1998) and Clara et al., (2001) found that the DASS-21 performed comparably to the DASS scale.

Wood et al., (2010) found that the DASS-21 sub scales have significant associations with a number of other validated outcome measures. These included the affective distress and interference sub-scales of the Multidimensional Pain Inventory, social functioning, general health, mental health, and vitality sub-scales of the SF-36, and for separate sub-scales between the depression scale and the role limitations-emotional subscale of the SF-36.

The scale is used both in individuals showing signs of depression and anxiety disorders (Clara et al., 2001), but also in a number of musculoskeletal condition such as
Rheumatoid Arthritis (Covic et al., 2012) and low back pain (Haggman et al., 2004; Parkitny et al., 2012).
Overall DASS has been shown to have high retest reliability of 0.99 (Akin and Cetin, 2007).

**2.5.4 Summary**

The importance of levels of disability and psychological influences on the prognosis of low back pain with particular reference to spinally referred leg pain has been presented. Different levels of disability or psychological factors could influence the effects of treatment modalities, therefore should be taken into account during analysis. In addition, some studies have suggested that individuals with neurogenic leg pain have greater levels of disability and presence of psychosocial factors than those with a somatic cause of leg pain, although this varies between studies, therefore further research is required to support or refute such assertions.

**2.6 Chapter Conclusion**

To summarise, this chapter has discussed the presentation of disorders resulting in spinally referred leg pain. It has supported the use of a pragmatic sub-grouping system for the identification of 3 main groups; radiculopathy, radicular pain and somatic referred leg pain. The influence of CS, and how this can be assessed using inexpensive time efficient equipment has been discussed. Finally, it has considered the effects of disability and psychological influences on the prognosis of spinally referred leg pain. A critical discourse around the use of the SLR test is pivotal to justify its use as an assessment and treatment tool. The next chapter provides a historical overview of the use of neurodynamic tests, and specifically the SLR test, and a critical evaluation of the use of the test as an assessment and treatment tool.
Chapter 3 Neurodynamic Assessment

The aim of this chapter is to provide evidence of the robustness of neurodynamic tests in clinical practice and establish the principles of using these tests to identify individuals with neuropathic pain. For the most part, this chapter includes a discussion of the literature which has looked at the SLR or slump test, but where necessary and appropriate, other neurodynamic literature is also reviewed.

3.1 Concept of neurodynamic tests

The concept of moving the nervous system to produce a change in an individual’s symptoms is not new. There is some documentary evidence that the use of SLR for diagnosing LBP was used as far back as 2800 BC by Imhotep who was chief minister to Zoser, the first King of the Third Dynasty (Beasley, 1982). However, Lasègue is often credited as being the first author to document the use of the SLR (Lasègue, 1864). The assessment of nerves in the upper limb was also given credence historically; tests for the median, ulnar and radial nerves were documented in the 1920s and 1950s (Bragard, 1929; Von Lanz and Wachsmuth, 1959).

In the Physiotherapy literature, Maitland described the use of SLR and slump tests in the 1970s (Maitland, 1973). Elvey introduced the brachial plexus tension test in 1979, and Butler wrote the book “Mobilisation of the nervous system” which became a popular text for Physiotherapists introduced to this seemingly new concept (Butler, 1991). However, prior to that time, studies had already been published which demonstrated movement of the nervous system during movements of the spine and leg. Authors such as O’Connell, (1946), Breig and Marions, (1962) and Goddard and Reid, (1965) had analysed excursion of the brain, spinal cord, lumbosacral nerve roots and sciatic nerve with movements of the trunk, head and leg. Later, studies looked at changes to the upper limb nerves during upper limb movements (Wright et al., 1996; Zoech et al., 1991). The focus of these pioneering studies was to assess the biomechanics of the nervous tissue, namely strain and nerve excursion as the nerve bed was lengthened.
The principle behind nerve testing in this concept is that as a series of joint movements occur, the nerve bed lengthens and the nerves are subjected to a number of biomechanical changes such as uncoiling, nerve excursion, strain and compression. These classic studies found that as the cervical spine and trunk were flexed, strain increased, and the spinal cord moved within the spinal column (Breig, 1960; O'Connell, 1946; Reid, 1960; Smith, 1956). Later studies focussed on tension changes within nerves as the nerve bed was lengthened (Kleinrensink et al., 2000; Kleinrensink et al., 1995a; Lewis et al., 1998). At this time many of the tests used were referred to as neural tension tests (Butler, 1989; Hall et al., 1998), and the dysfunction for which patients were seeking treatment was known as adverse mechanical tension.

As the 1990s progressed, the science behind the physiological changes involved with nerve dysfunction was developing rapidly, and research was published relating to changes to the peripheral and central nervous systems (e.g. Devor and Rappaport, 1990; Tal and Eliav, 1996). It became clear that pain and symptoms produced on movement of the nerves was not necessarily indicative of a biomechanical dysfunction. A more integrated approach, which combined both the mechanical aspects of nerve movement and nerve physiology, was developed. The physiological changes that occur after a compression neuropathy or chemical irritation to the nerve root have been discussed in chapter 2. The term neurodynamics was introduced by Shacklock, (1995) to try to marry the two important aspects of nerve assessment.

Shacklock, (2005a, pg 2) defines neurodynamics as “the clinical application of mechanics and the physiology of the nervous system as they relate to each other and are integrated with musculoskeletal function”. Such tests are designed to assess if movement of the nerve within the nerve bed, by applying a series of joint movements together which lengthen the nerve bed, produce the patient’s symptoms. Such altered tolerance to the application of these tests has been termed neural mechanosensitivity (Hall and Elvey, 2004).
3.2 Normal nerve mechanics

Nerves must move considerable amounts in order to cope with the large amounts of physiological movement which occur in the trunk and limbs during every day activities. They do so by a number of biomechanical and anatomical mechanisms, which help to protect them during the course of one’s lifetime. The peripheral nerves are continuous with the central nervous system due to the unique arrangement of the nerve sheaths, with the epineurium being continuous with the duramater (Butler, 1991; Rydevik et al., 1984). Its continuity is also apparent in chemical and electrical terms, since the same neurotransmitters occur throughout the system, and electrical messages are conveyed through the peripheral nerves, spinal cord and to the brain (Butler, 1991).

The presence of the connective tissue sheaths gives the nerves considerable biomechanical advantage during normal movement, since the sheaths are predominantly made up of connective tissues which are viscoelastic (Grewal et al., 1996; Millesi et al., 1995; Sunderland and Bradley, 1949; Topp and Boyd, 2006). The peripheral nerves have a more highly developed network of connective tissue sheaths (see fig 3.1) than the nerve roots and central nervous system, possibly due to the fact that there is less protection within the limbs for the nerves, and considerably more peripheral movement overall than within the trunk. In addition, within the spinal canal, the presence of cerebrospinal fluid together with the dura, pia and arachnoid mater may provide mechanical protection to these nervous tissues (Rydevik et al., 1984).

During normal activities, the nerves are placed under stress, which may be perpendicular or in parallel to the nerve resulting in transverse or longitudinal stress. The nervous system deals with such stresses via a number of biomechanical mechanisms. Firstly, the nerve trunk takes an undulating course through its nerve bed (Millesi, 1986; Millesi et al., 1995; Sunderland, 1989a; Topp and Boyd, 2006). These undulations also occur within the epineurium and within the nerve fascicles themselves. During limb movements, the undulations straighten out, hence the nerve’s initial adaptation to movement does not involve any elongation of the nerve trunk. As further limb movements occur, the nerve will begin to elongate. Strain is the biomechanical term...
used to describe nerve lengthening and is the change in length of the nerve divided by the original length; it is usually described as a percentage (Karduna, 2012; Topp and Boyd, 2006). Nerves which run on the flexor aspect of the joint will generally have smaller changes to make during limb extension, than nerves which run on the extensor aspect of the joint, where greater ranges of flexion (compared to extension) require a greater adaptation (Sunderland and Bradley, 1949; Sunderland, 1989a). Most large peripheral nerve trunks run on the flexor aspect of limbs, but the ulnar nerve in the upper limb and sciatic nerve in the lower limb run on the extensor aspects.

Most nerve movement and nerve strain occurs around the moving joint (Dilley et al., 2003; Boyd et al., 2005; Phillips et al., 2004). It had been thought that the sciatic nerve contained a greater number of fascicles as it passed over the hip joint to protect it from the greater amounts of longitudinal stress imposed on it during hip flexion (Sunderland and Bradley, 1949; Sunderland, 1989a). An increase in fascicles results in greater connective tissue surrounding the nerve fascicles, and may result in greater cushioning effects (beneficial for sitting down on the sciatic nerve as it passes around the ischial tuberosity), but also provides greater compliance for the nerve as the hip flexes. However, Phillips et al., (2004) found a greater number of fascicles in the non-joint
region of the sciatic nerve compared to the joint region in rats. Such differences may be due to a number of factors; Phillips et al. (2004), used rats, whereas Sunderland and Bradley (1949) used human cadavers, which may give more credence to Sunderland and Bradley’s results. However, technology had advanced considerably since 1949, and Sunderland and Bradley’s method of counting numbers of fascicles by enlarging the specimens on a micro projector and drawing out the sections, was undoubtedly less accurate than Phillips et al., (2004) who used digital micrographic images, and Adobe Photoshop to ascertain numbers of fascicles.

Despite this disagreement in fascicle numbers, Phillips et al., (2004) found that the compliance of the nerve was greater around the moving joint, than in non-joint areas. Such increases in compliance in the absence of increased fascicle numbers may be explained by changes to the diameter of collagen fibrils, with thinner fibrils thought to have greater compliance than thicker fibrils (Ottani et al., 2001). Indeed Mason and Phillips (2011) found that joint regions of the median nerve had a greater proportion of smaller diameter collagen fibrils than the non-joint regions in rats. Interestingly, this was not the case for the sciatic nerve, although this study confirmed the findings of Phillips et al., (2004) that there was greater compliance at the joint region compared to the non-joint regions. Hence, it is not known what causes the greater compliance of the sciatic nerve around the hip joint at present.

One way in which nerves around the moving joint are protected is by a mechanism known as convergence. The nervous tissue distal and proximal to the moving joint is pulled towards the moving joint, resulting in less overall strain of the nerve at the moving joint (Shacklock, 2005a). The initial movement of the nerve will be around the moving joint, and then progresses to the nerve further away from the joint (Dilley et al., 2003; Wright et al., 1996). Such accommodation from convergence is dependent on the position of the other joints. For example, if the knee is extended and ankle dorsiflexed and the hip then flexed (a SLR procedure), convergence distal to the hip will be restricted, since knee extension and dorsiflexion will have resulted in a distal pull on the sciatic and tibial nerves (Boyd et al., 2013; Coppieters et al., 2006).
Once undulations have been straightened out, and further increases in tensile stress occur, the nerve will continue to lengthen in vitro until it reaches the peak of its stress strain curve and failure occurs (Millesi, 1986; Millesi et al., 1995). It has been established that nerves exhibit a non-linear stress-strain relationship in both animal and cadaveric studies (Kwan et al., 1992; Sunderland and Bradley, 1949; Sunderland and Bradley, 1961a; Zoech et al., 1991), although the specific figures vary between animal and human studies. The animal studies suggest that there is a long toe region, where strain increases rapidly without an increase in stress until about 20% strain (Kwan et al., 1992), however a study using fresh cadaveric median nerve suggested a much shorter toe region, where stress increased proportionately with strain at less than 2.5% strain (Zoech et al., 1991). These large differences in range may be explained by a number of factors. Firstly, the different methods of fixation; for example the way in which the nerve is clamped may give rise to slippage. Secondly, excision of the nerve removes a structure called the paraneurium, which is thought to add friction in vivo (Millesi et al., 1995). Finally, greater increases in strain values will be found if the nerve is allowed to contract ex-vivo, which may occur if the nerve is placed under strain at the start of the experiment. These factors and purely the fact that animals have very different functional needs than humans reflect some of the issues with utilising animal studies to extrapolate to humans. A smaller toe region would expose the nerve to greater stress during movements than a larger toe region.

The connective tissue properties of nerve means that the nerves can tolerate forces of between 7.3 to 22.3kg of force for the median nerve, 6.5 to 15.5kg for the ulnar nerve, and 20.6 to 33.6kg for the tibial nerve (Sunderland and Bradley, 1961a). This equates to strain values of 7-30% for median nerve, 9-26% for ulnar nerve and 8-32% for tibial nerve. Forces above these levels will lead to rupturing of the nerve. The perineurium is generally accepted as the strongest connective tissue (Kwan et al., 1992; Rydevik et al., 1990), although the epineurium has been found to be the last tissue to rupture in one study (Haftek, 1970). In comparison, nerve roots fail at much lower loads (Sunderland and Bradley, 1961b), anterior roots were found to fail at between 0.2 to 2.2kg and posterior roots at between 0.5 to 3.3kg. Falconer et al., (1948) found slightly higher
(4.6kg) tensile forces were required for failure of the S1 nerve root. However, Sunderland and Bradley looked at 32 cadaveric nerve roots in total, whereas Falconer et al., (1948) only investigated 3 cadavers. The structural differences and simple parallel arrangement of the nerve roots in comparison to the peripheral nerves, helps to explain such differences. In peripheral nerves, the perineurium is considered to be the strongest structure, and as such will give the nerve greater tensile strength. In addition the funicular plexus arrangement of the nerve fibres gives the nerve both tensile strength and protection from compressive forces. However, in vivo it is unlikely that such levels would ensue unless a sudden stretch occurred where normal protective mechanisms such as muscle contraction of the antagonist muscle were overcome. However even slow, controlled stretch well below levels thought to rupture the nerve may be detrimental to nerve function (Driscoll et al., 2002; Jou et al., 2000; Kwan et al., 1992; Lundborg and Rydevik, 1973; Wall et al., 1992).

Deterioration in circulation has been found at around 8% strain (Driscoll et al., 2002; Jou et al., 2000; Kwan et al., 1992). Deterioration in nerve conduction has been found in rabbits at 6% strain held for longer than 20 minutes, or 12% held for 10 minutes or longer (Kwan et al., 1992; Wall et al., 1992). How these figures relate to humans during normal movements is difficult to gauge. In addition two other characteristics of nervous tissue is the presence of stress relaxation and creep (Millesi et al., 1995, Wall et al., 1991) both resulting in a reduction in stress at sustained loads, hence prolonged postures which cause altered strain on the nerves may have less of a detrimental effect on the tissue (Topp and Boyd, 2006).

A number of studies have looked at amounts of nerve strain that occur during normal movements (Fleming et al., 2003; Wright et al., 1996; Wright et al., 2001; Zoeph et al., 1991) and during neurodynamic tests (Boyd et al., 2013; Byl et al., 2002; Coppieters et al., 2006; Gilbert et al., 2007 a and b; Goddard and Reid, 1965; Smith et al., 1993). However, the levels found vary considerably (from <1% Gilbert et al., 2007b to 26% Fleming et al., 2003) depending on the nerve examined, methods used to assess strain, the exact location of the area of nerve studied, the exact combination of joint movement
and the order in which they were performed. The findings most pertinent to the overall focus of this thesis (Chapter 1, pg7) are those for excursion and strain during the slump and SLR.

### 3.2.1 Biomechanics of Slump and SLR Tests

A number of studies have assessed the biomechanics of a number of neural structures during movements which make up components of the slump test (O’Connell 1946; Smith 1956; Reid 1960; Breig 1960) and SLR (Boyd et al., 2013; Breig and Marions, 1963; Breig and Troup, 1979; Coppieters et al., 2006; Fleming et al., 2003; Gilbert et al., 2007a; Gilbert et al., 2007b; Goddard and Reid, 1965; O’Connell, 1946; Smith et al., 1993).

The slump test consists of cervical and trunk flexion, hip flexion, knee extension and then ankle dorsiflexion or plantar flexion with inversion to stress tibial or common peroneal nerves respectively (Butler, 2000; Shacklock, 2005a). Studies that have examined changes to spinal cord and meninges support the use of the cervical and trunk flexion components of the slump test as they show marked nervous system excursion and strain (Breig, 1960; O’Connell, 1946; Reid, 1960; Smith, 1956). From a position of spinal and cervical extension to spinal and cervical flexion, the spinal canal has to lengthen by 50-90 mms (Breig, 1960; Louis, 1981), and the spinal cord has to accommodate for such changes. Generally during trunk or cervical flexion, the spinal cord accommodates first by uncoiling and then elongation (Breig, 1960; Breig and Marions, 1963; Breig, 1978). However, when the trunk extends, the diameter of the spinal cord increases through wrinkling or bunching of the nerves (Breig 1960; Breig and Marions, 1963; Breig, 1978).

Comparisons between studies need to be considered in terms of the exact location of where the nerves were examined, and the sequence of movements that ensued (details of studies can be found in appendix 11). The overall amounts of excursion vary due to the marked differences in methods in measuring the excursion. Some consistent findings however are as follows. Firstly, the direction of movement of the nerves that lie on the
lengthening side of the region is towards the moving joint. When the cervical spine is flexed, nervous tissue below the head moves in a cephalad direction (Breig and Marions, 1963; O’Connell, 1946). An exception to this was a study by Smith (1956) who found that the spinal cord above C4 moved in a caudad direction, but below this level the cord moved cephalad. This was further supported in a much later study using MRI scanning (Yuan et al., 1998). This may be due to the presence of tension points where the nerves in this region have limited movement compared to local tissues, and hence the cord above is relatively pulled towards this point during cervical flexion (Butler, 1991).

Indeed Yuan et al., (1998) found that the mid-cervical region had minimal displacement during cervical flexion.

Another consistent finding is that larger amounts of excursion occur closest to the moving region (Breig and Marions, 1963; O’Connell, 1946; Reid, 1960), hence with head and neck flexion greater excursion has been found at T1 (6.8 mm, Reid, 1960) compared to the cauda equina (1-2mm, Breig and Marions, 1963). When the head and trunk are flexed together, some studies have demonstrated less excursion in different parts of the neuraxis compared to cervical flexion alone (Reid, 1960) whilst others have found greater excursion (Breig, 1960). This may be because Breig (1960) measured nerve excursion in overall sections (cervical, thoracic and lumbar) whereas Reid (1960) looked at nerve excursion between vertebral segments. Only one study attempted to assess strain during trunk movements. Smith (1956) found up to 24% strain at the level of C6 during trunk and cervical flexion in 4 monkeys. However, although monkeys share certain characteristics with humans, their gait varies between biped and quadruped, and their functional activities vary significantly from humans. Another limitation of both the animal and cadaveric studies is that both excursion and strain are likely to be more when surrounding bone and connective tissue are dissected out (Gilbert et al., 2007a), and when protective muscle contraction mechanisms are not at work (Hall et al., 1998; van der Heide et al., 2001) as they should be in vivo.

The results of the studies at this point are summarised for clarity and to link this with the purpose of this section, which is to evaluate the evidence in support of the use of
neurodynamic tests. The critical aspect of neurodynamic testing is that the movements of the trunk and limbs must lengthen the nerve bed of the nerve being examined, so that the nerve undergoes a change in its resting position, this may consist of sliding through the tissues, elongation (and therefore increase in tension), and possible compression as it passes through surrounding interfaces (Butler, 1991; Butler, 2000; Shacklock, 2005a). The studies that have been discussed indicate that both excursion and strain occur when individuals are placed in trunk and cervical flexion. The strain values which have been described are of importance as it has been shown that lengthening nerve tissue beyond 8% may have detrimental effects on function (Driscoll et al., 2002; Jou et al., 2000; Lundborg and Rydevik, 1973). The high levels of strain of up to 26% shown by Smith (1956) during cervical and trunk flexion may indicate that prolonged or repeated cervical and trunk flexion could predispose the cervical cord to pathology. When considering the static postures that humans tend to hold themselves in however, without neuropathic signs and symptoms, some degree of adaptation must occur which protects the nervous system from such pathology. In vivo, human nervous tissue has enormous potential to adapt, and this is seen commonly in conditions such as slow growing intrathecal spinal tumours, where symptoms do not develop until the tumour has grown dramatically in size (Mercer, 2010). However, with respect to the slump test, increasing strain on tissue which is already mechanosensitive is most likely to reproduce symptoms, and as such the use of these movements during the slump test give these tests face validity.

Whilst the studies above have considered movements of the spinal cord, many individuals seen in out-patient physiotherapy departments present with disorders of the nerve root. As described in chapter 2, nerve root disorders may be classified as radiculopathy (or nerve root compression) and radicular pain (nerve root irritation). Slump and SLR tests are purported to affect the nerve root as well as the spinal cord, and the studies presented below demonstrate this to be the case.

Studies looking at the effects of trunk movements on the nerve root suggest that there is increased tension placed upon them during flexion (Breig, 1960; Breig and Marions,
1963), and small amounts of nerve root excursion. Breig and Marions (1963, page 1154) concluded that their findings “establish without doubt” that the lumbosacral nerve roots are stretched during cervical flexion. However the method of assessing tension was to wrap a fine thread around the nerve root attached to a spring balance with 20g of force applied. With this weight it was possible to lift the nerve root away from the lumbar canal. With cervical flexion it became more difficult to lift the nerve root from the lumbar canal, indicating increased tension. One to 2 mm of cephalad movement of the nerve roots in the cauda equina were found using observational methods. However, because of a lack of robust methodology, these studies provide only an indication of what might be occurring.

Movements of the nerve roots during SLR have received more attention probably as this test, sometimes known as Lasègue’s test, was originally devised to diagnose lumbar radiculopathy (Deville et al., 2000; Goddard and Reid, 1965; Smith et al., 1993). Studies have demonstrated that excursion and strain occurs from L4 and below, and that excursion is in a caudal direction during SLR (Gilbert et al., 2007 a; Gilbert et al., 2007 b; Goddard and Reid, 1965; Smith et al., 1993). However, ranges of nerve root excursion varied from as much as 5mm at S1 in cadavers from younger age groups (Goddard and Reid, 1965) to as little as 0.48mm at L5 in more aged cadavers (Gilbert et al., 2007a). Such wide variations in ranges of nerve root excursion may be explained in part by the marked differences in methodology. For example many of the cadavers in Goddard and Reid’s (1965) study were in rigor mortis and forcible breaking of the rigor was required in order to move the leg. It is possible that such strong forces could have had an impact on the normal mechanics of the nerve roots. In addition an anterior dissection method was used by Goddard and Reid (1965) which may have disrupted the perineal connective tissues (Peretti et al., 1989; Spencer and Dalton, 1995).

Gilbert et al., (2007a) used a novel fluoroscope method of assessing nerve root excursion, and the data was analysed using Matlab which gave a 3d co-ordinate system referenced to a screw implanted into the sacral base. The anterior dissection method criticised above in Goddard and Reid’s (1965) study was also used, but attention was
given to avoiding transection of the foraminal ligaments. Such transection may increase the amount of caudal movement of the nerve roots during SLR since these ligaments connect the nerve root sleeves to the foramen. In Smith et al.’s (1993) study a posterior approach was taken, which would have resulted in transection of such ligaments and may have resulted in artificially larger excursion values (1.4 mm, 2.1 mm and 2.5 mm for L4, 5 and S1 respectively; see appendix 11 for details). Whilst Gilbert et al., (2007a) argue that their smaller values (0.53, 0.48 and 0.51 mm for L4, 5 and S1) are related to both the robust measuring methods and careful dissection, the age of the cadavers pre-mortem may also explain these smaller excursion values (aged between 72-88). Both Smith et al., (1993) and Goddard and Reid (1965) had younger aged cadavers; Smith et al., (1993) aged from 55-77, and Goddard and Reid from less than 35- over 75 years. Indeed Goddard and Reid (1965) found 0 mm of movement at L4, 0-1.5 mm at L5 (greatest in the intervertebral foramen), and between 0 and 2 mm at S1 in cadavers over 75 years.

One final explanation for the large differences found by Gilbert et al., (2007a) was that the pelvis was fixated in order to have a stable base for the fluoroscopy marker. During SLR a degree of pelvic tilting is likely to occur, and such control of the pelvis may have produced less nerve excursion because the trunk was not allowed to reverse its lordosis and flex. Hence it appears that whilst some of the limitations of the Smith et al., (1993) and Goddard and Reid (1965) studies may have caused inflation in excursion values, the results of Gilbert et al., (2007a) are limited as a result of the advanced age of the cadavers at death, and the restriction of the movement of the pelvis.

With regards to strain values, Smith et al., (1993) found that strain was exerted on the nerve roots during SLR in the region of 3.2, 2.7 and 3.4% for L4, 5 and S1 respectively, whereas Gilbert et al., (2007a) found negligible strain in the nerve roots.

During SLR, it has been proposed that additional movements can be added to further stress the nerve roots (Butler, 1991; 2000; Shacklock, 2005a). Ankle dorsiflexion, hip medial rotation and hip adduction are frequently used as further components of the SLR
when symptoms are not reproduced from a straightforward SLR. Gilbert et al., (2007b) found that the addition of the dorsiflexion significantly reduced the amount of caudal excursion of the nerve roots and increased the strain up to 1.89% at S1. Whilst the increase in strain was not statistically significant compared to no dorsiflexion, the effect size was moderate to large with dorsiflexion, indicating a tendency to greater strain in this group. Hip medial rotation was found to cause between 2-10mm of excursion towards the greater sciatic foramen of the S2 and S3 nerve roots in 4 cadavers (Breig and Troup, 1979), whilst hip adduction resulted in a 3mm excursion in 1 cadaver. The gross methods of assessment and limited number of cadavers does restrict the extrapolation of this study, however it does demonstrate that such movements can cause changes to the nerve root, which may explain any changes to patient’s symptoms with these manoeuvres. A further study (Sugiura et al., 1979) found an increase in pressure around the nerve root with the addition of adduction to a SLR in 5 fresh cadavers (measured by the insertion of a water filled rubber tube inserted between the nerve root and disc).

To summarise, the studies (Goddard and Reid, 1965; Smith et al., 1993; Gilbert et al., 2007a;b) exploring nerve root excursion and strain during SLR indicate a small to moderate caudad movement of the nerve roots from L4 to S1, and that low levels of strain occur with increased hip flexion. In addition there is limited work which also supports the use of further manoeuvres such as dorsiflexion and medial rotation and adduction to add further proximal load to the nerve roots. These studies support the use of SLR to mechanically load the lower lumbar nerve roots, but SLR is also used to load the nervous tissue as it continues into the sciatic nerve (Boyd et al., 2013; Coppieters et al., 2006; Fleming et al., 2003; Gilbert et al., 2007 a; b; Goddard and Reid, 1965).

Ranges of sciatic nerve excursion during SLR vary from 28mm (Coppieters et al., 2006) to around 4mm (Goddard and Reid, 1965), but because of the differences in location of the nerve studied, combinations of movements and methods of assessment, these values cannot easily or sensibly be compared. It is most pertinent to consider trends and the first of these is that regardless of differences in methods, the direction of excursion of
the nerve (on the lengthening aspect of the joint) towards the moving joint was consistent in all excursion studies (Boyd et al., 2013; Coppieters et al., 2006; Goddard and Reid, 1965). Most nerve excursion occurs closest to the moving joint (Boyd et al., 2013; Coppieters et al., 2006; Goddard and Reid, 1965). In Coppieters et al., (2006) 9.5mm of distal tibial nerve excursion was found around the ankle during dorsiflexion, compared to 3.1mm at the knee and 0mm of sciatic nerve just distal to greater trochanter. The reverse was seen when hip flexion was added first; 28 mm sciatic nerve, 12.2mm tibial nerve knee, 6.4mm tibial nerve ankle. Details of the other studies can be found in appendix 11, but the above trends remain the same regardless of study.

An important aspect of some of these studies is the fact that some used embalmed cadavers (Boyd et al., 2013, Coppieters et al., 2006), whereas Goddard and Reid (1965) used fresh cadavers. Kleinrensink et al., (1995b) found a close relationship in tensile force data between embalmed and unembalmed cadavers during various components of the upper limb tension tests. However, there were marked differences in magnitude of tensile force during the tests. For example during the upper limb neurodynamic tests for the median nerve, tensile forces measured at the median nerve in the axilla were 32.44 N in embalmed cadavers and 19.99N in unembalmed cadavers. Such marked differences in magnitude suggest that the mechanical properties of the tissues have been significantly altered by the embalming process, although the positive correlation between the 2 types of cadavers suggests that the behaviour towards applied stress shows similarities. What is clear is that the absolute values found in biomechanical studies using embalmed cadavers should not be extrapolated directly to in vivo situations, but general trends such as increases or decreases in excursion may be relevant.

In addition to nerve excursion, some studies have also investigated nerve strain during the SLR. Fleming et al., (2003) found that the sciatic nerve posterior to the hip joint underwent elongation of 26% when the hip was flexed to 45° and the knee extended. These values (Fleming et al., 2003) are substantially higher than those found by Coppieters et al. (2006) and Boyd et al., (2013). During hip flexion with the ankle dorsiflexed, strain measured by 2 linear displacement transducers fixed into the sciatic
nerve was 6.61% (Coppieters et al., 2006). However the exact location of the
transducers was not clear, which could have implications because most excursion and
strain occur close the moving joint (Boyd et al., 2005; Phillips et al., 2004). Boyd et al.,
(2013) found a maximum of 8% increase in strain at the sciatic nerve measured 5cms
below the ischial tuberosity during SLR regardless of whether dorsiflexion was added
prior to hip flexion or subsequently. It has been suggested that the application of
different sequences of movements during neurodynamic tests, may increase the strain
within different aspects of the nerve. This study raises questions as to the relevance of
adding sequences of movements in different orders with respect to strain. Both
Coppieters et al., (2006) and Boyd et al., (2013) used embalmed cadavers and as such
the magnitude of strain may not be the same as unembalmed cadavers, or more
importantly in vivo. In addition, Fleming et al. (2003) measured closer to the moving
joint, which may partly explain the greater strain found compared to Coppieters et al
(2006) and Boyd et al. (2013).

These studies suggest that SLR produces both sciatic nerve excursion and strain, but the
levels that occur vary between studies due to differing methodologies. More studies are
required to establish the actual amounts of movement during SLR, and importantly these
are required in vivo on human participants where possible.

To summarise, nerve excursion and strain occur during flexion of the cervical spine and
trunk and during SLR. The amounts of these vary depending on the methods used, but
tend to show that an increase occurs with increasing applications of movements which
lengthen the nerve bed. It may be that pre-loading the nerve with movements which
lengthen the nerve bed distal and/or proximal to the site of the nerve reduce nerve
excursion, but increase strain (Gilbert et al., 2007b). The direction of nerve movement
of nerves on the elongation side of the moving joint is always towards the moving joint,
except in circumstances where tension points within the spine exist. Such results
indicate that the slump and SLR tests substantially influence the nervous system which
supports their use in clinical practice.
3.2.2 Other biomechanical considerations with neurodynamic tests: concept of sliders and tensioners

One aspect of neurodynamic assessment and treatment is to consider the effect of excursion and strain depending on the combination of movements that are applied. Some authors have specifically named these techniques sliders and tensioners due to the application of components of limb movement which will predominantly tension or slide the nerve within the nerve bed (Coppieters and Butler, 2008; Coppieters et al., 2009; Shacklock, 2005a). With regards to tensioners, a series of movements of the joints are applied which all aim to lengthen the nerve bed (Shacklock, 2005a). For example for SLR, the foot is dorsiflexed, knee extended and hip flexed to exert most tension on the sciatic nerve and it’s tibial nerve component (Boyd et al., 2009). With slider techniques joints at one end of the limb are positioned so that lengthening of the nerve bed occurs, whilst the joints at the other end are positioned so that the nerve bed is shortened (e.g. for SLR with tibial nerve bias, the hip could be flexed, and knee extended whilst the ankle is plantar flexed). Slider techniques are considered to be less provocative as they are thought to generate less tension and induce most movement (Shacklock, 2005a). Recent studies have verified this theory in the upper limb using cadavers (Coppieters and Alshami, 2007; Coppieters and Butler, 2008) and in vivo using diagnostic B mode ultrasound in both upper and lower limbs (Coppieters et al., 2009; Ellis et al., 2012 ). Appendix 12 gives the detail of each study.

Coppieters and Alshami (2007) and Coppieters and Butler (2008) showed similar findings for median nerve excursion and strain during upper limb neurodynamic test with a median nerve bias (ULNT1). Fig 3.2 shows the 6 sequences chosen in these two studies for median nerve.
Fig 3.2 Sequence of movements in Coppieters and Alshami, (2007) and Coppieters and Butler, (2008) (From Coppieters and Butler, 2008 Manual Therapy 13:213-221 with permission from Elsevier limited)

The sliding technique (b) produced greater amounts of excursion of the median nerve measured proximal to the wrist by the use of a vernier caliper, than all other positions (12.4 mm) (p=0.0002, Coppieters and Alshami, 2007). No statistical testing was performed by Coppieters and Butler (2008) possibly due to the use of only 2 cadavers. Strain was greatest in the tensioner position (4% Coppieters and Alshami, 2007, 6.4% Coppieters and Butler, 2008). Of interest, excursion of the median nerve measured proximal to the elbow was greatest during the tensioner movement (a) (13.7mm Coppieters and Alshami, 2007, 16.5mm Coppieters and Butler, 2008), than the slider or other joint positions. This seemingly paradoxical finding is explained by the mechanical events that occur during these movements. The measurement was proximal to the elbow, and during elbow extension the nerve would move distally (Coppieters et al., 2009). The addition of wrist extension would result in a further distal movement at the proximal
elbow, therefore resulting in greater, not less excursion in this location. Proximal to the wrist however, elbow extension would result in a proximal movement, but wrist extension would result in a distal movement; the cumulative effect resulting in an overall reduction in nerve excursion. Hence, the effect with regards to nerve excursion during a tensioner manoeuvre, is very much dependent on the exact location of measurement in relation to joint movements. Importantly, proximal to the elbow an increase in peak strain was still found during the tensioner manoeuvre compared to the slider. Even at the highest peak strain (6.8%), this was below the levels that most animal studies have found to be harmful in terms of circulation, nerve conduction or structural changes (Driscoll et al. 2002; Jou et al., 2000; Kwan et al., 1992; Lundborg and Rydevik, 1973). However, since participants were cadavers, these values may not accurately portray figures found in vivo, although Boyd et al. (2005) found no significant differences in either strain or nerve excursion between live and fresh euthanized rats during the SLR test. If this similarity between fresh cadavers and living tissue exists in humans, a more important consideration may be the use of embalmed cadavers used in the aforementioned studies.

As mentioned in section 3.2.1, although a close relationship between the biomechanical behaviours of median nerves in unembalmed and embalmed cadavers has been found (Kleinrensink et al., 1995b), actual figures for tensile forces were markedly different, with considerably greater tensile forces in embalmed compared to fresh cadavers. This may suggest that embalmed tissue is stiffer, which may result in less overall nerve strain. This may mean that strain values measured in embalmed tissue is less than in unembalmed tissue.

In support of Coppieters and Alshami (2007) and Coppieters and Butler (2008), Coppieters et al. (2009) found a decrease in median nerve excursion during a tensioner technique compared to a slider technique in vivo utilising ultrasound imaging in 15 asymptomatic participants. The sequence of movements of ULNT1 were similar but incorporated cervical contralateral and ipsilateral lateral flexion (CLLF/ ILLF) of the cervical spine, with a neutral wrist position. A mean of 10.2 mm of nerve excursion was
found at the proximal elbow during the slider compared to 3.3 mm of excursion during CLLF with the elbow extended. Whilst this may seem to contradict Coppieters et al.”s earlier studies since greater excursion was found at the proximal elbow during the slider technique, this is explained by the same biomechanical principles as for the other studies. CLLF moved the median nerve proximally and elbow extension moved the nerve distally in all participants (Coppieters et al., 2009), hence the 2 movements together resulted in a cumulative effect of an overall reduction in nerve excursion. Interestingly, the combined effect of both CLLF and elbow extension resulted in a difference in participants in overall direction of movement. The nerve moved distally in 10, and proximally in 5 participants, demonstrating the difference in compliance in different areas of the nerve between individuals.

The only study to date which has demonstrated this effect in vivo for the lower limb is by Ellis et al., (2012). Utilising ultrasound to provide images of the sciatic nerve in the posterior thigh during slump test, greater nerve excursion was found during the slider manoeuvre (slump test, with knee extension and cervical extension) than the tensioner position (slump test with knee extension and cervical flexion). However, the difference in excursion between the 2 positions, although reaching statistical significance was around 0.6mm only just above the smallest detectable difference of the technique (0.55mm, calculated from standard error of measurement (SEM) 0.2mm in Ellis et al., 2012), indicating that some of the change could be attributed to measurement error of the technique. Such small differences in values between participants can be explained by the control of knee extension to only minus 20°, in full slump position, hence small mean excursion values (mean 3.2mm for slider movement) were found at the sciatic nerve. Such small amounts of excursion make it difficult to demonstrate sufficient changes between movements, whereas in the Coppieters et al., studies above, the mean excursion value for the slider techniques were all over 10mm.

These studies together demonstrate the effect of a combination of joint manoeuvres on strain and excursion of the nervous system during these neurodynamic tests. The
considerations of producing more or less excursion and greater or lesser strain during these tests will be discussed in the next chapter with regards to neurodynamic treatment.

Showing biomechanical changes of the nerve with the application of joint movements is only part of the picture, because other tissues also move in response to such manoeuvres. It is therefore essential that the test can discriminate between neural and non-neural structures, and this next section provides evidence that done correctly, these tests have such discriminative ability.

### 3.3 Structural Differentiation between neural and non-neural structures.

The crucial aspect of being able to discriminate between non-neural and neural structures during a neurodynamic test forms the basis of structural differentiation. Movements are added or taken away at a joint most distant to the site of symptoms. A change in symptoms implies neural structures are the source of symptoms, since local structures around the area of symptoms have not been influenced (Boyd et al., 2009; Butler, 1991; 2000; Coppieters et al., 2006; Shacklock, 2005a). However, it has been suggested that due to the continuation of the body’s fascial systems (Barker and Briggs, 1999; Gajdosik et al., 1985), movements of joints distant from the site of injury could increase symptoms in the presence of a myofascial injury. This would result in a falsely positive neurodynamic test. However, there is a small but growing body of evidence that suggests the influence of these fascial systems do not invalidate these neurodynamic tests (Coppieters et al., 2005; 2006).

One way of ascertaining if fascial systems are influenced by neurodynamic tests is to assess the effects of structural differentiation manoeuvres during a neurodynamic test on relevant fascial tissue. Coppieters et al., (2006) found that the addition of hip flexion significantly increased the strain in the tibial, medial and lateral plantar nerves, but not the plantar fascia in cadavers. These results suggested that local soft tissue was not influenced by more proximal movements during SLR. In support of these findings,
Coppieters et al., (2005) found that a localised muscle pain was not influenced by the addition of structural differentiation in 25 asymptomatic participants. Muscle pain was induced by injecting hypertonic saline into either tibialis anterior or soleus muscles. SLR or slump tests were performed with the ankle maintained in a plantar grade position with the use of an ankle foot orthosis. Symptoms either remained the same, or reduced during the two tests. These results suggest that myofascial structures which have theorised connections to both soleus and gastrocnemius did not induce an increase in tension sufficient to change symptoms. It must be noted however that injection of saline into the muscle, whilst producing local pain, does not reflect the changes to muscle that occur during trauma. It may be that in such cases where there is inflammation or fibrosis, movement of fascial structures may influence the muscle tissue to a greater level.

Further investigation into the effects of structural differentiation during SLR or slump tests have shown changes to both final range of motion of the test (Boland and Adams, 2000; Boyd et al., 2009; 2012; Fidel et al., 1996), activation of muscles which are positioned to counter the movement (e.g. hamstrings muscle during SLR) (Boyd et al., 2009; Hall et al., 1998), and changes to symptoms (Boyd et al., 2012). Restriction in range of hip motion during SLR was found with the addition of dorsiflexion compared to a 30 degree plantar flexed foot position, with a greater restriction if SLR was taken to maximally tolerated symptoms (P2) compared to first onset of symptoms (P1), (5.5° P1, 10.1° P2) (Boyd et al., 2009).

A slightly greater restriction in range between the 2 foot positions (around 7.8°; mean of left and right legs) was found in a later study at P1 (Boyd et al., 2012). Slightly higher differences still were found by Boland and Adams (2000). A mean difference between SLR with and without dorsiflexion of 9° was found when tested to P1. Male asymptomatic participants were found to have a similar mean difference between SLR with and without dorsiflexion (9.5°) to Boland and Adams (2000), but a much larger mean difference in females (15.2°) (Herrington et al., 2008). Boyd et al., (2012) found a moderate significant correlation between gender and overall range of motion of SLR.
The larger differences found by Herrington et al., (2008) compared to the other studies described could be attributed to the lack of standardisation of the ankle range of motion since a neutral starting position was estimated to be around 10° plantar flexion, but this was held by the Physiotherapist, and not maintained by the use of a splint. Despite this, intra rater reliability was excellent (ICC =0.93) with a standard error of measurement of 2.8°, although it was not clear if this was for both ankle positions or just one of them. Regardless of the actual figures, a trend can be seen demonstrating a reduction in range of motion with the addition of dorsiflexion.

Similar trends in reductions in final range of movement have been found during the slump test (Fidel et al., 1996; Herrington et al., 2008). Herrington et al., (2008) found a slightly smaller mean difference in end range knee extension between cervical extension and flexion (6.6°, 5.4° for males and females respectively) compared to Fidel et al., (1996) (P1 8.1°, P2 7.3°). The differences may be explained because Fidel et al., (1996) used an AFO to stabilise the ankle.

Overall, such findings suggest that as the nerve bed becomes further lengthened by the addition of the structural differentiation manoeuvres, symptoms increase earlier in range limiting range of motion. However, in addition to joint movement decreases, another restriction to final range of motion may be due to an increase in activation of the local muscles, theorised to become activated in order to limit further ranges of motion, and protect the neural structures (Hall et al., 1998; Boyd et al., 2009).

Abnormal muscle activity during SLR has been found in the posterior thigh muscles and erector spinae in some individuals with restrictions in forwards bending and contralateral SLR (Goeken et al., 1994). Goeken et al., (1994) found that earlier and greater activation was seen particularly in semimembranosis during SLR in individuals with “abnormal defence reactions”. Such individuals tended to have reduced ipsilateral SLR compared to those with normal defence reactions (median of 38°, compared to 68°). Such defence reactions have been considered an important clinical aspect of
physiological responses during neurodynamic testing, however it is not clear if this protective response is related to protection of nervous tissue or other soft tissues.

With respect to structural differentiation, Hall et al., (1998) found that increase in muscle activity in hamstrings occurred earlier during SLR with the addition of dorsiflexion in both asymptomatic participants and those with radiculopathy. Results regarding muscle activation were less clear by Boyd et al., (2009). There was a wide variability in EMG activity during SLR, but noticeably significantly higher levels in soleus and tibialis anterior at P1 between dorsiflexion and 30° plantar flexion. The authors suggested this was due to a protective response in the distal muscles to prevent further nerve lengthening from the far ends of the nerve bed, but if this theory is correct, it would be more logical for the hip extensors to have increased their activation between conditions in order to limit hip flexion. As there was no significant difference between conditions for the hip extensors, the effect of structural differentiation on protective muscle activity during SLR is not well supported from this study, however participants were asymptomatic; it is possible that symptomatic individuals may demonstrate more abnormal muscle activation patterns as found by Goeken et al., (1994).

With regards to the slump test, Lew and Briggs (1997) found no change in the EMG activity of hamstrings in slump test between cervical flexion and extension; but a marked difference in pain response between the 2 positions (much greater in cervical flexion). The conclusion from the study was that this supported the use of neurodynamics, since an increase in activity would have been suggestive of a change to the myofascial structures. Since there was no increase in activity, this suggested that the change in pain response was a result of the neural tissues. This conclusion seems at odds with the theory about protective muscle activation during neurodynamic tests. The hip and knee were maintained in the full test position and then cervical flexion and extension were added; it may be that any protective activity would be more likely to be from the trunk muscles in an attempt to limit the cervical flexion.
Overall, structural differentiation appears to be an important aspect of neurodynamic testing. It increases strain in the neural tissues whilst not producing strain in the local soft tissues, it does not appear to increase pain from a local soft tissue source, and it restricts final ROM during neurodynamic tests. However, it is not clear what role muscle activation has in terms of protection of the neural tissues, and at this stage does not help to support the use of structural differentiation. The limitation of most of the studies discussed above is that participants have been asymptomatic. Indeed, it has been found that in individuals with severe polyneuropathy due to type II diabetes, mechanosensitivity during SLR is diminished, and the effect of structural differentiation limited (Boyd et al., 2010). This highlights the need for appropriate exclusion criteria in studies assessing the effects of SLR, and in sub-grouping individuals using SLR as one of the criteria.

3.4 Repeatability of neurodynamic tests

Good to excellent repeatability of SLR has been found in both symptomatic (Boland and Adams, 2000; Strender et al., 1997) and asymptomatic populations (Boland and Adams, 2000; Chow et al. 1994; Herrington et al. 2008). Boland et al., (2000) found intraclass coefficients (ICC) of 0.89 and 0.86 for SLR with and without dorsiflexion respectively for inter therapist reliability. However, standard error of measurements (SEM) were relatively high, (5.62° and 6.81° with and without dorsiflexion respectively), indicating that measures greater than this would be required to be convinced of change attributed to the technique. As mentioned previously, Herrington et al., (2008) found intra therapist reliability to have an ICC of 0.93 and SEM of 2.5°, but it is expected that intra therapist reliability is superior to inter therapist and Boland and Adams’ (2000) participants were both asymptomatic and symptomatic.

Overall these studies suggest that there is good to excellent reliability when using SLR.
3.5 Conclusion

This section has presented supportive evidence for the use of SLR and slump tests in clinical practice and for research purposes. Both tests have been demonstrated to induce nerve excursion and strain. In addition the use of structural differentiation seems to be able to discriminate between neural and non-neural structures. Together these studies provide justification that the SLR and slump tests have appropriate validity. The repeatability of the tests has been demonstrated to be high. However, whilst the evidence to date supports the use of these neurodynamic tests, more research is needed in vivo and in symptomatic groups.
Chapter 4 Neurodynamic treatment

The principles behind neurodynamic assessment have been discussed in chapter 3, and the treatment of such conditions must be chosen appropriately. The focus of this thesis was to analyse the effects of a 3 x 1 minute SLR treatment in individuals with different causes of referred leg pain and therefore this chapter is pivotal to the rationale for the thesis. Neurodynamic treatment as described by Shacklock (2005a), can be classified into two basic forms; movements of the limb plus or minus the trunk resulting in an overall longitudinal movement of the nerve within its nerve bed, and an indirect form of treatment often called an interface technique where tissues around the nerve are mobilised (Shacklock, 2005a).

Whilst this thesis specifically relates to the effects of a SLR treatment, there is limited literature which has analysed the effects of SLR treatment, therefore in this chapter, other neurodynamic treatment literature is presented. In this chapter the rationale underpinning the different forms of neurodynamic treatment techniques is described, and the literature on the effects and effectiveness of these techniques is critically appraised.

4.1 Types of Neurodynamic Treatment

There are broadly two types of neurodynamic treatment; longitudinal (direct) or interface (indirect) techniques. As described in chapter 4, nerves move in response to changes in the nerve bed which in turn is influenced by joint movements. Whilst nerves moving within the nerve bed do not simply move in a longitudinal fashion (there is also movement transversely and superficially or deep (Dilley et al., 2003; Greening et al., 2001; Hough et al., 2000), this is the direction of most movement. Longitudinal neurodynamic treatments consist of applying a series of joint movements resulting in (mainly) longitudinal excursion through the nerve bed, before repeatedly moving one (or more) joints, resulting in a proximal and distal movement of the nerve (or vice versa). These series of movements may aim to produce more excursion, with minimal or no
increase in strain (a slider technique), or potentially less movement, with greater strain (a tensioner technique). The biomechanical changes that occur during these techniques have been discussed in chapter 3.

Another common form of neurodynamic treatment is interface treatment. A number of authors have advocated the use of techniques which move the structures surrounding the nerve, rather than moving the nerve itself (Butler, 2000; Nee and Butler, 2006; Shacklock, 2005a). The theoretical basis for these techniques include mobilising adhesive tissues around the nerve which may have resulted from some sort of traumatic event and may directly influence the nerve (Sunderland, 1989b), and to reduce the forces which interfacing structures may have on sensitive neural tissues (Nee and Butler, 2006). Examples of interface techniques include mobilising the fibular head to affect the peroneal nerve (Butler, 1991), mobilising the carpal bones to influence the median nerve in the carpal tunnel (Tal-Akabi and Rushton, 2000), and lateral glides to the cervical spine to influence the nerve roots within the intervertebral foramina (Hall et al., 1998; Nee et al., 2013).

An advantage of these techniques is that if the nerve is compromised by an external structure, and becomes mechanically sensitive as a consequence, then moving the surrounding tissues may reduce the compression or inflammatory effects on the nerve. However, a disadvantage is that in some conditions there may not be one specific interface that is causing the problem, and locating the problematic interface may be difficult as palpation anywhere along the length of a mechanosensitive nerve may reproduce the patient’s symptoms (Schäfer et al., 2009; Walsh and Hall, 2009c). In addition, it may not be possible to analyse whether the improvement in any symptoms is due to the underlying change to the nerve, or the effect of mobilising the structure itself.

4.2 Longitudinal movement (direct) treatment

As discussed in chapter 3, movements of the joints can be applied to produce excursion with little or no increase in strain (sliders) or to produce increases in strain (tensioners)
The rationale for the choice of each is not clear, but more recently it has been suggested that sliders may be more appropriate for most neuropathic pain conditions as a larger excursion, with minimal strain may aid resolution of oedema (Schmid et al., 2012), improve blood and axoplasmic flow and settle down the inflammatory environment of the nerve (Coppieters and Butler, 2008; Nee and Butler, 2006). In addition, it has been suggested that tensioner techniques may be detrimental to the nerve because of the larger increases in strain (compared to sliders), and that stretching nerve fibres may cause an increase in ectopic discharge of inflamed nerves (Dilley et al., 2005). However, more recent studies have demonstrated beneficial effects of tensioner techniques in both animal (Bertolini et al., 2009; Santos et al., 2012) and in vivo studies (Adel et al., 2011; Bialosky et al., 2009; Cleland et al., 2006; Kavlak et al., 2011; Nagrale et al., 2012). The supportive and negative evidence for the use of longitudinal treatments is presented in the next section.

4.2.1 Proposed mechanism of effects of longitudinal treatments

Regardless of the pathophysiology of the underlying nerve dysfunction, the main aims of treatment are to restore normal nerve gliding and neurophysiology to the nerve and surrounding tissues, with the result of decreasing pain and increasing function. A number of neurodynamic treatment effects have been proposed, but most are theoretical and are yet to be proven (Nee and Butler, 2006).

*Axoplasmic flow, intraneural circulation and decreased inflammatory responses*

Postulated longitudinal treatment effects include improving axoplasmic flow and intraneural circulation. Both of these effects are thought to occur due to the build-up and release of intraneural pressure that occur during an oscillatory longitudinal neurodynamic treatment technique (Coppieters and Butler, 2008; Nee and Butler, 2006); the so called milking effect. In addition, such alterations in pressures may lead to dispersal of intraneural oedema, which may be particularly beneficial since inflammatory exudate is acidic, and may enhance peripheral nerve sensitivity (Steen et
The presence of oedema within the endoneurium is particularly detrimental since the perineurial barrier prevents the leakage of fluid out of endoneurium (Lundborg, 1988; Lundborg and Dahlin, 1992). The oedema can contribute to the compressive effects on the nerve fibres, resulting in greater pathology and pain (Olmarker and Rydevik, 1989; Rydevik et al., 1984). The resulting intraneural fibrosis (Sunderland 1989b) may cause changes to the normal viscoelastic elements of the nerve, with increased activation of nervi nervorum endings and greater mechanosensitivity (Bove and Light, 1997; Nee and Butler, 2006). In addition, the inflammatory soup contains many substances which enhance peripheral nerve sensitivity, such as macrophages which release cytokines and other pro-inflammatory mediators. Another proposed side effect of nerve inflammation is ectopic discharging of afferent nerves. Dispersal of these inflammatory exudates could theoretically reduce the occurrences of such discharges (Coppieters and Butler, 2008). The removal of oedema and underlying inflammatory soup may therefore be an important response to neurodynamic treatment.

There is some preliminary evidence that longitudinal nerve mobilisation techniques may be effective in reducing oedema. Brown et al., (2011) found that ankle mobilisation was effective in the dispersal of injected intraneural dye in the tibial nerve of 6 unembalmed cadavers. The increase in spread of dye was significantly greater than on the control side (p<0.02). The conclusion of the study was that that ankle mobilisation would help to disperse oedema. However, the fluid was injected just beneath the epineurium, and hence it is not known how much entered the endoneurium (where the intraneural oedema would be situated), and how fluid specifically located around the axons would disperse. Since oedema becomes more organised after a period of time (Underwood, 2009), it is unclear how this more viscous fluid would disperse. It is also unknown what alterations in fluid dispersal would occur in vivo compared to cadavers. Despite all of these factors, the study does demonstrate that movement of a peripheral joint has the ability to disperse fluid intraneurally; perhaps the added benefit of elevating the limb (as in SLR) would further enhance this effect simply by the effect of gravity.
Further support for a reduction in oedema was offered by Schmid et al., (2012), who found a reduction in the signal intensity of MRI images of the median nerve at the wrist in individuals with carpal tunnel syndrome post longitudinal nerve mobilisation. Increase in signal on MRI T2 weighted scans reflects increases in fluid content (Kleindienst et al., 1996), and hence reduction in signal represents a decrease in oedema (Cudlip et al., 2002). Nerve tendon gliding exercises, and a slider technique for the median nerve (fig 3.2) were given to 10 patients to perform 10 times per day for 1 week, and the wrist was scanned prior to and after 1 week of intervention. A comparison group (N=10) received a night splint for 1 week. Both groups showed significant differences in signal intensity of the median nerve at the radio-ulnar level, but neither group showed any changes either at the pisiform or hook of hamate level, indicating that improvements occurred more proximal to the site on injury. Increase in swelling in CTS patients proximal to the site of compression has been demonstrated previously (Nakamichi and Tachibana, 2000), and therefore significant changes here may reflect the improvement in oedema in the most affected area. Whilst both night splinting and neural mobilisations were found equally to improve oedema, the particular relevance to the present study is that previously, opponents of longitudinal mobilisations have suggested that it is detrimental in nerve compression injuries due to potentially increasing oedema or nerve sensitivity (Dilley et al., 2005). However, individuals with severe signs and symptoms of CTS were excluded from the study, and the follow up was very short (1 week), hence the longer term effects of nerve and tendon mobilisation on oedema are not currently known.

Reducing oedema may be of value in restoring normal nerve mechanosensitivity, but affecting inflammatory and immune system cells could also be important as this may demonstrate an augmentation in healing, and an improvement in resting nerve sensitivity (Martins et al., 2011; Santos, 2012). The sciatic nerve in rats were either crushed for 30 seconds (Martins et al., 2011), or were subjected to a chronic constriction injury (CCI) by the use of chromic gut suture around the nerve (Santos et al., 2012). A tensioner SLR technique with the addition of cervical flexion for the final minute of treatment (Santos et al., 2012) was applied for 10 minutes in rats with CCI and control rats. Significant
reduction in mechanical hyperalgesia (paw withdrawal) was found from the second day of treatment, compared to the rats who did not receive treatment. Thermal hyperalgesia significantly decreased from the 4th treatment. Both mechanical and thermal hyperalgesia remained constant for the duration of the study (10 sessions; 20 days).

Santos et al., (2012) also explored the effects of the SLR treatment on glial cells and nerve growth factor (NGF). Glial cells in the spinal cord, have been demonstrated to become activated after nerve injury (DeLeo and Yezierski, 2001; Garrison et al., 1991), resulting in the production and release of an array of pro inflammatory mediators such as pro-inflammatory cytokines, prostaglandins and neurotropic factors. NGF is produced by a form of glial cell called an astrocyte, and has been associated with development of hyperalgesia after sciatic nerve constriction (Herzberg et al., 1997). NGF was demonstrated to increase after CCI, but was normalised in rats after neural mobilisation in the DRG. Glial cell changes were assessed by analysing the presence of a protein called glial fibrillary acidic protein (GFAP), which demonstrated a marked increase in the CCI rats, which was normalised in the mobilisation group in both the DRG and spinal cord.

Similar findings of improvements in mechanical hyperalgesia and changes to glial cell activation were found by Martins et al., (2011) after ankle joint mobilisation in sciatic nerve crushed animals. However, improvements in cold hyperalgesia were only observed at day 3, with changes equivocal to the crushed rats without ankle mobilisation thereafter (up to 35 days). Interestingly, mechanical hyperalgesia returned to almost normal after 35 days in both crushed and crushed mobilised groups, but cold hyperalgesia continued to increase up to 35 days, suggesting a continued hypersensitivity of the small diameter afferent nerves. This was not seen in the Santos et al., (2012) paper; neither mechanical nor thermal thresholds recovered in the CCI rats without mobilisation (up to day 34 post injury), but both improved (up to 34 days) in the nerve mobilisation group. Disagreement in these thermal results could be attributed to 2 differences in methodology. Firstly the neural mobilisation in the Santos et al., (2012) study did not start until 14 days after the CCI was imposed, whereas rats in Martins et
al., (2011) began ankle mobilisations 24 hours after crush injury. This may suggest that it is beneficial not to perform mobilisation techniques on acute inflammatory conditions, which supports most recommendations for management in the inflammatory stages of healing: POLICE (protection, optimal loading, ice, compression and elevation) (Bleakley et al., 2012). Secondly, Martins et al., (2011) used an ankle joint mobilisation, which although has an effect on the sciatic nerve via its tibial nerve connections (Boyd et al., 2013; Coppieters et al., 2006), would exert less mechanical load on the nervous tissue than a tensioner mobilisation, used by Santos et al., (2012). It may be that an overloading effect, considered to be a positive influence on other soft tissues during the proliferation and regenerative stages of healing, may be beneficial. It is unknown which, if any, of these theories could explain the differences in thermal changes found between the two studies, however, in clinical practice care is taken to avoid overload during inflammatory phases, and load is applied to tissue bearing in mind the patient’s symptoms, and underlying severity and irritability (something that is not possible to take into account in either of these studies).

Overall, the results of these 2 studies (Martins et al., 2011; Santos et al., 2012) are important in the understanding of the potential effects that nerve mobilisation may have on nerve inflammation. Improvements in oedema and inflammation are potentially important effects of nerve mobilisation and another proposed effect of longitudinal oscillatory movements may be to directly mobilise intra or extra funicular fibrosis once it is formed (Hall et al., 1998). Other postulated mechanical effects include, restoring nerve and fascicular gliding (Walsh, 2005), and mobilising the viscoelastic connective tissue elements of the nerve.

**Mechanical Effects**

At present there is little supportive literature to demonstrate any changes to the length of the connective tissue of the nerve after neural mobilisation techniques. Some degree of extrapolation may be taken from literature looking at the effects of mobilisation on other soft tissue structures, since the fundamental structure of the nerve sheaths is similar to other connective tissue within the body, such as ligaments. As mentioned in chapter 4,
the nerves possess similar stress strain curves to other soft tissues due to the viscoelastic nature of the tissue, and also exhibit stress relaxation, or creep (Millesi et al., 1995; Wall et al., 1991). Lengthening of soft tissue is thought to occur due to creep and hysteresis (Lee and Evans, 1994, McGill and Brown, 1992; Threlkeld, 1992). Hysteresis is the change in length that occurs simultaneously with energy loss into the tissue due to cyclical loading (Soderberg, 1997; Flanagan, 2013). Both of these effects may enable tissue to increase in length, however this is only a temporary change (Lee and Evans, 1994; McGill and Brown, 1992; Threlkeld, 1992). It has been suggested that for permanent length changes to occur, that the tissue should be taken to the point of failure (Threlkeld, 1992), however this would not be warranted in nervous tissue due to the deleterious effects of neurogenic inflammation, potentially compounding an already inflamed nerve.

McGill and Brown (1992) demonstrated a temporary (20 minutes) increase in forward spinal flexion in asymptomatic individuals after 20 minutes of sustained forward flexion. However, neural mobilisation techniques are generally not held for periods of time. Lee and Evans (1992) found an increase in segmental posteroanterior displacement of the vertebral segments of 28 young, asymptomatic participants, after both sustained and oscillatory mobilisations. This study demonstrated a creep and hysteresis effect of spinal manual therapy. The majority of creep occurred within the first 30 seconds, although additional gains in displacement were made after this time (up to 2 minutes). Only 3 cycles of the oscillatory load were applied, with greatest effects between the first and second loads.

The studies discussed above, suggest that manual therapy techniques are capable of increasing motion around a vertebral segment, however, it is unknown if the same effects occur to nerve during neural mobilisation techniques. One way of establishing biomechanical changes to the nerve after neurodynamic treatment in vivo, is through the measurement of nerve excursion analysed from ultrasound images (Dilley et al., 2001; Ellis et al., 2012, see chapter 5). Whilst excursion is not a direct measure of elongation, it has a close relationship to it. Excursion relates to length changes in that during the
first 2 phases of the stress-strain curve, the tissue initially uncrimps, then moves (excursion) before entering the third phase where lengthening (and less excursion) of the tissue occurs (Fig 4.1). Hence changes to tissue length may first demonstrate a greater amount of excursion before lengthening begins.

**Fig 4.1 Stress Strain Curve**

*Descending Inhibitory Pathways*

Inhibition of pain utilising pain gate mechanisms or descending pain inhibitory mechanisms may also have a role in explaining the beneficial effects of neurodynamic treatments (Katavich, 1999). It appears that the descending inhibitory pain mechanism previously demonstrated in joint mobilisation studies (Sluka et al., 2006, Sluka and Wright, 2001), may also be responsible for positive outcomes of nerve mobilisation techniques (Bertolini et al., 2009; Martins et al., 2011; Santos et al., 2012). In these studies, improvements in pain were demonstrated in rats post nerve injury after nerve mobilisation techniques. Martins et al. (2011) and Santos et al. (2012) have been discussed above (page 86) in consideration of changes to glial cell activation and neurotrophic factors. Previous joint studies have suggested a predominantly supraspinal
noradrenergic or serotonergic pain relieving system post joint mobilisation (Sluka and Wright, 2001; Sluka et al., 2006; Skyba et al., 2003). Some studies suggest that short term mobilisation effects are more likely produced via the noradrenergic systems, and therefore influence more mechanical hyperalgesia (Vincenzino et al., 1996; Wright, 1995). Martins et al., (2011) found only a change to mechanical rather than thermal pain thresholds after ankle joint mobilisation, which could suggest a more noradrenergic pain relieving mechanism. Prolonged changes to both thermal and mechanical thresholds were found by Santos et al., (2012), which may suggest that a tensioner mobilisation affects both descending inhibitory systems, or it may be that the long duration of treatment (10 minutes) imposed by Santos et al., (2012), may have had an additional effect on the serotonergic systems, a proposed effect of longer duration treatments such as acupuncture (Takeshige, 1992).

Bertolini et al., (2009) only looked at changes to mechanical hyperalgesia, but found an improvement in both a sustained stretched SLR group and a tensioner SLR treatment group after CCI of the sciatic nerve in rats compared to a sham treatment group. Mechanical thresholds (paw withdrawal) significantly improved immediately and 24 hours after the fifth and final treatment (5 consecutive daily treatments, starting on day 3 post injury), compared to immediately post CCI in both stretch and tensioner groups. However, 24 hours post final treatment, the tensioner group (but not the SLR stretch group) had reduced hyperalgesia that was not significant to pre- CCI levels, indicating that levels were returning to pre-injury status. This suggests that whilst sustained stretch improves hyperalgesia, some degree of hyperalgesia remains (8 days post injury), whereas the tensioner technique normalised hyperalgesia within this time frame. However, despite results being presented which demonstrated statistical significance within groups, no results were presented for between analyses, which may suggest that no differences were found between the groups, and this may limit the conclusions drawn from the study.

Activation of the dorsal and ventral periaqueductal gray areas within the mid brain have been suggested as being responsible for non-opioid descending inhibitory events post
manual therapy (Wright, 1995). Such changes will induce a systemic pain relieving effect, rather than a localised or segmental effect which may occur with pain gate response (Schmid et al., 2008; Wright, 1995). At present however, there is insufficient evidence that the non-opioid descending inhibitory mechanism is the sole mechanism responsible for such changes (Schmid et al., 2008). Relating the hypoalgesic effects found in the studies discussed to the glial cell activation changes found by Santos et al., (2012) and Martins et al., (2011), suggests an interesting link between descending pain mechanisms and altered neuro-inflammatory mechanisms.

It has been suggested that the descending release of noradrenaline and serotonin inhibit the release of glutamate from the Aδ and C afferent nerve endings (Yoshimura and Furue, 2006). Since chronic glial cell activation has been found to result in a decrease in glutamate uptake (Milligan and Watkins, 2009), a combination of both decreased glial cell activation, and descending inhibition of release of glutamate may result in an overall decrease in glutamate in the dorsal horn, with resulting decreased excitatory synaptic transmission (Milligan and Watkins, 2009), and reduction in pain.

The literature discussed above demonstrates a positive change after longitudinal nerve treatments, however there has been some suggestion that such techniques may cause an increase in sensory nerve firing, and could increase the pain felt by individuals with neuropathic pain (Dilley et al., 2005, Jaberzadeh et al., 2005). One study which supports such assertions was done in rats whose nerves were inflamed experimentally by exposing the nerves to a substance called complete Freund's adjuvant (CFA) (Dilley et al., 2005). It was found that a small percentage of C and A fibres ectopically fired when they were stretched. The authors suggest that in situations where patients have signs of neural inflammation, lengthening the nerve bed should be avoided, as this may contribute to wind up within the central nervous system and therefore central pain. It must be noted, however that only 1.8% of C fibres and 1.3% of A fibres ectopically fired when stretched after exposure to CFA. A slightly larger proportion of rats with CFA applied directly to the axons within the perineurium (by sectioning the perineurium first), showed spontaneous firing (6.5% C and 8.8 % A fibres). Such sectioning of the
perineurium could have effects on the normal function of the nerve and so does not best represent a neuropathy in humans. In addition, the axon was directly stretched using forceps; this clearly does not reflect the situation in vivo, where the axons are protected by the connective tissue coverings. These connective tissues limit the imposed tensile forces direct to the axons during longitudinal movements of the nerve (Butler, 2000; Grewal et al., 1996).

Taken in conjunction with the animal studies discussed above (Bertolini et al., 2009, Martins et al., 2011, Santos et al., 2012), it appears that the mechanism of increased firing after stretching the axon does not occur in the same way when a compression or crush neuropathy is applied to the whole nerve structure, and a longitudinal nerve treatment applied. In addition, Bialosky et al., (2009) has demonstrated a reduction in temporal summation post neural mobilisation in individuals with carpal tunnel syndrome, suggesting a dampening down of nerve sensitivity after treatment (this study will be discussed further in the next section). The combination of clinical and animal studies overall, reflect that longitudinal nerve mobilisation in compression neuropathy and crush injury do not increase afferent firing. However, regardless of the results of these studies, individuals with neuropathic pain present in a variety of ways. In individuals with severe and irritable symptoms, tensioner techniques, or indeed any extreme movement of the affected area, could aggravate symptoms, and therefore these techniques would not be appropriate.

Whilst there is evidence that pain may be improved by nerve treatment techniques, patients with neuropathic pain commonly have sensory changes including anaesthesia of an area (Bogduk, 2009; Greening and Lynn, 1998). There has been some suggestion that longitudinal nerve treatments could diminish nerve conduction even further, if strain values reach those levels sufficient to decrease blood supply to the nerve, in an already compromised region (Boyd et al., 2005; Humphreys et al., 1998).
Nerve conduction

The suggestion that nerve conduction could be affected by nerve mobilisation could be considered to be a positive or negative aspect of neurodynamic treatment. If blood circulation improves post nerve treatment then theoretically, conduction could improve. However, since strain levels during neurodynamic positions have been found to vary between studies (1% up to 26% (Fleming et al., 2003; Gilbert et al., 2007b), and strain greater than 8% could cause changes to circulation, nerve conduction and inflammation and oedema (Driscoll et al., 2002; Kwan et al., 1992; Lundborg and Rydevik, 1973), it is difficult to predict how nerve conduction could be affected during these treatment techniques.

Humphreys et al., (1998) found that tibial nerve F wave latency\(^7\) deteriorated after SLR to 50° in 10 asymptomatic participants. A mean difference of 1ms was found before and during the SLR position, which are below levels considered to be clinically significant (2ms Humphreys et al., 1998). In addition, it has been found that normal side to side differences are around 3.5ms for tibial nerve F wave latency (Alavian-Ghavanini and Haghpanah, 2000). Since Humphreys et al., (1998) initially measured the latency in both legs, compared to a single leg such small differences are unlikely to be attributed to the SLR position itself. In contrast to this study, Ha et al., (2012) found an improvement in motor nerve conduction velocity (NCV) of the median nerve after sustaining the median nerve upper limb neurodynamic test. Results were significantly different to pre-measures and to a group who received a home regime of the same neural mobilisation exercises. However, motor NCV may not be an accurate measure of change after minor nerve dysfunction, since sensory changes may be the initial finding in minor nerve dysfunction (Greening and Lynn, 1998). In addition, mean differences were only in the region of 2m/s. It has been demonstrated that variation in motor NCV may be around 6% within subjects (Galloway et al., 2011). The mean pre-readings for the neural mobilisation groups were 58.71m/s, hence a 6% difference would be 3.5mm. This suggests that the 2mm change found by Ha et al., (2012) could be attributed to normal

\(^7\) F wave latency is a measure of motor nerve conduction; it measures the action potential of the smaller number of fibres which propagate towards the dorsal horn, causing a firing of the cells at the anterior horn and returning efferent action potential.
variation in readings, although the variation may be more relevant to individual differences in readings. Nevertheless, such small differences in motor NCV may not be relevant despite the statistical differences found.

A more sensitive method of detecting early changes in minor peripheral nerve dysfunction may be the use of vibrametry (Dellon, 1981; Greening and Lynn, 1998; Goldberg and Lindblom, 1979). No significant changes to vibration thresholds (VT) were found in a group of 30 asymptomatic individuals after a SLR tensioner treatment (Ridehalgh et al., 2005), indicating that in individuals without neuropathy there are no detrimental changes to the large diameter afferent nerves. However, in rats with nerve injury, it has been found that greater levels of strain are reached during the SLR (mean 22.6% with ankle dorsiflexion), than in uninjured animals (mean 9.7% with dorsiflexion) (Boyd et al., 2005). However, this was 7 days after the crush injury had been induced; 21 days later, there was no significant difference in strain between uninjured and injured animals during the SLR, suggesting that changes to the connective tissue behaviour was short term. Hence if a similar restoration of mechanical characteristics occurs after 3 weeks, it is possible that techniques which lengthen the nerve bed may not have deleterious effects. As with all animal nerve compression studies, rats with induced nerve crush injury, may not reflect the normal pathogenesis that occur in humans with nerve compression or irritation.

In support of longitudinal neurodynamic techniques, Kavlak et al., (2011) found an improvement in light touch and 2 point discrimination in the foot supplied by the tibial nerve in individuals with tarsal tunnel syndrome after slump tensioner treatments added to a usual practice exercise regime. However, mean or median differences were very small. Indeed, the median difference between pre and post readings of light touch, despite reaching significant difference was zero. In addition, a series of T tests or non-parametric equivalent tests were performed on the data, rather than analysis of variance or equivalent, making the statistical results less convincing. However, regardless of whether positive changes were found post mobilisation, the study demonstrated that there was no deterioration in these sensory measures. This indicates that sensory
conduction may not be detrimentally affected by these types of neural mobilisation in individuals with compression neuropathy.

4.3 Effectiveness of longitudinal neurodynamic treatment

There has been an increase in longitudinal neurodynamic treatment research over the past decade, with most showing positive responses to treatment (Adel, 2011; Beneciuk et al., 2009; Bialosky et al., 2009; Cleland et al., 2006; De-La-Llave-Rincon et al., 2012; Kavlak et al., 2011; Nagrale et al., 2012, Nee et al., 2012b; Sarkari and Multani, 2007; Schäfer et al., 2011; Schmid et al., 2012), although some have found less positive effects (Heebner and Roddey, 2008; Scrimshaw and Maher, 2001) (see appendix 13 for summary of studies). Some of the studies looking at effectiveness of longitudinal neurodynamic treatment have looked at the addition of neurodynamic treatment to standardised exercise programme (Heebner and Roddey, 2008; Scrimshaw and Maher, 2001), or combination of exercise and hands on treatment or provision of orthotics or other modalities such as ice (Adel, 2011; Cleland et al., 2006; Kavlak et al., 2011; Kornberg and Lew, 1989; Nagrale et al., 2012; Sarkari and Multani, 2007). In these studies, the comparative group were given the physiotherapy programme without the addition of the neurodynamic treatment.

Other studies have focussed on the effectiveness of the neurodynamic treatment compared to a control or sham treatment (Beneciuk et al., 2009; Bialosky et al., 2009; Nee et al., 2012b, Schmid et al., 2012; Tal Akabi and Rushton, 2000). In the former case, the usefulness of the addition of neurodynamic treatment portrays a more realistic presentation of how neurodynamic treatment is used in clinical practice, but does not give an indication of how effective the treatment is in isolation. The difficulty with this scenario is that cumulative effects of a treatment may give a false improvement in outcome measures since more treatment is being provided, and where this is applied by the Physiotherapist may create a stronger placebo effect. Conversely, results could be falsely worsened because of the additional treatment on top of an often overloaded programme. Results from these studies have been varied. Using a similar physiotherapy
programme in individuals with spinally referred leg pain (without signs of neurological compromise) 3 studies have found significant improvements in the neurodynamic treatment group compared to the physiotherapy programme alone on a range of outcome measures (Adel, 2011; Cleland et al., 2006; Nagrale et al., 2012). Slump tensioner (Cleland et al., 2006; Nagrale et al., 2012) and SLR (Adel, 2011) were sustained for differing periods of time. Such sustained techniques in individuals with neuropathic symptoms have been thought to be potentially detrimental (Boyd et al., 2005; Dilley et al., 2005) due to levels of strain reached, changes to intraneural circulation and potentially ectopic firing of small diameter nerves. However, these techniques in two of these studies demonstrated not only significant improvements, but changes to a number of outcome measures which were greater than the minimal clinically important difference (MCID) (Cleland et al., 2006; Nagrale et al., 2012). Unfortunately whilst Adel (2011) found significant changes in a number of outcome measures, the data provided did not permit any analysis of MCID, in addition a series of multiple T tests were performed which increases the risk of a type I error, or in other words may have meant that the null hypothesis was falsely rejected. However, even if this error did occur, individuals in both groups all had improvements in a number of relevant outcome measures, suggesting that the addition of a strong SLR tensioner did not aggravate the individuals involved in the study, which diminishes the suggestion that these techniques may be harmful.

Using physiotherapy management techniques plus neurodynamic techniques has also resulted in positive findings in other studies in individuals with spinally referred leg pain (Sarkari and Multani, 2007), hamstring strains with postulated sciatic nerve involvement (Kornberg and Lew, 1989), and tarsal tunnel syndrome (Kavlak et al., 2011). Kornberg and Lew (1989) concluded that the addition of slump stretching to standard physiotherapy care resulted in significant reduction in missed games of Australian Rules football. However, neither a standardised physiotherapy management programme, nor a standardised slump treatment prescription was utilised; physiotherapists were free to decide on the most appropriate treatment for the patients. This sort of pragmatic trial may be useful when considering that Physiotherapists should apply techniques based on
a thorough assessment of the patients, but the lack of any standardisation of treatment makes it difficult to account for improvement in the main outcome measure solely on the addition of the slump technique.

Sarkari and Multani, (2007) also had a number of limitations which made the statistically significant greater improvement in hip ROM and VAS scores after SLR treatment compared to physiotherapy management alone, less conclusive. The detail of the physiotherapy programme was scant, there was no detail of how the range of motion of the hip was measured, and no p values were presented. Likewise, whilst Kavlak et al., (2011) found improvements in an array of outcome measures in participants with tarsal tunnel syndrome after a slump tensioner, numbers of limitations made the results less convincing. Details of numbers of exercises performed, or how many times per day participants repeated them were omitted from the method. One of the outcome measures used was range of motion of the subtalar joint and this was measured with a universal goniometer. Reliability has not been found to be consistently high in patients with neurological disorders; ICC for inversion has been found to be only 0.53, whilst that for eversion was 0.65 (Elveru et al., 1988). It is unknown what the smallest detectable difference for such measurements would be, but mean differences found were around 6° in the study group, it is not possible to say whether these values could be related to error or a real difference in range of motion. Significant improvements were found in Tinel’s sign and 2 point discrimination in 2 out of 3 sites after neurodynamic treatment, but not in the usual physiotherapy management alone. However, mean differences for 2 point discrimination were small (around 0.3), unlikely to be clinically meaningful. Measuring Tinel’s sign may not be accurate as the measure could vary depending on the amount of force applied by the examiner.

Taken together the results of the latter 3 studies (Kavlak et al., 2011; Kornberg and Lew, 1989 and Sarkari and Multani, 2007), do not provide strong evidence of the effectiveness of neurodynamic treatment as part of a package of care. In addition, 2 studies have suggested that the addition of a neurodynamic treatment to a standardised
physiotherapy management programme does not improve outcome (Heebner and Roddey, 2008), and may even have a negative effect (Scrimshaw and Maher, 2001).

Participants with CTS (Heebner and Roddey, 2008) did not improve any more than the standard care alone, and the carpal tunnel specific questionnaire was marginally (0.7), but significantly better (p=0.016) in the standard care group. However, a number of limitations of the study may account for some of these findings. A total of 31 patients were lost during the course of the 6 month study, resulting in only 14 participants in the standard care group and 15 in the standard care plus neural mobilisation group, which was below the minimum required (21 in each group) from the power calculation. Compliance appeared to be worse in the neurodynamic group than the standard care alone (p=0.01), which could also, in part account for the result. One other consideration which may account for the difference in these results compared to other studies that have been discussed, is the fact that participants were instructed to do the exercises at home and were not offered any treatment by the Physiotherapist. Their technique was not reassessed even at the one month follow up and hence progression or regression of exercises at home may not have been properly carried out, and it is possible that some participants may have not been performing exercises optimally.

In agreement with Heebner and Roddey (2008), Scrimshaw and Maher (2001) found that the addition of neurodynamic exercises (SLR) to standard care post spinal surgery did not improve outcomes compared to standard care alone. Indeed in further analysis of between group differences for improvement, overall there was a slightly worse outcome than the standard care group. However, such analysis was not supported by the statistical findings and a suggestion that individuals were worse in the SLR group cannot be concluded from the results of this study. Overall the conclusion as to the effectiveness of a longitudinal neurodynamic treatment in conjunction with standard physiotherapy management is equivocal.

Stand-alone neurodynamic treatments have been applied in a number of studies (Beneciuk et al., 2009; Bialosky et al., 2009; De-La-Llave-Rincon et al., 2012; Schmid
et al., 2012; Tal Akabi and Rushton, 2000), with a predominance of positive findings. All of these studies however, have been conducted using upper limb neurodynamic test 1 (median nerve bias) as the neurodynamic treatment on asymptomatic individuals (Benecuik et al., 2009) or individuals with CTS (Bialosky et al., 2009; De-La-Llave-Rincon et al., 2012; Schmid et al., 2012; Tal Akabi and Rushton, 2000). One study assessed the effect of a slider SLR technique on different groups of individuals with spinally referred leg pain (Schäfer et al., 2011), and is discussed further below (page 102).

Benecuik et al., (2009) and Bialosky et al., (2009) demonstrated a significant improvement in temporal summation after an ULNT1 tensioner technique in asymptomatic participants and individuals with CTS respectively. Temporal summation is considered to be an important phenomenon in the contribution to central sensitisation, where tonic C fibre activity leads to wind up at the dorsal horn (Rygh et al., 2005), and has been found to increase in conditions where central sensitisation predominates (Staud et al., 2007). However, Benecuik et al., (2009) only found this to be of significance immediately after the initial treatment, not at the end of the 9th Rx session nor one week subsequently. The authors suggest that this may be due to a ceiling effect which occurred because the participants were asymptomatic.

Some support of this is offered by the results of Bialosky et al., (2009) since the participants with CTS had significant improvements in temporal summation compared to the sham group after 3 weeks of treatment. Unlike Benecuik et al., (2009), where additional improvements in other outcome measures occurred compared to the sham treatment (VAS and ROM of elbow during the ULNT), Bialosky et al. (2009) found no other significant differences in an array of other outcome measures (see appendix 13 for details) between the sham and tensioner technique, although significant improvements from baseline were found in both groups. This suggests that apart from a change in temporal summation, no other benefits were specifically seen from the tensioner technique. However, it must be noted that the sham treatment given, whilst limiting the amount of strain through the median nerve, would have resulted in nerve excursion at
the wrist during the wrist and finger extension (Dilley et al., 2003, Hough et al., 2007; Ugbolue et al., 2004), hence it could be considered to be a neural treatment of sorts.

Improvements in outcomes in individuals with CTS were found in another 3 studies (De-La-Llave-Rincon et al., 2012; Schmid et al., 2012; Tal Akabi and Rushton, 2000) after neurodynamic treatment. However, despite significant improvement after the neurodynamic treatment compared to the control group, a carpal bone mobilisation also improved outcomes similarly in participants (Tal Akabi and Rushton, 2000). Such carpal bone mobilisation could be considered a neural interface technique, and may suggest therefore that in entrapment neuropathies, both direct and non-direct forms of nerve treatment can be equally effective. Caution should be taken when extrapolating this data due to the small numbers of participants in each group (7 in each group).

Schmid et al., (2012) also did not find a difference between a night splint group and a slider neurodynamic treatment group, although both demonstrated significant differences from baseline in MRI signal (indication reduced oedema) and functional outcome measures from one week of treatment. Whilst this study demonstrates that neurodynamic treatment is not superior to rest, it does provide evidence of no harm in patients with nerve entrapment. It had been suggested that these sorts of techniques could increase oedema in the CT (Brahme et al., 1997), and this study counters that argument.

De-La-Llave-Rincon et al., (2012) found that whilst significant improvements in pressure pain threshold (PPT) were observed at C5-C6 after ULNT slide technique in participants with CTS, no other sites, including the carpal tunnel showed significant improvement compared to baseline. Improvements were found in numeric pain rating scale (NPRS) after treatment, but a lack of comparative group or treatment, means that the changes could be attributed to natural progression or placebo effect alone.

Cumulatively, there is some limited evidence that longitudinal neurodynamic treatments may be beneficial, and stronger evidence that they do not cause harm in individuals with nerve entrapment syndromes.
This is further supported by Nee et al., (2012b), who specifically investigated harmful and adverse effects, in addition to beneficial effects of neurodynamic treatment (both sliders and tensioners) in individuals with non-traumatic nerve related neck and arm pain. A significant improvement (specific p value not reported) in global rating of change scale (GROC) was found in the experimental group (who also had cervical interface treatment and general cervical and shoulder mobilisation exercises; see appendix 13) compared to the control group (advised to stay active). Three out of 38 participants in the experimental group, and 4 out of 18 in the control group reported a worsening in the GROC scale, demonstrating that deterioration in condition was no worse than a control group. In addition, adverse effects, whilst reported in 16 out of 38 participants in the experimental group, were found to last for less than 24 hours, did not require additional treatment, and did not result in a worse outcome at the end of the trial compared to those who did not complain of any adverse changes.

One study, found a better outcome in individuals in a specific sub-group of individuals with low back and leg pain (Schäfer et al., 2011). Four sub-groups were identified by Schäfer et al., (2011): 1. Neuropathic sensitised (NS) (i.e. >12 on LANSS scale), 2. Denervation (D) (+ve neuro integrity), 3. Peripheral nerve sensitised (PNS) (<12 LANSS scale and +ve SLR, nerve palpation and lumbar flexion), 4. Musculoskeletal (M) (somatic). The results suggested that patients who were grouped within the PNS group, had significantly better outcomes (Roland Morris disability scale and global perceived rating scale) than all other groups, but not NPRS, which was not significantly different between the PNS and the NS group. Two treatment techniques were applied over a 2 week period (5 x weekly); the first technique was a lateral flexion technique designed to open the intervertebral foramen (interface technique, 5 x 60 secs), and the second a hip and knee mobilisation technique in side lying (slider technique, 5 x 30 secs). The use of two different types of neurodynamic treatment techniques used together means that any effects of treatment cannot be attributed to any one technique, making it difficult to rationalise the use of individual treatment techniques.
Other limitations of the study affect the strength of the results; one clear issue being that the group in which most positive effects were seen only had 9 participants. Recruitment of participants with specific criteria can be unpredictable and within the time period of the study, such small numbers in this important group was unavoidable. However, such small number of individuals does affect the extrapolation into clinical practice; that being that in participants classified in a PNS group a neurodynamic intervention is more likely to be effective. Perhaps more importantly since the definition of neuropathic pain has been updated (Cruccu et al., 2010) all three sub groups who had neurological cause for their leg pain could have positive responses to this scale (NS, denervation and PNSG). This has quite major implications for the study’s outcomes as the comparisons between groups may not be discriminatory.

One difficulty of interpreting the effectiveness of such neurodynamic techniques described in the above studies is the lack of consistency of treatment dose and timings of measurement of outcomes (see appendix 13 for details). Whilst literature has been published analysing optimal treatment dose for joint mobilisations, no such work has been established for nerve treatment. In addition the joint mobilisation studies have been performed on asymptomatic participants (Krouwel et al., 2010; Pentelka et al., 2012; Willett et al., 2010) or in rats (Sluka and Wright 2001), and therefore extrapolation of these studies is even more difficult in justifying neurodynamic treatment doses. Three times 30 seconds treatment dose was advocated for many years as a starting point by Maitland (1973), with some support from biomechanical studies such as Lee and Evans, where 30 seconds provided the greatest proportion of a creep effect. However Sluka and Wright (2001) found that longer treatment durations (>6 mins) were required to demonstrate a hypoalgesic effect in rats. Until more published literature is provided on optimal treatment doses, clinicians establish the best dose based on reassessing outcome asterisks between and after chosen repetition and durations, however the starting dose may be less clear.

The timings of assessment of outcome measures may also have an impact on the considered effectiveness of the treatment intervention. Measuring immediately after
treatment may produce different effects than if measured 10 minutes, a few hours or even days later. Benecuik et al., (2009) found a significant difference in temporal summation immediately after treatment, but not after other time frames. However, it is not clear what the immediate effects are after one neurodynamic treatment in most of the studies described. Whilst long term outcome is of great importance in establishing overall effectiveness of such treatments, it is helpful to establish immediate changes since subsequent measures can be affected by other extraneous variables.

4.4 Summary and Conclusions

There is a growing body of literature which supports the use of neurodynamic treatments. Research has demonstrated support for a number of physiological and mechanical changes which may account for improvement after neurodynamic treatments found in some studies. Such changes include the reduction in inflammation, oedema and pain behaviours. The use of longitudinal treatment techniques has been controversial, with numbers of authors suggesting potential detrimental changes in individuals with nerve dysfunction (Boyd et al., 2005; Dilley et al., 2005). However as this chapter has demonstrated, there is little evidence to support such assertions, but there still remains a need for robust research looking into the effectiveness of such longitudinal neurodynamic techniques, using outcome measures which reflect both mechanical and neurophysiological mechanisms. In addition, preliminary work looking at a standardised neurodynamic treatment dose with immediate measurement of outcomes is essential to determine any early changes to outcome.

The following chapter assesses the methods that may be useful in analysing both mechanical and neurophysiological effects of a neurodynamic SLR treatment.
Chapter 5 Measurement of nerve excursion, pain and nerve conduction.

There are a number of ways in which an intervention like SLR can be assessed to evaluate its effectiveness. Analysing how the nerve moves before and after treatment may give an insight into differences in the way in which the nerve behaves mechanically. However, measurements of nerve excursion alone, would not explain any neurophysiological changes. Since most individuals with painful conditions visit the Physiotherapist for relief of their pain, a measure of pain is commonly used in studies looking at the effectiveness of a treatment modality. In addition, because individuals with neuropathic pain often have changes to nerve conduction, measures to assess any changes to their nerve conduction is of importance to not only determine effectiveness, but to ensure that the treatments are not detrimental to nerve function. This chapter aims to assess and critically evaluate appropriate methods of assessing nerve excursion, pain and conduction.

5.1 Measuring nerve deformation in vivo

As presented in chapter 1, the overall focus of the thesis was to explore the difference in responses of individuals with spinally referred leg pain to a 3 x 1 minute SLR tensioner treatment. Such neurodynamic techniques aim to move the nerve through its interfaces resulting in mechanical and neurophysiological changes (Coppieters and Butler, 2008; Nee and Butler, 2006). Such mechanical changes could manifest themselves as a change to nerve excursion during SLR. Historically, methods of assessing nerve excursion have included cadaveric research (e.g., Boyd et al., 2013; Breig et al., 1960; 1963; Coppieters et al., 2006; Goddard and Reid, 1965), during surgery (Fleming et al., 2003), or animal studies (Boyd et al., 2005; Kwan et al., 1992; Millesi et al., 1995). Recently, real-time ultrasound imaging (USI) has been utilised to measure nerve motion (Coppieters et al., 2009; Dillely et al., 2001; Dillely et al., 2003; Ellis et al., 2008; Erel et al., 2003; Greening et al., 2005; Hough et al., 2000). This technology has made great advances in researchers’ ability to comment on not only what happens to nerves during normal movements in asymptomatic individuals, but also in pathological situations such as
carpal tunnel syndrome, non-specific arm pain and whiplash (Erel et al., 2003; Greening et al., 2005; Hough et al., 2000).

5.1.1 History of musculoskeletal ultrasound

The first recorded use of USI in medical fields was in the early 1940s when a neurologist Karl Dussik, used the technology to investigate brain tumours (Ylinen et al., 2005). Subsequently in the 1950’s it was developed for the use of pelvic and breast tissues (Shampo and Kyle, 1997) utilising both brightness (B) and amplitude (A) modes. It was with the development of antenatal scanning in the 1960s that ultrasound technology exploded onto the medical diagnostic scene (Ylinen et al., 2005).

Adipose tissue, tendon, cartilage and bone characteristics were reported using USI in the late 1950’s (Dussik et al., 1958); the first reported use of USI for musculoskeletal structures. With the increasing advances in technology, its use in musculoskeletal diagnostics has rapidly developed (Jacobson and van Holsbeeck, 1998). USI is also used in rehabilitation by assessing changes to muscle during exercise and functional activities (Whittaker and Stokes, 2011). In addition, measuring tissue motion is possible with the use of Doppler (Anderson and McDicken, 1999; Hough et al., 2000; Hough et al., 2007) and computer assisted techniques which detect motion of a section of tissue and track its relative change in position through a sequence of moving images (Dilley et al., 2001; Korstanje et al., 2009; Korstanje et al., 2010; Varghese et al., 2000). One of the common types of computer-assisted analysis is frame-by-frame cross correlation.

5.1.2 Theoretical basis of ultrasound

Ultrasonic sound waves are produced by a transducer which contains a piezoelectric crystal; this crystal vibrates and produces high frequency sound waves (ultrasound). These longitudinal waves are capable of travelling through solids, liquids and gases and are therefore ideal for use within the body (Pope, 1999). Different tissues have their own opposition to sound waves; this is known as acoustic impedance (Pope, 1999). Such acoustic impedance is a consequence of 2 factors, the speed of the propagated sound
wave, and the density of the measured tissue. For example, bone has high acoustic impedance whereas air has relatively low impedance. The sound waves travel through the tissues until they reach a soft tissue interface which has different acoustic impedance; at this point reflection or transmission occurs (Whittaker and Stokes, 2011). Where a good acoustic match occurs, the sound waves will be transmitted and little reflection will occur. If there is a large mismatch then the sound waves are strongly reflected. The transducer detects the reflected sound waves and converts them into electrical current and produces an image (Jacobson and van Holsbeeck, 1998). Hence, in situations where there is a large acoustic mismatch, a bright image is produced (hyperechoic), and when there is a good acoustic match a dark image results (hypoechoic or anechoic). Examples of this are soft tissue- bone interface (hyperechoic) and soft tissue-soft tissue interface (hypoechoic) (Jacobson and van Holsbeeck, 1998; Pope, 1999).

The depth of penetration of the ultrasound wave is dependent on the frequency of the transducer; higher frequencies penetrating more superficially than lower frequencies. However, there is a compromise, with lower frequencies which penetrate more deeply having poorer resolution than the more superficially penetrating ones. There are 2 types of resolution to consider; lateral and axial resolution. Lateral resolution is the ability of the beam to detect 2 objects side by side, with better resolution being able to detect the 2 objects which are closer together (Pope, 1999). Higher frequencies and narrow beam widths enhance lateral resolution. Axial resolution detects the position of the 2 objects along the axis of the ultrasound beam, so is often termed depth resolution. Shorter pulse durations result in improved axial resolution, and since there are the same numbers of cycles in a single pulse, short wavelengths and hence higher frequencies give a superior axial resolution (Pope, 1999).

A number of modes of ultrasound exist which are used for a variety of different usages. B mode or brightness ultrasound provides a real time 2 dimensional grey scale image and is commonly used in USI to diagnose lesions within a variety of soft tissues, but also in both rehabilitative USI and tissue motion analysis. More recently 3 and 4
dimensional versions of the B mode image are being utilised with increasing popularity, particularly for foetal scanning (Messing et al., 2007). M mode or motion mode is a modification of the B mode image. Changes in depth of the tissue can be calculated using a single beam tracked over time. It has been used successfully in measuring the valves in the heart (Pope, 1999). Doppler ultrasound scans were originally devised in the 1950s in Japan where they were used to assess blood flow in the peripheral vessels, eye ball movements and heart movements (Sigel, 1998). Recent advances have provided an array of different modes of Doppler, including colour, spectral and power Doppler, which all work on the Doppler shift principle (see below) which was originally used in radar.

5.1.3 Safety of Ultrasound Imaging

Ultrasound is considered to be a safe method of imaging structures of the body. In fact there have been no reported cases of safety breaches since the 1950s (Szabo, 2004). Two bioeffects of ultrasound are mechanical effects and thermal heating. Thermal heating is related to absorption of the energy produced by the movement of molecules subject to insonation. The loss of energy (attenuation) into the tissues, and therefore potential to heat tissues is greatest in higher frequency modes (Duck, 2008). The power of the ultrasound machine may determine the extent of the heating effect, since some of the heating effects are directly related to the heating effect of the transducer itself (Duck, 2008). However the power and intensities of modern ultrasound machines mean that rises in temperature of more than 2° are extremely rare (Duck, 2008). In addition, heating of a large mass of tissue is prevented because the rise in temperature is broadly limited to within the constraints of the ultrasound beam, and depth of penetration in higher frequency prevents heating of more deeply located tissues. Another important factor in the consideration of heating tissues is the length of time that the transducer is stationary. Greater amounts of heating occur with longer scanning durations. Generally, in most scanning contexts, the transducer is only held in one position for seconds, and the risk therefore is further limited.
Another bioeffect of ultrasound is acoustic cavitation. Gas bubbles within fluid undergo marked changes when placed within an ultrasound beam, with expansion and contraction of the bubble during decreased and increased pressure components of the sonic wave (Duck, 2008). The bubble may become unstable when it contracts and result in collapse. However, the likelihood of acoustic cavitation occurring is extremely unlikely in most situations because there is an absence of free bubbles, and the pressures and frequencies used in modern day machines are low (Duck, 2008). Indeed according to the American Institute of Ultrasound in medicine, “there is no basis in present knowledge to suggest an adverse nonthermal bioeffect from current diagnostic instruments not exceeding the US FDA output limits” (Fowlkes et al., 2008 p 510). Greater risks occur in areas within the body where there are stabilised gas bodies, such as the lung or abdomen, and particularly where gas filled contrast agents are injected into the blood stream. These will not be considered further as they are not relevant to this thesis.

5.1.3.1 Best Practice to minimise adverse effects of diagnostic ultrasound

Guidelines for safe practice of diagnostic ultrasound have been published, and a principle is used which is the ALARA principle (Fowlkes, 2008), which means that the output used should be as low as reasonable achievable. Two indices exist which help the operator to consider the likely thermal and non-thermal bioeffects. It has been recommended that the thermal indices (TI) be as low as possible, particularly in at-risk groups such as foetal or intracranial scanning, where absorption of ultrasound is high, and temperature increases have been demonstrated (Fowlkes et al., 2008). There is guidance as to the length of time that scanning should continue where TI are set and cannot be changed. According to the British Medical Ultrasound Society (BMUS) Safety guidelines (2009), TI of between 1 to 1.5 should be used for no longer than 120 minutes, and as with all outputs, should aim to be in contact with the individual for as short a time as possible. The mechanical index (MI) relates to the potential for ultrasound to cause a non-thermal bioeffect. However, since the risk is so low in sonographic evaluation of most diagnostic applications (as discussed above), this may be less relevant (Fowlkes, 2008).
The Titan ultrasound machine (SonoSite Ltd, Hitchin, UK) which was used in both the repeatability and clinical studies in this thesis, has a TI of <1 and a maximum MI of 1. The transducer was held in position over the posterior thigh for 3 seconds, for each component of knee extension during the modified SLR movement sequence (a total of 3 components). This falls well below the TI guidance by the BMUS (2009). The nerve and surrounding tissue that were scanned in these studies, do not fit within the guidelines for at-risk structures during ultrasound imaging with regards to non-thermal effects.

All scans performed in the studies for this thesis were performed by the researcher who is an experienced Physiotherapist, and successfully completed an ultrasound module on the Medical Imaging MSc at the University of Leeds in 2006. Many hours of practice were required to enhance the researcher’s technique of USI the sciatic nerve in the posterior thigh prior to data collection.

5.1.4 Measuring nerve motion with ultrasound

Soft tissue motion has been measured with USI for some time. As the resolution of ultrasound transducers developed, the ability to scan peripheral nerves became more common place (Walker et al., 2004). The sciatic nerve has been successfully identified in the posterior thigh (Ellis et al., 2008; Graif et al., 1991) and the popliteal fossa (Ellis et al., 2008). It is described as being a homogenous tubular echogenic structure when scanned longitudinally and a round echogenic structure with interspersed echoes when scanned in its transverse view (Graif et al., 1991).

An array of techniques have been developed to measure soft tissue excursion. These include Doppler (Hough et al., 2000, Hough et al., 2007), elastography (Lalitha et al., 2011) and frame-by-frame cross correlation or speckle tracking (Coppieters et al., 2009; Dilley et al., 2001; Dilley et al., 2003; Ellis et al., 2008; Ellis et al., 2012).
**Doppler**

Doppler has predominantly been used in medical imaging to analyse the flow of blood through vessels pre and post-natally and to detect abnormalities in heart valves and blood vessels (Yagel et al., 2010). This technique utilises the Doppler Effect, where there is an apparent change in frequency when movement occurs between a source and observer (Pope, 1999). This change in frequency is dependent on a number of factors including the angle between the probe and the moving tissue, the speed of the moving tissue, and the frequency of the wave emitted from the ultrasound machine (Hough et al., 2000). Hough et al. (2000) developed a new method in order to use this technology to analyse nerve motion. One problem with the use of Doppler to analyse movement is that if the probe is held perpendicular to the nerve, the resulting Doppler shift and therefore velocity would be equal to zero. This is because the Doppler shift equation is:

\[ \Delta f = \frac{2fv \cos \theta}{c} \]

(where \( \Delta f \) = doppler shift, \( f \) = frequency of the source, \( v \) = relative velocity, \( \theta \) = angle of the ultrasound beam in relation to the moving structure and \( c \) = velocity of ultrasound waves in the body).

Hence if \( \theta = 90^\circ \), cosine of 90 is zero. In order to limit this scenario from happening, Hough et al. (2007) added a beam steering angle of 15°, which reduced the angle between the nerve and the beam to between 45 and 60°.

This method was utilised to analyse median nerve motion at the wrist in 37 asymptomatic participants and 19 individuals with carpal tunnel syndrome (CTS) (Hough et al., 2007). Repeatability of the technique was performed on 5 participants over 3 occasions. Intraclass correlation coefficients (ICC) ranged from 0.58- 1 with a standard error of measurement (SEM) of between 0.012 and 0.49 mm depending on the position of the elbow, and if nerve or nerve/tendon ratio was analysed. The SEM of nerve movement was 0.32 mm with the elbow flexed and 0.49 mm with the elbow extended, which are small when compared to the mean longitudinal nerve movement found (4.2- 15.8 mm in the CTS group and 5.2 to 17.4 mm in the control group).
One issue with the use of this technology is the fact that velocity of the moving tissue needs to be sufficiently high enough in order for the Doppler shift to be accurately calculated. Very low velocities would result in negligible values for the Doppler shift. High velocity movement may be less appropriate in situations where symptomatic individuals are being moved into potentially pain provocative positions. Slower movements of the limb mean that the position can be stopped early in range if symptoms prevent further movement.

Elastography
One method that has shown great potential in estimating tissue strain is elastography. This method is based on the premise that applying a force to a tissue results in a returning force which enables one to ascertain the resulting stiffness of the underlying tissue. This method has been utilised by applying pressure to tissue with an ultrasound probe and analysing the echo signals obtained before and after the compression is applied using frame-by-frame cross correlation methods described below (Varghese et al., 2000). This method has been used successfully in detecting tumours, as they are harder than other soft tissue (Krouskop et al., 1987) and as such the strain exerted by the underlying tissue and detected by cross correlation is higher than in normal tissue. More recently elastography has been used to help to diagnose soft tissue lesions such as tendinopathy (Drakanoni et al., 2009; Lalitha et al., 2011).

This technique appears to be a robust method of analysing axial tissue strain in response to a compressive load (Varghese et al., 2000). Promisingly, longitudinal excursion and strain of tendon has been accurately measured using elastography on dissected porcine flexor tendons (Chernak and Thelan, 2012). However this very new technique has not been assessed in vivo on nervous tissue, although it has great potential for nerve deformation studies in the future.

Frame-by-frame -cross correlation method
In studies looking at changes in muscle, excursion has been calculated by comparing the movement in relation to other structures because of the heterogeneous nature of
muscular structures. For example, Fukunaga et al., (1996) were able to calculate longitudinal motion of tibialis anterior by identifying and comparing the muscular tissue with the musculotendinous junction. However, as explained earlier, nerve in its longitudinal section is broadly a homogenous tubular echogenic structure, and as a result there are no distinctive points along the nerve with which to compare movement. Hence, another method is required to assess longitudinal excursion of the nerve during movement of the limbs.

The cross correlation method is a form of “speckle tracking” which utilises the speckled grey pattern, which is interference of echo signals from within the tissue (Anderson and McDicken, 1999). This speckle is relatively consistent between frames of images, and as such can be followed as the tissue moves (Anderson and McDicken, 1999). Various software has been developed to analyse the amount of movement using this mathematical method. Once the moving image is saved, a series of regions of interest (ROI) are selected on the image. These ROI can vary in shape and size, and are selected by the researcher. Each ROI contains a portion of the image and has a unique number of grey scale pixels. There are advantages and disadvantages of different sizes of ROI. A large ROI will contain a less equivocal, but still distinctive pattern, but may not be able to follow the nerve so well if there is a large deformation during the movement. A small ROI might have a more indistinct pattern, but is better able to continue to track with larger nerve deformation (Korstanje et al., 2010). Some authors have recommended particular sizes of the ROI, for example to measure carotid artery wall motion, a ROI of 3.2 X 2.5 mm² was found to be optimal (Golemati et al., 2003). To the present author’s knowledge, no specific recommendations have been made as to the specific size of a ROI for measuring nerve motion. Dilley et al., (2001) used ROI between 500 X 30 pixels to cover most of the median nerve, or multiple ROI of ~ 80 X 30 pixels where the nerve was obliquely orientated. However, no attempt was made to assess the accuracy of different sizes of ROI. Ellis et al. (2008) used the same software programme as Dilley et al., (2001) to establish the reliability of the technique in measuring sciatic nerve motion, however the authors did not comment on the best size of ROI to use. However, Korstanje et al., (2010) used software which allowed the use of multiple concurrent
ROI, and used the ROI size with the best match, demonstrated by the highest correlation (see below). Such software is not routinely available, and therefore it is pertinent to use a number of ROI of varying shapes and sizes.

The cross-correlation procedure works by the software recognising the region by its grey scale; each pixel is assigned a specific number based on its brightness (or echogenicity), from 0 (black) to 256 (white). For each successive frame, the programme identifies this same area and calculates the amount that the region has moved by offsetting the co-ordinates of the ROI along the horizontal image plane, and shifting them one pixel at a time; the pixel shift (Dilley et al., 2001). A correlation coefficient is calculated for each pixel shift. The pixel shift that has the highest correlation coefficient is identified as the “true” value. Dilley et al., (2001) noticed that comparisons of sequential frames resulted in an underestimation of movement, and therefore recommended that analysis is performed on every other frame, however this is dependent on the speed of movement in relation to the frame rate (Korstanje et al., 2010). The output of the analysis produces the vertical and horizontal movement, and the overall horizontal movement from these two values, in addition it provides this for each ROI and an average for all of the ROI. A useful aspect of the programme is that it is possible to observe the movement of each area for each successive frame and ensure that all areas appear to be following the nerve appropriately.

Dilley et al., (2001) found that the method of frame-by-frame cross correlation was accurate in assessing nerve excursion in a number of string and avian phantoms (n=unknown) and control subject (n=1), and repeatable in 10 control participants. The string and avian sciatic nerve phantoms were fixed within a water bath and the bath moved a set distance by a chart recorder, whilst simultaneously collecting series of ultrasound images. The control participants placed their forearm in a water bath and the transducer was moved a known distance over the forearm whilst the median nerve was imaged.
For repeatability, the median nerve was imaged longitudinally 6-12 cms proximal to the wrist crease during extension of the wrist in 3 participants, and during index finger extension in 7 participants. The movements were performed between 3-4 times, and for wrist extension one subject returned 5 days later for a repeat of the procedure. Movements performed at very low velocities of < 0.25mm/sec were not accurately estimated.

Error measurements were found to be less than 10% of the overall excursion. With regards to repeatability, the average median nerve movement between the two trials on 2 separate days in one subject varied less than 10% during passive wrist extension. The authors considered that variability was low as standard deviations varied between 0.2-0.4 mm for within session readings for wrist extension, and between 0.16 and 0.67 mm during the passive index finger extension. Average nerve excursion for wrist extension was between 2.85 and 3.74 mm and for index finger extension was between 1.38 and 4.48 mm.

The technique described by Dilley et al. (2001) has enriched the field of nerve motion research. A number of studies have used this method to assess changes to nerve motion in groups of individuals (Dilley et al., 2003; Dilley et al., 2008; Erel et al., 2003), and to assess how different types of neurodynamic exercises can influence the amount of nerve motion (Coppieters et al., 2009; Ellis et al., 2012). However, there are limitations of the original study which must be taken into account. Firstly, the numbers of phantoms used was not disclosed making the use of statistical methods impossible. Limited numbers were used for the repeatability study and more robust reliability statistics such as ICC or SEM were not used, which would have given more critical values to estimate the errors of measurements that may occur using this technique.

More detail was given by Coppieters et al., (2009) who found excellent reliability of the technique for assessing median nerve excursion at the proximal humerus (ICC 0.96, SEM 0.66mm, smallest detectable differences (SDD) 1.84mm). However, some lower limb nerves, such as the sciatic nerve, are deeper, and the image may have poorer
resolution. Ellis et al., (2008) assessed the reliability of measuring sciatic nerve motion in the back of the thigh and behind the knee using the same frame-by-frame cross-correlation method as Dilley et al., (2001) devised. The sciatic nerve was imaged with participants in sitting with the knee flexed to 50°, whilst participants extended their cervical spine and their ankles were passively dorsiflexed.

Mean longitudinal nerve excursion of 3.47 mm was seen at the posterior thigh with an ICC of 0.75 and SEM of 0.79 mm, indicating good reliability and relatively low error measures. Longitudinal movement of the nerve behind the knee could only be recorded in 3 participants because the nerve moved beyond the field of view and therefore could not be further analysed. Whilst the study helps to support the technique for analysing sciatic nerve excursion in the posterior thigh, the movements of the nerve were small because the moving joint was distant from the site of imaging. If the knee or hip had been moved, greater amounts of sciatic nerve excursion at the posterior thigh would be expected since the nerve will follow the moving joint. This may explain why Ellis et al., (2008) found scanning behind the knee, (closer to the moving ankle) more difficult, and means further work is required to establish repeatability of the technique when nerves closer to the site of movement are analysed.

**Transverse plane nerve movement**

Whilst longitudinal nerve excursion has been successfully analysed by the Doppler and frame-by-frame cross correlation methods, transverse plane movement (i.e. superficial and deep, and lateral/medial) has had limited attention. Most studies have measured longitudinal movements, and where measurements of transverse plane motion have been used, no reference to reliability or error measures have been cited (Erel et al., 2003). However, more recently (Boyd et al., 2012) used a method which has been shown to be reliable for transverse plane tibial nerve excursion at the knee.

The method consists of importing the transverse image sequence into image J and manually outlining the border. The most central pixel (centroid) of the nerve can be identified by the software, and movement is calculated by comparing the centroid value
in last frame to that in the first frame. Boyd et al., (2012) found the reliability of the technique to be high for the tibial nerve behind the knee (ICC (SEM) 0.97 (0.42mm), 0.98 (0.47mm) for med/lat and sup/deep respectively) during ankle dorsiflexion. However, the tibial nerve is more superficial than some other lower limb nerves such as the sciatic nerve, and since resolution may be poorer it is not known if the technique is robust for all nerves.

5.1.5 Summary

This section has reviewed the use of USI to analyse nerve excursion. At the current time, frame-by-frame cross correlation appears to be the most robust method of assessing nerve excursion in vivo. Transverse plan nerve motion however has only recently been investigated, using a potentially reliable technique.

Analysing nerve excursion before and after a neurodynamic treatment reveals one aspect of a treatment effect, but since studies have suggested potential changes to pain and nerve conduction (chapter 4), appropriate methods of measuring these outcomes are necessary. The following two sections will evaluate methods of assessing pain and nerve conduction.
5.2 Methods of assessing nerve conduction

5.2.1 Introduction

Patients with neuropathy are commonly diagnosed by electrodiagnostic tests, such as sensory and motor nerve latency and nerve conduction velocity tests. However, these tests may be inconclusive in conditions where a number of nerve fibres continue to function, and thus propagate an action potential (Greening and Lynn, 1998). This has been demonstrated in both clinical studies (Atroshi et al., 2003; Finsen and Russworm, 2001) and in animal studies. Yoshizawa et al. (1995) found that nerve conduction velocity did not alter until 6 months after a silicone tube was inserted around the 7th lumbar nerve root in dogs despite marked changes to the large diameter afferent nerves after just 3 months. In a clinical study, Finsen and Russworm (2001) found that 14 out of 63 patients with successful outcome post-decompressive surgery for carpal tunnel syndrome had negative electrodiagnostic tests prior to the surgery. Atroshi et al., (2003) found that nerve conduction studies had low positive predictive values for individuals with carpal tunnel syndrome.

Due to such poor ability to detect the presence of alteration in nerve conduction in individuals with confirmed neuropathy, such tests are unlikely to be useful in showing changes in individuals with neuropathic low back pain. Quantitative sensory testing (QST) protocols for diagnosis of neuropathic pain have been supported by a number of authors (Felix and Widertröm-Noga, 2009; Rolke et al., 2006). The battery of tests which are used in the overall protocol are extensive (7 tests measuring 13 parameters), and take around 30 minutes to test (Rolke et al., 2006). In addition, the equipment which is required to fully investigate all parameters is expensive, and not widely available. In addition, QST protocol aims to test if individuals are suffering from neuropathic pain, rather than testing solely for nerve conduction, although some of the individual tests also assess conduction.
Vibration threshold testing (VTT) is one of the measures used in the QST protocol. It has been proposed as a measure for identifying individuals with common entrapment neuropathies such as carpal tunnel syndrome and work related upper limb disorders (Greening and Lynn, 1998; Greening et al., 2003; Tucker et al., 2007) and is a measure of the large diameter afferent nerves, the A beta fibres. It consists of applying a vibrating probe to the surface of the skin and the individual being tested informing the tester when they feel the sensation of vibration. It has been used in a number of conditions such as work related upper limb disorders (Greening and Lynn, 1998), carpal tunnel syndrome (Dellon, 1981; Lundborg, 2004), diabetes (Goldberg and Lindblom, 1979), compartment syndromes (Phillips et al., 1987), and to assess changes in nerve conduction after neurodynamic mobilisation (Ridehalgh et al., 2005). It is considered to be a useful tool in the early diagnosis of a neuropathic condition, as it assesses the function of the large diameter afferent fibres (Aβ) which are postulated to be the first fibres to show dysfunction after neural compromise (Dahlin et al., 1989; Fink and Cairns, 1982). In addition, most animal studies that have assessed changes to the nerve root and dorsal root ganglion post trauma have found greatest changes to the large diameter afferent nerves, and greatest pain behaviours to mechanical stimuli rather than thermal stimuli (Hou et al., 2003; Kawakami et al., 1996; Obata et al., 2002; Omarker and Myers, 1993). Further, individuals with radicular leg pain were found to have a disruption in the large diameter fibres (as tested with VT) but not the small diameter fibres (Freynhagen et al., 2008).

The use of a test to assess the function of the nerves after a neurodynamic intervention is useful for a number of reasons. Firstly, patients with neuropathic pain may already have deterioration in nerve function. It has been suggested that neurodynamic treatment may improve axoplasmic flow, blood flow and thus encourage dispersal of oedema (Coppieters and Butler, 2008; Nee and Butler, 2006). Such improvements could theoretically reduce the compression on the nerve and help to restore normal function, and VTT may help to capture this change.
In contrast, if strain over 8% is imposed on the nerve and the vessels which supply the nerve during the neurodynamic treatment technique, deterioration in blood flow may occur (Driscoll et al., 2002; Lundborg and Rydevik, 1973). If strain exceeds 12% then nerve conduction may deteriorate (Kwan et al., 1992). It is difficult to assess if such strain values occur during a technique like the SLR as strain of the sciatic nerve during the SLR has been found to vary between 6 and 26% (Boyd et al., 2013; Coppieters et al., 2006; Fleming et al., 2003). However, there may be an increase in strain values when the nerve is injured (Boyd et al., 2005).

An elevation of VT suggests deterioration in nerve function of the Aβ fibres, and such rapid changes if they occurred after a neurodynamic mobilisation, would likely to be caused by a reduction in circulation (Ochs et al., 2000). It is unlikely that structural changes or increased oedema would occur immediately after the technique. In a study looking at the effects of a longitudinal SLR treatment using repeated ankle dorsiflexion (3 x 60 secs) with the leg in SLR, no changes were found to VT in both control participants and participants who ran greater than 20 miles per week (Ridehalgh et al., 2005). Runners are considered more at risk of injury to the peroneal nerve due to repeated movements of the foot and ankle, and the high incidence of ankle sprains in this group of individuals (Fabre et al., 1998; McCrory et al., 2002; Pahor and Toppenberg, 1996). The study results (Ridehalgh et al., 2005) suggested that even in more at-risk groups, SLR assessment and treatment is not detrimental to nerve function. However, only 10 runners and 20 control participants were recruited to the study, therefore it is possible that such low numbers may have resulted in the non-significant changes. In addition, none of the participants were currently complaining of symptoms, and therefore it is not known if individuals with symptomatic neuropathy would behave in the same way.

As with all outcome measures, the analysis of the robustness of the technique is crucial in order to ensure that any change is attributed to the intervention and not because of variability in measurements between testing sessions. This chapter will assess the validity, repeatability and factors which may compromise VTT.
5.2.2 Validity of Vibration threshold testing

The validity of the technique has been considered in older observational studies (Dellon et al., 1980; Phillips et al., 1987), and in combination with other sensory tests for diagnosis of neuropathic pain (Rolke et al., 2005; 2006). VTT was found to be diminished in 9 out of 11 patients with suspected compartment syndrome (Phillips et al., 1987). On testing the pressure within the compartments, 9 out of 11 patients had an elevated pressure, and all of these patients had elevated VT. A further study in 12 healthy participants subjected to an experimental increase of up to 35-40 mm Hg in their lower leg by the means of an inflated pneumatic antishock garment had elevations in VT (Phillips et al., 1987). Participants also complained of numbness and change to sensation in the distribution of the deep peroneal nerve which matched the VT loss. The results of this study suggest that in situations where nerve function was altered by marked compression, VT was not only sensitive (i.e identified correctly all nerve dysfunctions), but also specific, since 2 out of the 11 patients with suspected compartment syndrome who did not have elevated pressures were found to have normal VT. The small sample sizes, and lack of statistical methods do limit the extrapolation of the results, but show a clear link between an elevation in VT and deterioration in nerve function.

In agreement, Dellon et al., (1980) looked at the use of VT to diagnose nerve dysfunction in people with different causes of nerve injury including 56 patients with direct nerve injuries (e.g. nerve divisions and neuromas) and 61 with compression injuries (e.g. crush, CTS). Following on from VT, additional tests were performed to analyse the construct validity of VTT. Surgical exploration was performed on the acute nerve injuries (n =47). In all cases where VT was elevated, there was evidence of nerve injury. In addition, VT was found to closely follow the stage of injury in 3 burns patients. One, who had normal VT on admission, subsequently developed marked swelling and inflammation and deterioration in VT. After escharotomy VT returned to normal. Whilst these studies are more observational and therefore not conclusive in terms of validity, they suggest that VTT is a clear indicator of deterioration in nerve function.
Construct validity of VTT was examined in 78 individuals with diabetes (Valk et al., 2000), by comparing the VT with sensory dimensions on the Diabetes symptom checklist-Type 2 (DSC-2). Examples included tingling or strange sensations in the hands and legs. The authors concluded that the use of VTT was valid for the assessment of sensory changes in individuals with diabetes. However Pearson’s correlation, whilst statistically significant (0.02 and 0.04 for foot and hand respectively), was only 0.3 and 0.26. An r value of 0.3 represents only a moderate correlation (Cohen, 1992), and 0.26 suggests a weak to moderate correlation.

A higher correlation (r=0.447) was found by comparing composite nerve conduction tests to VTT in 247 individuals with diabetes (Burns et al., 2002). One potential issue with this study is that the nerve conduction studies themselves may not be accurate in individuals with early stages of neuropathy caused by diabetes, since the intact axons may continue to propagate the signal as discussed above.

Whilst this raises some questions over the absolute validity of VTT, a plethora of studies have demonstrated elevations in VT in discrete groups of individuals with neuropathy including carpal tunnel syndrome (Borg and Lindblom, 1986; Winn and Putz Anderson, 1990), work related arm pain (Greening and Lynn, 1998, Greening et al., 2003), compartment syndromes (Dellon et al., 1980), diabetes (Martina et al., 1998; van Deursen et al., 2001), and polyneuropathies from a number of causes (Martina et al., 1998). These indicate that elevations in VT are an indicator of conduction changes that occur due to dysfunction of the nervous system.

There are a number of considerations when using VTT, which must be taken into account to ensure repeatable, accurate testing, these will be discussed below.

5.2.3 Methods of testing vibration thresholds

There are a number of approaches used for testing VTs. The mode that appears to be most commonly used is the method of limits (Greening and Lynn, 1998; Greening et al.,
This method consists of the subject informing the tester when they first feel the onset of a sensation of vibration as the stimulus is gradually increased, called vibration perception (VP), and then to let them know when the sensation disappears as the stimulus is first increased above VP, and then gradually decreased (vibration disappearance (VD)). Generally three measures of each are taken, and a mean of the 6 readings taken to give a value of vibration threshold (VT). One of the issues with such a method is that there is a reaction time consideration, as the stimulus continues to rise whilst the subject becomes aware of the sensation of vibration (Yarnitsky, 1997). The idea of using both perception and disappearance is that there will be a delay in true perception and also in disappearance, so using a mean of the two, aims to cancel out the reaction time component (Hilz et al., 1998).

Another method for testing VT, called the method of levels which excludes reaction time, delivers a pre-set stimulus and the subject is asked to inform the tester if they can feel vibration or not. If not, the stimulus is doubled until a yes is given, before reducing the stimulus by half until the participants says they can’t feel it anymore. This continues to be raised and decreased until the step between yes and no is within a predetermined range. The mean of the last yes and no is taken as the VT (Yarnitsky, 1997). The advantage of this method is that it excludes the issue of reaction time, although it can take considerably longer to test. In addition, this method of using discrete sensory stimulus increments appears to be more commonly used for thermal thresholds (Yarnitsky, 1997). Only one paper describing the method of levels for VTT was identified in this review (Hagander et al., 2000), and this may restrict comparisons between studies. The specific method of attaining VT is important when assessing studies because direct comparison between vibration thresholds cannot be made, as ones using method of limits, even with a mean of VP and VD, are likely to be higher than those using method of levels (Yarnitsky, 1997).

Whilst the method of limits is used more commonly, it has been suggested that simply taking VP is as accurate as taking the mean of both VP and VD to produce VT
Goldberg and Lindblom (1979) found that VPT correlated well with VT, and better than VDT in 110 healthy male volunteers. However this was established by assessing the correlation between VDT and VT, and VPT and VDT; i.e. no figures were given for VPT and VT. In addition, only male participants were used, and as it has been shown that VT differ between men and women (Halonen, 1986; Hilz et al., 1998), it is unclear from this study alone if this trend would be the same in women.

Hilz et al., (1998) found that all three measurements (VT, VPT and VDT) were closely correlated in a study of 530 healthy participants with a large variation in age range (3-79 years). This was apparent regardless of age or gender, suggesting that any of the three measurements would be acceptable.

Whilst the method of limits is likely to yield most accurate and comparable results to other studies, other factors may affect VTT.

### 5.2.4 Factors affecting vibration thresholds

There are many factors which may influence VT including gender, age, site tested, medication, temperature, and intake of substances such as caffeine or alcohol; these will be discussed in turn.

*Gender and age*

As mentioned, some studies have demonstrated a difference between men and women, but this is not consistent between studies. Hilz et al., (1998) found a difference in VT measured at the 2nd metacarpal and 1st metatarsal between men and women, but only in ages above 50 years. Halonen et al., (1986) also demonstrated that with increasing age, men’s VT deteriorated more than women’s in a study on 202 participants tested at the dorsum of the 1st metatarsal, although the age where this occurred was not specified. A limitation of this study was that it was not clear if participants had been asked to refrain from medication or caffeine, which could influence VTs (Gregg, 1952).
In contrast, Martina et al., (1998) only found a difference between men and women in one site; the medial malleolus whereas the other sites (index finger, ulnar styloid and great toe) did not show a difference between gender, even with increasing age. The method of testing VT was different in this study, in that a Rydel-Seiffer tuning fork was used, however this study also compared the tuning fork to a vibrameter and reported that the two correlated well (Spearman Ranks correlation coefficient 0.46 index finger and 0.65 big toe in asymptomatic group, and 0.46 and 0.71 respectively in a polyneuropathy group).

Although these studies together do not conclusively support the difference between men and women in all sites tested, most have demonstrated that VT deteriorates with age. These studies combined suggest such changes start at about the age of 40 years, but whilst they continue to deteriorate with age, they are still useful measures as long as age related corrections are applied (Hilz et al., 1998).

Choice of test site

A variety of testing sites are used in the literature, but most testing is performed on the hand or foot (Greening and Lynn, 1998; Hagander et al., 2000; Halonen, 1986; Hilz et al., 1998; Martina et al., 1998; Phillips et al., 1987; Ridehalgh et al., 2005). Higher VT have been demonstrated in the feet than the hands (Hilz et al., 1998; Martina et al., 1998), with the difference being more apparent with age (Goldberg and Lindblom, 1979). Such elevations may be due to either a difference in the number of mechanoreceptors between the two areas, or because the neural pathways are longer in the lower limb than arm, and therefore action potentials have further to travel (Hilz et al., 1998).

Differences in VT have been found between bony sites and soft tissue sites (Hagander et al., 2000). VTs were tested on the pulp, dorsum and middle phalanx of the index finger and dorsum of proximal phalanx and nail of the great toe. At the index finger the pulp had lower VTs than the nail, but no differences were found in the great toe. In addition
the narrowest percentile range was at the pulp followed by the phalanx and least at the nail in the index finger, suggesting that there is less variability in the readings at the pulp. No differences were found between sites at the great toe. Such differences between sites may be due to dampening of the vibration by soft tissue. However it has been found that even bony surfaces have differing dampening effects (Goldberg and Lindblom, 1979). The tibia was found to have greater dampening than the metatarsals, and the carpal bones had the least dampening of the three sites.

Other Parameters

Pressure exerted
Depending on the type of vibrameter used, it is possible to apply different amounts of pressure during vibration testing. Hagander et al. (2000) found that vibration thresholds were not statistically different between 3 different levels of pressure (30, 50 and 100g) in the foot. However, VT was significantly lower measured at 30g in the hand. The Somedic vibrameter which has been used in a number of studies assessing changes to VT in individuals with neuropathy (Greening and Lynne, 1998; Greening et al., 2003) uses a standardised pressure of 650g. Hagander et al. (2000) suggested that pressures over 100g were considered uncomfortable in some participants, therefore the comfort of participants should be assessed when using this instrumentation for VT testing.

Temperature
Skin temperature may have an effect on VT. Halonen (1986) found that temperatures below 20° centigrade significantly elevated VTs in men (compared to men’s baseline measures), but not in women. Warming does not seem to affect VT (Hilz et al. 1998) in temperatures up to 34°. However, both of these measures were carried out under artificial conditions; the cooling was imposed by putting the hand into ice and then measuring the VT every 0.5° rise, and the warming study by heating with an infra-red lamp. It is not clear if systemic rather than localised heating or cooling would have the same effect.
Medication

No significant changes to VT occurred 30, 60 and 90 minutes after ingestion of diazepam, but the spread of values increased considerably, suggesting that there was more variability in readings after diazepam (Meh and Denislic, 1995). At 90 minutes, this variability reduced to similar ranges as before ingestion. The authors recommend that ingestion of diazepam should be avoided prior to testing, but do not give a specific time frame for this, however their results suggest that taking diazepam greater than 1 ½ hours prior to testing may be acceptable. This part of the study was only conducted on 6 normal individuals, which may explain the lack of significant data, and may warrant caution over time frames after which it is appropriate to test VTs.

Both caffeine and aspirin were found to have an effect on VTs (Gregg, 1952). Participants were found to have a reduction in VT with caffeine intake, whereas aspirin tended to increase VT. Fifty three participants showed a marked reduction in VT (between 66-82% change from pre-ingestion) after taking caffeine, whereas aspirin elevated VT by around 70% in 70 participants. A placebo group was apparently used, although not all of the results were presented, and it did not appear that any statistical testing was performed between the placebo and intervention groups or between pre and post injection figures. Bearing these limitations in mind, the study suggests that there may be a trend for increases in VT post aspirin intake and decreases in VT post caffeine intake. The length of time that VT remained reduced after caffeine intake was not clear, as only data for 2 participants, who had taken a combination of both caffeine and aspirin, was presented. As caffeine and aspirin had opposite effects on VT the length of time shown (approximately 60 minutes) may not be reliable. VTs, after ingesting aspirin alone, remained elevated after 120 minutes. No studies have been found in the literature that have assessed the effects of non-steroidal inflammatory medication or paracetamol on VT, but based on the effects of aspirin it is possible that these types of medication may also have an effect on VT.
As there is a lack of robust information on length of time that VTs may be affected, it is pertinent to ask individuals to avoid caffeine or taking any pain medication for 24 hours prior to VT testing.

**Alcohol**

The effects of the use of alcohol are somewhat unclear due to the limited literature and different methodology used. It has been demonstrated that there is a strong correlation between individuals with high levels of alcohol intake and an elevation in VT (Melgaard et al., 1986). Whilst this suggests that alcohol may affect VT, these were individuals who had sought help for an alcohol addiction or had major signs of alcohol abuse. It is not clear if simply drinking alcohol prior to testing VTs would affect the results in some way. Another study (Sosenko et al., 1989) found that occasional use of alcohol did not affect VT, however it was not disclosed how this information was sought, nor how long prior to testing the participants had drank the alcohol.

Whilst there is limited evidence as to the effects of alcohol on VTs, it may be pertinent for individuals to avoid alcohol for 24 hours prior to testing.

### 5.2.5 Retest Reliability

A number of studies have demonstrated that VT measurements are reliable. Hilz et al. (1998) found substantial short term repeatability in 530 asymptomatic individuals (Spearman $0.87 < R_s < 0.99$). Unfortunately the time frame of this short term re-test was not specified. Longer term repeatability was correlated, but to a lesser degree ($0.43 < R_s < 0.59$). This reflects a moderate, but not substantial relationship. In addition, whilst this gives an idea of the relationship, it does not indicate the error within the data, and so the measures on the 2 occasions may correlate well against each other, but there may be a large variability in measurement (Bland and Altman, 1986). Such variability would impact on responsiveness of the measure to detect clinically meaningful change and may lead to either very large sample sizes being required or null hypotheses being incorrectly accepted.
Halonen (1986) found no significant difference between successive tests of VT measured at the great toe and tip and metacarpal bone of the index finger in 202 participants (p>0.1) analysed with paired T tests. However, this is not the best way to ensure repeatability; it only indicates that they are not statistically different from each other, and provides no detail about measurement error (Bland and Altman, 1986).

A more robust study, in terms of choice of statistical analysis looked at reliability in a small sample of asymptomatic participants, and a group of patients with spinal cord injury and neuropathic pain (Felix and Widerström-Noga, 2009). There were only 10 participants in each group, but even with such low numbers the repeatability of measures is of relevance, poor agreement can still be ascertained in small sample sizes, and likewise for good agreement. Using the mean of 3 VPTs over 8 different sites in the upper limb, trunk and lower limb resulted in ICCs of 0.86 (95% CI 0.45-0.76) for the asymptomatic group and 0.9 (95% CI 0.84-0.94) for participants with spinal cord injury, showing substantial reliability. More credence could have been given to the study if additional methods such as Bland Altman and SEM had been undertaken, but such strong ICCs and small confidence intervals (especially for the spinal cord injury group) indicate that VTT is a reliable method to use in patients with neuropathic pain.

Slightly lower correlations (r=0.77) for repeatability of VTT were found for 78 individuals with diabetes (Valk et al., 2000). Importantly SDD values were given, and found to be in the region of 9%, indicating that changes greater than 9% would be needed in future studies to ensure that the changes were attributed to a treatment effect.

The studies discussed suggest that reliability of VTT is acceptable. However, the technique is operator dependent and therefore it is essential to assess researchers’ repeatability measurements prior to any intervention studies.
5.2.6 Summary

VTT appears to be a robust method of assessing the function of large diameter afferent nerves. However, there are a number of factors that must be taken into consideration when testing this sensory modality; the most important being age of the subject, the choice of method of ascertaining the VT, and the effects of any medication and other stimulating substances. With regards to age, VT starts to deteriorate in men after the age of 40, therefore when participants in studies using VT as an outcome measure are over 40 years of age, age adjustment methods are necessary. The method of limits (mean of three vibratory perception and three vibratory disappearance) appears to be an accurate method for ascertaining VT.

5.3 Pressure Pain Thresholds

5.3.1 Introduction

Individuals seeking treatment for painful conditions predominantly seek to relieve their pain. Therefore measurements which assess changes in pain perception are essential in order to assess for a treatment effect. There are many methods of assessing pain including the use of pain scales, and indirectly by measuring the function of small diameter pain fibres with responses to hot and cold (Lautenbacher et al., 2005). All of these measures have their advantages and disadvantages, but one disadvantage of using pain scales such as the numerical pain rating scale is in studies where participants all receive the same intervention, and cannot therefore be blinded to a treatment intervention. Here, participant bias may lead to inflated improvement in pain measures. Measuring the function of small diameter fibres requires time consuming and expensive equipment (see QST in 5.2.1), and may have limitations for research because of these reasons.

An increasing number of studies assessing effectiveness of manual therapy techniques, have used a measure which evaluates the change in response to the first onset of pain.
caused by the gradual build-up of pressure (De-La-Llave-Rincon et al., 2012; Krouwel et al., 2010; Moss et al., 2007; Sterling et al., 2000; Willett et al., 2010). Pressure pain thresholds (PPTs) have been shown to be repeatable (Antonacci et al., 1998; Persson et al., 2004; Sterling et al., 2000), but are subject to within subject variability (Rolke et al., 2005).

Of particular relevance to this thesis, patients with nerve pain have been found to have increased mechanosensitivity to both movement and palpation of the affected nerve trunk (Fidel et al., 1996; Schäfer et al., 2009; Sterling et al., 2000), and PPTs have been used to assess such tenderness to palpation. In addition, PPTs have been found to be affected by manual therapy both local and distant to the site of treatment, suggesting that there are both segmental and systemic inhibitory mechanisms at play (Krouwel et al., 2010; Moss et al., 2007; Sluka et al., 2006; Willett et al., 2010). The following section evaluates the literature relating to testing PPTs with standardised algometers.

5.3.2 Reliability and validity of measuring pressure pain thresholds

The construct validity of the Wagner Force one algometer has been assessed by comparison to a force plate (Kinser et al., 2009). The algometer was placed in the centre of the force plate and the reading on the algometer was compared to the force plate output. Highly significant Pearson’s correlation (r=0.99) was found between force platform readings and the algometer. This demonstrates that this algometer accurately measured the pressure applied, but the authors’ claim that this demonstrates validity is not correct, since force plates are not used as a measure of pain. However, whilst the validity cannot be assumed from this study, it is well established that if you press on an area of the body hard enough, this will trigger polymodal nociceptive endings, and produce a sensation of pain (Dafny, 2000). Although, the amount of pressure that is required to produce such a response is variable between individuals, and subject to many factors. These will be discussed later in this section.

A number of studies have looked at the repeatability of measuring PPTs and found that both inter and intra tester reliability is good to excellent (Antonacci et al., 1998; Persson
et al., 2004; Sterling et al., 2000; Vanderweeën et al., 1996; Walton et al., 2011). The earliest of these studies (Vanderweeën et al., 1996), measured the PPTs in 14 trigger points around the shoulder and spine, and found an ICC of between 0.64-0.96 (intra tester). This indicates substantial to excellent reliability (Fleiss, 1986); unfortunately no CI, SEM or SDD were given which limits the appreciation of the error size during such measurements. In addition, only one PPT for each site was tested, which is not normal practice, and it has been found that the first PPT is significantly different on the first reading to subsequent readings (Kosek et al., 1999; Persson et al., 2004). Higher ICC values were found by Antonaci et al. (1998) for intra tester reliability of 15 points over three consecutive sessions (ICC 0.85), and acceptable ICCs for inter tester reliability (ICC 0.75). Whilst SEM and CI were not provided, the authors worked out the intra and inter examiner variations which were 15% and 18% respectively. This suggests that variation of measurements between sessions and testers is relatively high. The gap between sessions however was only 2-3 minutes, and each point was tested 3 times in each session. Such large numbers of points and repetition could either increase the PPTs due to habituation of the stimulus (Kosek et al., 1999), or reduce them if the points became sensitive from successive testing.

Persson et al., (2004) also found excellent intra tester reliability (ICC 0.7-0.94) within one session, of 7 points in the shoulder tested 4 times with 10 mins between each test. As with the previous studies, no SEM data was provided, but 95% CI varied between each test site and were as wide as 0.54-0.84, and as narrow as 0.82-0.95. The largest CI was a distal and lateral point in deltoid, which may have indicated the difficulty in maintaining the probe perpendicular to the tissue. This highlights the importance of establishing the best sites to test with pilot work prior to any intervention studies.

Walton et al., (2011) assessed SEM and SDD in addition to reliability in individuals with and without neck pain. Three measurements of PPT were taken from the upper fibres of trapezius and tibialis anterior. Inter rater reliability was performed with only a 5 minute gap between testing which may not have allowed for any sensitive areas to have recovered from the stimulus of the first tester’s assessment. Repeated measures
were taken with a 3-5 day gap between tests. Excellent intra (ICC 0.94-0.97) and substantial inter rater reliability (0.76-0.84) were found in the asymptomatic group, and were equally matched in the symptomatic group (0.96-0.97, intra and 0.81-0.9 inter rater). SEM and SDD were lower in the asymptomatic group than the symptomatic groups and at the trapezius site compared to the tibialis anterior site (asymptomatic trapezius SEM 18.2 kPa (7%), SDD 42.7 (17%), symptomatic trapezius SEM 20.5 (8.6%), SDD 47.2 (19.8%), asymptomatic tibialis anterior SEM 37.4 (11.2%), SDD 86.3 (26%), symptomatic tibialis anterior SEM 42.3 (10.5%), SDD 97.9 (24%)). Such relatively high error measurements must be taken into account when considering the effects of any treatment interventions. However, it is not known from this study if error measures would alter if PPT were tested in the same session, rather than between days. This would provide useful information for studies where immediate effects of treatment are being investigated.

In conclusion, PPTs appear to be a reliable method of assessing pain perception in a variety of points around the body. The repeatability of any technique however, is in part related to the skill of the operator, and therefore the reliability of the technique used by any researcher should be assessed prior to intervention studies.

### 5.3.3 Factors to consider when testing pressure pain thresholds

Several factors may have an impact on PPT testing and include gender, site, age and number of repetitions.

#### 5.3.3.1 Gender

Some studies have found lower PPTs in females than men (Chesterton et al., 2003; Manning and Fillingim, 2002; Sterling et al., 2000; Vanderweeën et al., 1996), although one study found no difference in PPTs between genders (Lautenbacher et al., 2005). Chesterton et al. (2003) tested the first dorsal interosseous muscle of the hand in 240 participants, evenly divided between men and women. Women had PPTs of between
12.2 to 12.8 N (1.2 kg) (28% lower than men). This was a well-controlled study, with a large sample group which was suited to simply assess the difference in gender.

Sterling et al. (2000) found in a study on 45 men and 50 women, that women had significantly lower PPTs (p=0.006) then men in all three upper limb nerves tested (radial, median and ulnar). An approximate (calculated from the published figures) 28% difference between men and women were found at the median nerve, with smaller differences (around 23%) for radial and ulnar nerves. These compare well to Chesterton et al.’s (2003) study findings, despite differences in units of measurement and sites tested.

Vanderweeen et al., (1998) and Manning and Fillingim (2002) also found lower PPTs in women compared to men, but these were not consistent. In Manning and Fillingim’s (2002) study, differences were only found between genders in non-athletic individuals. One area of confusion in this paper was the definition of non-athlete population, who were individuals who participated in sports for more than 3 hours per week (the group varied between >3 and 15 hours). The number of hours of training that the competitive college athletes participated in was not divulged, meaning that the differences between groups for a number of factors including muscle bulk, cardiovascular fitness, circulating endorphins may not have been sufficiently different.

Vanderweeen et al., (1996) found significantly lower PPTs in women in 6 out of 14 points on acquisition of the first PPT, but re-testing the points 5 minutes later revealed only 2 of the points were significantly lower. This may suggest that repeated measures on women may even out the differences between men and women, however, Chesterton et al., (2003) found that the difference between men and women remained significant even after 6 measurements of the same points.
5.3.3.2 Site

A difference in PPT has been found between types of tissue (nerve/muscle interface being lower than bone or muscle) (Kosek et al., 1999), and upper limb compared to lower limb (hand being lower than the foot) (Rolke et al., 2005). Within the foot it was also found that the nail bed had highest PPTs followed by bone then muscle (Rolke et al., 2005).

5.3.3.3 Age

There does not appear to be a consensus in the literature about the effects of age on PPTs. Sterling et al., (2000) found age not to be a significant factor in PPTs performed over the upper limb nerves, whereas Lautenbacher et al., (2005) found that PPTs were significantly lower in an elderly group (63-88 years compared to a younger group (21-35 years). The differences between the study results could be due to the differences in the upper age range; 88 years in Lautenbacher et al.’s (2005) study, but only 65 years in Sterling et al.’s (2000) study. Hence, age may have an impact on PPT, and as such age adjusted methods may be required in any analysis of studies using older participants.

5.3.3.4 Body Mass Index

Some authors have specifically excluded participants with a BMI of greater than 26 kg/m^2 (Krouwel et al., 2010) or 32 Kg/m^2 (Letchuman et al., 2005). However, there is no justification for doing so in these studies and there appears to be no literature to the present researcher’s knowledge to support such exclusion. Participants with anorexia have been shown to have an elevation in PPTs compared to those within normal ranges of BMI (Raymond et al., 1999), suggesting that weight could alter PPTs, but these participants suffer from many other physical and psychological factors than simply reduction in BMI, and these factors may be more important than the weight alone. BMI did not alter PPTs in 26 asymptomatic participants (Defrin et al., 2003). In agreement, a study on 87 individuals with non-specific LBP and 64 asymptomatic participants (Farasyn and Meeusen, 2005) found no difference in PPTs in participants with BMI below 26 kg/m^2 compared to those over 26 kg/m^2. Whilst exclusion of participants with
higher BMI may reduce the effects of extraneous variables to testing, to do so potentially reduces the extrapolation of study results to the wider public. In addition, some symptomatic groups, such as those with LBP, have a higher BMI than the general population, and therefore exclusion would result in a lack of a representative sample from that specific group (Farasyn and Meeusen, 2005).

5.3.3.5 Number of Repetitions

A consensus of repetitions per site does not seem to have been reached within the literature. Some authors have used just 1 repetition (Vanderweeen et al., 1996), 2 repetitions (Chesterton et al., 2003), mean of 3 readings (Sterling et al., 2000), median of 3 readings (Lautenbacher et al., 2005), and 4 repetitions with a 10 minute gap between (Persson et al., 2004). Persson et al. (2004) found that the 1st PPT reading was significantly different from the others, and the 1st PPT compared to the 5th PPT was significantly higher in 3 different sites in the arm (Kosek et al., 1999). Further assessment is required to analyse the most repeatable method of assessing PPT, and should form part of the pilot work of studies using PPT as an outcome measure.

5.3.4 Summary

Measurements of PPT are repeatable and stable over time. Females tend to have lower PPTs than a similar matched group of males, and it may be that older individuals have lower PPTs. It is not known if BMI has an effect on PPT, although it has been postulated that individuals with BMI over 26 kg/m² have higher PPT. Nerve areas tend to have lower PPTs than muscle or bone and the first measure of PPT may be different from subsequent measures.

5.4 Conclusion

This chapter has discussed the use of measures which assess nerve biomechanics, nerve conduction and pain. Longitudinal nerve excursion can be reliably measured using offline analysis (frame-by-frame cross correlation) of B mode ultrasound images, but
further studies are required to assess whether this method is suitable for measuring sciatic nerve excursion in the posterior thigh with movements close to the moving joint. Methods to analyse transverse plane nerve excursion are still in their infancy.

Since nerve conduction may be affected by increased nerve strain, which is thought to occur during neurodynamic tests like the SLR, nerve conduction is a useful measure to assess if such changes occur after neurodynamic treatments. VTT is repeatable and detects changes to the large diameter afferent nerves. This chapter has provided some considerations of factors which affect VT, which need to be taken into consideration in research using VTT as an outcome measure.

Pain measures are important tools to analyse improvement in painful conditions after treatment. PPT appears to be repeatable, but is subject to variation due to certain factors. This chapter has presented the factors which influence the robustness of PPT testing, and these should be taken into account when this outcome measure is used in studies.
Chapter 6 Rationale and aims and objectives of the experimental work

The five previous chapters have provided a rationale for the study and the choice of outcome measures that were chosen. Chapter 2 outlined the cause and sub-grouping of individuals with spinally referred leg pain. It also determined the main causes of these types of pain, and how individuals with each of the three types of leg pain could be identified clinically. It also discussed how the presence of central sensitisation could have detrimental effects of prognosis, and how disability and psychosocial factors can impact on prognosis in individuals with spinally referred leg pain. Hence identifying these characteristics is important when analysing the effects of treatment.

Chapter 3 examined the use of neurodynamic testing in practice. It outlined some important biomechanical factors which are essential in interpreting the literature on nerve excursion, and provided supporting evidence for the validity of such tests. Chapter 4 examined the literature which has supported the use of neurodynamic techniques as a treatment intervention. Whilst the literature is expanding in this area of Physiotherapy practice, there is still insufficient literature which has examined the immediate effects of nerve treatments on both mechanical and neurophysiological effects in symptomatic individuals. In addition, it also highlighted the concern that some authors have expressed in applying tensioner techniques in individuals with neuropathic pain, but demonstrated the lack of conclusive evidence to support such views, and even presented some literature which showed beneficial effects to pain and the potential for the reversal of central pain processes.

Chapter 5 critiqued the potential outcome measures which could be used in a study looking at the effects of a neurodynamic treatment intervention and identified three main outcome measures which would be useful in a study of this sort; ultrasound imaging to measure nerve excursion, pressure pain thresholds to measure pain, and vibration thresholds to measure nerve conduction. These three measures would give both a
narrative for any changes that occurred to the mechanics of the nerve being moved and the neurophysiological changes.

The main aim of the study was to determine what effects a 3 x 1 minute SLR tensioner treatment had on pressure pain thresholds, vibration thresholds and sciatic nerve excursion between 3 different sub-groups of individuals with spinally referred leg pain (somatic, radicular and radiculopathy).

The objectives underpinning this aim were to:-

I. Determine the validity and repeatability of the frame-by-frame cross correlation method to analyse nerve motion

II. Determine normative excursion data for the sciatic nerve during a modified side lying SLR test

III. Determine the repeatability of the VT and PPT tests in individuals with spinally referred leg pain.

IV. Determine the immediate effects of a SLR treatment dose on nerve excursion, PPT and VT.

V. Analyse the differences in the 3 outcome measures between the 3 groups of individuals with referred leg pain.

A second aim was to assess if the presence of central sensitisation, levels of disability and psychosocial factors were different between the three groups and interacted with the effect of treatment.

The objectives underpinning this aim were:-

VI. Determine any baseline differences between the sub-groups

VII. Introduce each factor into the main statistical analysis as covariates to establish any interaction with the main analyses.

A third aim was to assess how well the psychosocial factors and levels of disability were related to each other.
In order for these objectives to be achieved, initial studies which explored the validity and repeatability of the three outcome measures proposed were performed. In addition, since the data collected in the repeatability study for nerve excursion consisted of asymptomatic participants, the data were also analysed to gain information about normative nerve excursion. The clinical study explored the main aims of this thesis and consisted of two main parts. The initial part was the sub-grouping of individuals with spinally referred leg pain, which was done by Physiotherapists who volunteered to assist in the study. The second part was the data collection to assess the effects of the SLR mobilisation on pain (PPT), conduction (VTT) and nerve excursion (ultrasound imaging) in individuals with spinally referred leg pain. Fig 6.1 shows the flow chart of studies which form the next 2 chapters.
Fig 6.1 Flow chart of Studies

Validity study of cross correlation method of speckle tracking of ultrasound images of nerve (Chapter 7)

Reliability/normative study of cross correlation method of speckle tracking of ultrasound images of sciatic nerve during SLR (Chapter 7)

Reliability study of VTT and PPT in participants with referred leg (Chapter 7)

Clinical Study (Chapter 8)

Part 1 Physiotherapist recruitment and subgrouping of participants

Part 2 Laboratory study
Chapter 7 Validity and Repeatability Studies

The overall aim of the present study was to determine what effects a 3 x 1 minute SLR tensioner treatment had on pressure pain thresholds, vibration thresholds and sciatic nerve excursion between 3 different sub-groups of individuals with spinally referred leg pain. The outcome measures proposed for the clinical study were sciatic nerve excursion during the SLR measured using a frame-by-frame cross correlation method of ultrasound images, VTs of areas of the foot and ankle supplied by the lumbosacral plexus and PPTs of the leg (tibial nerve behind the knee and gastrocnemius as it is supplied by the lumbosacral plexus), and contra lateral deltoid to assess if any improvements in pain are segmentally or systemically mediated.

The validity of the ultrasound technique has been assessed, but in small numbers on avian or string (Dilley et al., 2001), and it was felt that this was not sufficient to support the use of the technique in this study. Good repeatability of all three measures had been found in previous studies, but all of the techniques are subject to operator skill, and therefore it was important to establish reliability for the researcher prior to the main data collection.

Therefore three studies were performed:

1. The validity of using a frame-by-frame cross correlation method of analysis of excursion on real time B mode ultrasound images of pig nerve.
2. The repeatability of using this same cross correlation method of analysis of excursion of the sciatic nerve in the posterior thigh during the SLR.
3. The repeatability of VT and PPT measurements in the areas described above.

In addition, because asymptomatic participants were used in the ultrasound repeatability study and there is limited in vivo description of normative movement during the SLR, a separate section is given to the analysis and discussion of these data.
The objectives of the studies were as follows:

1. To assess if frame-by-frame cross correlation technique was a valid measure of nerve excursion.
2. To assess if frame-by-frame cross correlation technique was a reliable measure of sciatic nerve excursion during a modified SLR technique in side lying.
3. To describe the trends in sciatic nerve excursion during a modified SLR test in asymptomatic participants.
4. To assess if VTT of the lateral malleolus and 1st metatarsal was repeatable in individuals with spinally referred leg pain.
5. To assess if PPT at contralateral deltoid, ipsilateral tibial nerve and ipsilateral gastrocnemius sites was repeatable in individuals with spinally referred leg pain.

7.1 Ultrasound cross-correlation method

7.1.1 Validity

As mentioned in chapter 5, there is limited work on the accuracy of utilising the cross correlation method to measure nerve movement. Error measurements of <10% were found on avian nerve and string phantoms (Dilley et al., 2001), but it was not stated how many phantoms were used and in addition such phantoms may not best represent human nerve.

The purpose of this study therefore was to analyse the use of frame by frame cross correlation on B mode ultrasound images of movements of pig sciatic nerve, and establish if the technique was robust for measuring excursion.
7.1.1.1 Method

Materials
Eight fresh porcine forelimbs were obtained and the neurovascular bundle was identified, before the nerves (musculocutaneous and median, n=16) were dissected free of surrounding tissues. Pig nerve was used as it is has a close relationship to human nerve (Wall et al., 1991). These were frozen and stored at -30°C until required. Nerves were thawed at room temperature for 4 hours before testing (Clavert et al., 2001).

Each nerve was mounted in a water bath by fixing one end to a rigid stand; and the other end was passed around a pulley with a baseline weight of 0.49 N (50G) which was hung to the nerve. The ultrasound transducer was positioned immediately above the nerve in the water, and held in place by a clamp and stand. A plastic ruler was positioned underneath the nerve so that markings of the ruler were visible from outside the water bath (Fig 7.1). This allowed the magnification of the photographic image of the nerve to be determined.

![Fig 7.1 Lateral view of porcine nerve mounted in water bath](image)

**Fig 7.1 Lateral view of porcine nerve mounted in water bath**

Instruments
Nerve displacements were tracked by both optical and ultrasonic methods. These two measurements were compared so as to establish the validity of using ultrasound
images to track nerve sliding. A camera mounted on a tripod, was positioned in front of the water bath so that the ultrasound probe, nerve and ruler were visible. The camera was placed as far away as possible (approximately 2 metres) with the zoom on to ensure a clear image, so that parallax was kept to a minimum. The exact distance was not required as the photographs were subsequently analysed by image J software which allowed conversion of mms to pixels by measuring the distance of 10mm on the ruler and assigning this distance a set number of pixels.

A FF Sonic UF-750XT (Fukuda Denshi) ultrasound machine with a 7.5 MHz linear array transducer, connected to an image grabber (Global lab image Data Translation, Bietigheim-Bissingen, Germany, with a 25 frames per second capture rate ) was used to scan the porcine nerve.

Procedure
A static photograph was taken of the baseline position. The stand that clamped the ultrasound transducer was then moved a short distance so that the transducer moved longitudinally over the nerve to mimic sliding of the tissue (the distance was not set, as the amount was calculated from the photographic images subsequently). The images were captured and saved with the image grabber onto an external hard drive. A static photograph was taken of the new position of the probe over the nerve.

Analysis
The ultrasound images were saved in MPeg format and converted to bitmap images. Subsequently all images were analysed off line using frame-by-frame cross correlation which was developed by Dilley et al., (2001) using Matlab (Mathworks Inc, Natick, MA). For the chosen frame a cluster of three to five regions of interest (ROI) were selected along the nerve of slightly different shapes and sizes depending on the size of the nerve (Fig 7.2). The programme recognises the region by its grey scale; each pixel is assigned a specific number based on its brightness (or echogenicity), from 0 (black) to 256 (white). For each successive frame, the programme identifies this same area and calculates the amount that the region has
moved by offsetting the co-ordinates of the ROI along the horizontal image plane and shifting them one pixel at a time; the pixel shift (Dilley et al., 2001). A correlation coefficient is calculated for each pixel shift. The pixel shift that has the highest correlation coefficient is identified as the “true” value. Dilley et al., (2001) noticed that comparisons of sequential frames resulted in an underestimation of movement. Therefore, the researcher analysed a selection of different options; tracking sequential frames, every other frame and between every third frame. The best frame selection appeared to be on every other frame, and therefore this method was used for the analysis.

The output from the programme produces the vertical and horizontal movement, and the overall horizontal movement from these two values, in addition it provides this for each ROI and an average for all of the ROI. A useful aspect of the programme is that it is possible to view an image clip showing how the programme is tracking the movement. This provides an element of quality assurance to ensure that all ROI appear to be following the nerve movement. At times, certain ROI did not follow the movement of the nerve and these were discounted from the analysis; in these cases the mean value was used unless there was substantial one sided outliers, when the median value was used.

![Fig 7.2 Regions of interest](image)

The cross correlation procedure described above was carried out tracking the position of the three to four ROI, before and after the probe was moved.
longitudinally above the nerve. The photograph images were opened into image J, and the edges of the ultrasound probe were compared before and after the probe was moved. The pixels were converted to mms by measuring the length in pixels of a 10mm section of ruler in the photographs.

**Statistical Analysis**

The data were assessed for normality and then intraclass correlation coefficients (ICC 2,1), confidence intervals, standard error of measurements (SEM) and a Bland Altman plot was drawn to see if the measures were in agreement (Bland and Altman, 1986). The results from the SPSS spread sheets can be found in appendix 29 and the attached CD.

### 7.1.1.2 Results

Table 7.1 shows the comparison between the amount of movement analysed by the photographic method and that by the cross correlation method on the ultrasound images. As can be seen, the distance that each nerve moved varied considerably between trials, but is similar between both the photographic and ultrasound methods for each nerve.
Table 7.1 Amount of movement (sliding of each nerve) measured by cross correlation method of ultrasound images and photographs.

Statistical Analysis
All data were normally distributed (Shapiro Wilk ultrasound p=0.31, photographs p=0.15), and therefore ICCs were calculated on the data.
The ICC was 0.93 (C.I. 0.82-0.98) and SEM =1.19 mm.

A Bland Altman plot was produced (fig 7.3) which showed a good spread around zero, indicating good agreement (Rankin and Stokes, 1998). Two of the measures lie outside the upper limit of agreement and represent outliers.
The results indicate that the use of a cross correlation analysis of B mode ultrasound images of nerve motion is a valid method for assessing longitudinal nerve excursion. Dilley et al., (2001) suggested that the use of this method for assessing string and avian nerve phantoms was a valid measure of longitudinal excursion. Their results indicated that there was less than 10% error in the measurements. The results of the present study show an average error of 1.19 mm, which is an error of 8.5% when one considers the mean nerve movement to be 14 mm. This is slightly lower than Dilley et al.’s (2001) study. The present study analysed 16 porcine nerves, which may be more appropriate to compare to human nerve since the size and characteristics of porcine nerve are more similar to human (Rydevik, 1991). Dilley et al. (2001) did not present the numbers of nerves or string that they analysed in that part of the study, nor did they attempt to perform any statistical analysis on the data. The present validity study suggests that the technique may be more accurate than Dilley et al., (2001) indicated.

Fig 7.3 Bland Altman Plot of ultrasound v photographic sliding data

7.1.1.3 Discussion
The amount of sliding that occurred in nerves 11 and 15 were considerably less than the photographic data and as such deserves a comment. A blurred image was found for nerve 15. Such blurring may result in underestimation of the programme as it may reject movement from some frames, as the ROI does not match a region in these frames. In addition, looking at the photographs, the ultrasound transducer in these 2 nerves was at a slight angle to the nerve. Hence, both the tracking method and the method of analysing the movement of the probe from the photographs could be inaccurate. The clarity of the image is essential to ensure that the image analysis software is able to visualise the image sufficiently to recognise that same region throughout the entire period. It is vital therefore that the operator has sufficient skill to produce clear images. This element to scanning the sciatic nerve was assessed during the repeatability study.

7.1.1.4 Conclusion

The use of frame-by-frame cross correlation method using B module ultrasound images appears to be a valid method of analysing longitudinal nerve excursion. This method appears to measure longitudinal nerve movement with an error of 1.19 mm. This must be taken into account when assessing any change to nerve movement after longitudinal SLR treatment and also when comparing between the different sub groups of participants with referred leg pain.
7.1.2 Reliability of nerve motion using ultrasound

Ensuring the technique is measuring what it should be measuring is an essential element when ensuring a robust outcome measure, but in addition, ensuring that the measure is repeatable enables the researcher to be sure that any changes to the outcome are due to the intervention, and not just due to fluctuations in readings between measurements.

Excellent intra-rater reliability was found for measuring longitudinal movement of the sciatic nerve in the posterior thigh (Ellis et al., 2008); however this was done in a seated slump position and during ankle dorsiflexion and cervical extension only. In the clinical study (chapter 8), the nerve was scanned in the posterior thigh during knee extension, which was likely to produce larger levels of excursion than Ellis et al., (2008) for 2 reasons. Firstly, nerves move most around the moving joint (Dilley et al., 2003; Phillips et al., 2004; Boyd et al., 2005), and the posterior thigh scanning location was much further from the ankle (Ellis et al., 2008) than the knee in the clinical study. Secondly, a greater range of joint movement occurs at the knee than at the ankle, hence the nerve has to adapt to greater amounts of joint range, and will do so by increasing excursion (as well as strain).

Dilley et al. (2001) also found good intra-rater reliability for measurements of the median nerve in the forearm, although very small numbers (3 and 7) were examined meaning that statistical methods appropriate for assessing reliability were not performed (more details of this study can be found in chapter 5). The median nerve is more superficial than the sciatic nerve, and therefore the resolution of the image may be superior compared to the sciatic nerve, since ultrasound waves emitted from higher frequency transducers are absorbed faster, with increasing depth (Rizzatto, 1998).

The ultrasound technique requires much practice to perfect (Beekman and Visser, 2004), and so it was important to establish that the researcher was sufficiently skilled in obtaining clear images, because the frame-by-frame cross correlation method is likely to be less reliable if poor images are used.
For these reasons it was essential to test the repeatability of the method planned for the clinical study with the same operator.\(^8\)

### 7.1.2.1. Method

**Participants and Recruitment**

Ethical approval was gained from the Faculty of Health and Social Sciences Research Ethics and Governance Committee at the University of Brighton (appendix 14).

Eighteen asymptomatic participants (9 women, 9 men, mean age (SD) 28.9 (14.3), range 19-68 years) were recruited for the study. All participants were required to read an information sheet and sign a consent form prior to participating (appendix 15). A list of exclusion criteria was assessed including any neuromusculoskeletal conditions, systemic disorders such as rheumatoid arthritis and pregnancy (appendix 15).

**Instruments**

A Titan ultrasound machine (SonoSite Ltd, Hitchin, UK) with a 5-10MHz linear array transducer connected to an image grabber (Global lab image with a 25f/s capture rate) was used to scan the sciatic nerve in the posterior thigh.

A universal goniometer and an electrogoniometer (Biometrics ltd, dataLINK goniometer) were used to measure the position of the knee.

A purpose made jig was used to enable the hip to be positioned in 30 and 60° of hip flexion, and the knee allowed to move from 90° through to 0° (see fig 7.4)

**Procedure**

The order of left or right leg to be tested was randomly chosen by participants asked to pick out a piece of paper from a bag which consisted of 20 pieces of paper, 10 with left

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8 This reliability study was published in Manual Therapy in 2012 (see appendix 31)
written on, and 10 with right. Participants were asked to undress to shorts and a top before their height and weight were taken. Lumbar spine, hip, knee and ankle measurements were taken to ensure that there was no joint restriction which would prevent the participants from being placed in the SLR position. Neurological integrity tests of the lower limbs were performed and consisted of light touch (tested with cotton wool), reflexes of the knee and ankle, and isometric muscle testing of the lower limb myotomes. Any participants who had positive tests would have been excluded, but this was not the case in any of the 18 participants.

The electrogoniometer was placed laterally over the knee joint by placing the upper end block in line with the greater trochanter and the lower end block in line with the lateral malleolus (Biometrics ltd dataLINK goniometer manual). The participants were then asked to lie supine whilst an ankle foot orthosis was placed on each foot and secured with bandages.

The participants then lay down on the jig with the chosen leg upper most, and the hip joint positioned over the joint of the jig (resulting in the hip being positioned in 30°), the knee was straightened as far as possible and the electrogoniometer zeroed. One or two pillows were placed under the subject’s head to prevent cervical lateral flexion occurring, and this varied between participants depending on the width of their shoulders. The subject was then secured onto the jig with a series of straps around the pelvis and lower leg (fig 7.4). The knee angle was measured with the universal goniometer, and the electrogoniometer reading repeated before the knee was flexed to 90° (measured by the electrogoniometer). The knee was held in this position by a peg placed anterior to the crease of the ankle, and then the position of knee flexion was measured with the universal goniometer. Whilst the knee position was held at 90°, it was noticed that small variations in the reading on the electrogoniometer occurred, and therefore the reading used for analysis was the reading shown immediately after the measurement with the Universal goniometer. The universal goniometer measurements were used to subsequently assess for agreement with the electrogoniometer. Universal goniometers have been demonstrated to have excellent intra tester reliability for
measurements of knee flexion and extension (ICC flexion 0.997 and 0.972 to 0.985 for extension, Brosseau et al., 2001), and accuracy as compared to measurements taken by X ray (r=0.97-0.98, Gogia et al., 1987).

The sciatic nerve was then located in the posterior thigh in its transverse view with the ultrasound transducer. The nerve was located on a line between the ischial tuberosity and the greater trochanter (Karmakar et al., 2007) and 10 cms distal to the gluteal fold (Bruhn et al., 2008). The best image of the nerve in its transverse view was found by moving the transducer slightly up and down along the course of the nerve. The position of the transducer was then marked on the skin with a non-permanent marker. The transducer was then rotated and a longitudinal image acquired (Fig 7.5). The movement of the sciatic nerve was captured between 90 to 45° of knee extension, 45 to 20° and 20° to 0° using the image grabber to save the images to a portable hard drive. These ranges of movement were chosen after pilot work discovered that between 45 to 0° of knee extension, there was considerably more out of plane movement which meant that keeping the transducer above the nerve was difficult. Utilising smaller ranges of movement made it easier to follow the nerve and ensured that the best image was maintained within the field of view. Once these images had been captured, the transducer was removed, and the marks measured from the ischial tuberosity and the knee crease.

The subject’s hip was then positioned in 60° of flexion with the jig, and the full procedure was repeated in the same way as described above. All ultrasound imaging was performed by the researcher, and the knee was extended, and images saved by a research assistant.

Participants returned for an identical test procedure between 48 hours and one week later.
Fig 7.4 Subject positioned on purpose made jig. Scanning of sciatic nerve in posterior thigh. Images from Ridehalgh et al. (2013) Manual Therapy 17(6):572-6 with permission from Elsevier limited.

Data Analysis
All longitudinal images were saved onto a portable hard drive and analysed off line using frame-by-frame cross correlation which was developed by Dilley et al., (2001) using Matlab (Mathworks Inc, Natick, MA). For the chosen frame a cluster of three or four regions of interest (ROI) were selected along the nerve of slightly different shapes and sizes (Fig 7.5). The detailed description of the procedure can be found in 7.1.1.

Fig 7.5 Regions of Interest
The cross correlation procedure described above was carried out tracking the position of the 3 to 4 ROI during knee extension, depending on the size of the nerve (see Fig 7.5). The images were also tracked visually and the mean value was used unless there was substantial one sided outliers, when the median value was used.

The total amount of movement measured during each hip position was used to compare between occasion 1 and occasion 2, hence for each subject there was an overall longitudinal movement calculated for hip at 30° moving the knee from 90 to 0° of flexion, and an overall longitudinal movement with the hip at 60° and knee moving from 90 to 0°.

Statistical Analysis
Repeatability of longitudinal sciatic nerve motion was calculated using intraclass correlation coefficients (ICCs) (2,1), with subsequent analysis using SEM and 95% confidence intervals (Bland and Altman, 1986). SDD for the 2 hip positions was calculated using the equation $1.96 \times \sqrt{2} \times SEM$ (Schuck and Zwingmann, 2003).

Agreement between the universal goniometer knee measures and the electrogoniometer measures were compared using ICCs (2,1) with subsequent analysis using standard error of measurement and 95% confidence intervals (Bland and Altman, 1986). All analyses were performed using SPSS version 18. The results from the SPSS spread sheets can be found in appendix 29 and attached CD).
7.1.2.2. Results

Two participants were excluded as the image quality was too poor for the motion analysis software to track longitudinal movement of the nerve. In both of these participants a depth of 6.5 cms had been used to be able to view the sciatic nerve, and as such the resolution was not as clear as more shallow depths.

Agreement between universal goniometer and electrogoniometer

Table 7.2 shows the figures for each subject’s knee range of movement for both the universal (UG) and electrogoniometer (EG).

<table>
<thead>
<tr>
<th>Subject</th>
<th>UG 0°</th>
<th>EG 0°</th>
<th>UG 90°</th>
<th>EG 90°</th>
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<td>0</td>
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<td>92</td>
</tr>
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<tr>
<td>16</td>
<td>5</td>
<td>1</td>
<td>92</td>
<td>88</td>
</tr>
</tbody>
</table>

*Table 7.2 universal v electrogoniometer measures at set up positions of zero and 90 degrees flexion*

The ICC for 0° was 0.51 (0.04 -0.8 C.I.) and SEM 1.39°. The ICC for 90° was 0.084 (-0.42-0.54), SEM 4.57°. However, such low ICCs for knee flexed to 90° with relatively low standard error measures required further analysis, since small differences between
measures is known to affect the robustness of ICC (Hopkins, 2000). Coefficient of variation (CV) (Hopkins, 2000) was therefore used for the 90° of flexion data, but was not possible for the 0° position, as the calculation uses the mean of the differences of the 2 measures to calculate the CV. Since the differences were zero in some cases, this inflated the CV values. CV for 90° of knee flexion were 5.04% for the Universal goniometer and 5.26% for the electrogoniometer (calculations for CV can be found in the attached CD), this indicated that the error measures for both goniometers were similar and low.

**Longitudinal Nerve Excursion**

Table 7.3 shows the amount of sliding for all participants with the hip in 30° of flexion and 60° of flexion. The total amount of movement is shown for the whole range of knee extension from 90 to 0° flexion. Mean (SD) movement at 30° hip flexion was 9.92mm (2.2) for test 1 and 10.06mm (2.5) for test 2. At 60° hip flexion mean (SD) for test 1 was 12.44mm (4.42) and test 2 was 12.54 (3.97).

It can be seen that there was a large amount of variability between participants in the amount of nerve motion occurring overall and between the two hip positions. Values between tests 1 and 2 showed relatively little variation for most participants, but participants 4, 13 and 16 had larger differences for one of the hip positions.
### Table 7.3

<table>
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<th>Subject no</th>
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<td>13.79</td>
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<tr>
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<td></td>
<td>Hip 60 flexion</td>
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<td>17.83</td>
</tr>
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</tr>
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<td>11.13</td>
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<td></td>
<td></td>
<td>Hip 60 flexion</td>
<td>20.21</td>
<td>19.11</td>
</tr>
</tbody>
</table>

*Table 7.3 Amount of nerve movement (mm) at different ranges of hip movement between 90 and 0 degrees of knee flexion. Participants 4, 13 and 16 are highlighted as they had relatively large differences between test days.*

All data was normally distributed (Shapiro Wilk test for hip flexion 30° p=0.19 and p=0.28 for occasions 1 and 2 respectively, and for hip flexion 60° p= 0.78 and 0.62 for occasions 1 and 2 respectively).

The ICC for 30° hip flexion was 0.92 (C.I. 0.79-0.97). The SEM was 0.69 mm, and SDD was 1.9 mm.
The ICC for 60° hip flexion was 0.96 (C.I. 0.89-0.99). The SEM was 0.87mm, and SDD was 2.41mm.

A Bland Altman plot was produced for each position of hip flexion to assess if any bias between the two readings occurred (figs 7.6 and 7.7).

*Fig 7.6* Bland Altman plot of sciatic nerve sliding (mm) with hip in 30 degrees flexion (knee 90 to 0 degrees) for test 1 and test 2

*Fig 7.7* Bland Altman plot of sciatic nerve sliding (mm) with hip in 60 degrees flexion (knee 90 to 0 degrees) for test 1 and test 2
Both plots show a good spread around zero which indicates good agreement (Rankin and Stokes, 1998). One of the data points lies outside the 95% limits of agreement in both plots. These two outliers represent two different participants, and the rationale for why this occurred is discussed below.

**7.1.2.3 Discussion**

These results suggest that the use of the cross-correlation method of analysis for measuring longitudinal sciatic nerve excursion using B mode ultrasound sciatic nerve images is a repeatable method. Very good to excellent ICCs values (Fleiss, 1986), and mean measurement errors < 10% were found for both the 30 and 60° hip flexion protocols. Two other studies have shown the cross correlation method to be reliable in assessing longitudinal nerve excursion (Dilley et al., 2001 and Ellis et al., 2008). Dilley et al., (2001) found that the average median nerve movement measured in the forearm between two trials on 2 separate days in one subject varied less than 10% during passive wrist extension. The authors also considered that variability was low for within session readings as standard deviations varied between 0.2-0.4 mm for wrist extension, and between 0.16 and 0.67 mm during the passive index finger extension. Average nerve excursion for wrist extension was between 2.85 and 3.74 mm and for index finger extension was between 1.38 and 4.48 mm. Since small numbers of participants were used (one for repeat measures on a separate day, and 3 for wrist extension group), no other statistical analysis was attempted and therefore it is not possible to compare the results of this study directly with Dilley et al., (2001).

Ellis et al., (2008) found mean longitudinal sciatic nerve movement of 3.47 mm during a modified slump test in the posterior thigh with an ICC of 0.75 and SEM of 0.79 mm. The ICCs found in the present study are slightly higher than Ellis et al. (2008) (0.92 and 0.96 for hip flexion of 30 and 60° respectively), but the SEMs are similar (0.69 and 0.87). The mean amounts of movement are understandably different between the two studies since the movements imposed, and starting positions for each study contrast considerably; participants in Ellis et al.’s (2008) study being held in slump position whilst the head was extended and ankle dorsiflexed. The nerve was scanned in the
posterior thigh, and since most movement occurs closest to the moving joint (Dilley et al., 2003; Phillips et al., 2004; Boyd et al., 2005), small movements would have been expected at this location. What is promising about the present study is that despite larger excursion values, where it may be considered more technically difficult to follow the nerve movement, it appears that the technique is still repeatable.

The SEMs found in this repeatability study were 0.69 and 0.87 mm and SDD 1.9 mm and 2.41 mm for the two hip positions. This means that in the clinical study (chapter 8) any differences in measurements were required to be greater than 1.9 mm (hip flexed to 30°) and 2.41 mm (with hip flexed to 60°) to be 95% certain that these differences are due to a real change and not due to error.

One potential problem with using the cross correlation method to analyse nerve motion is the speed at which the movement occurs (Dilley et al., 2001). Nerve movements recorded below 0.25 mm/sec were too low to be accurately measured by Dilley et al., (2001). Passive movements of the limb between each stage of knee extension were performed within 3 seconds. The smallest movement found between 90 to 0° of movement was 5.11 mm (subject 1 at 60° hip flexion). Assuming that all of that time was taken (9 secs), then the lowest rate of movement would have been 0.57 mm/sec. In reality much of the movement had finished within the first 2 secs, but even if this was not the case, the speed of nerve movement is likely to be well above those required to provide accurate data.

Goniometry measurements.
The results of the ICC for comparison between the electro and universal goniometers showed fair agreement for 0° (0.51) but poor agreement for 90° (0.084). The coefficient of variation was calculated since ICC may be inaccurate where the 2 compared measures are very similar. Both the electrogoniometer and universal goniometer shared similar error measures, suggesting that they were closely related. However, there were problems with using the electrogoniometer during the study. At times, the angle that the electrogoniometer indicated as being the position to stop the movement, did not appear
correct compared to eyeballing, and so the movement was stopped, the
electrogoniometer re-positioned, and the process was started again. This increased the
time that the participant was required to stay in the lab, and also meant that the leg was
moved an extra time. Whilst this was unlikely to significantly alter the amount of nerve
excursion during the movement (since changes to viscoelastic tissues are likely to
require sustained or repeated movements into resistance for over 30 seconds), minor
changes in starting position could have occurred. Therefore, a pragmatic decision was
made to use a universal goniometer in the clinical study. The SEM of the goniometer
was $4.57^\circ$ at $90^\circ$ knee flexion. Total nerve excursion during this modified SLR is due to
a combination of joint movement (hip, knee and ankle), and such small differences
between individuals are unlikely to significantly alter if the knee was positioned in just
over or just under $90^\circ$ of flexion.

Study Considerations and limitations
There are some considerations about the technique which are worth noting. In two
instances where the nerve was imaged at greater depths, poor resolution meant that the
software programme was unable to track the moving image appropriately. However in
some instances (3) even at depths of greater than 6 cms the programme was able to track
the nerve movement. It may be that differences in soft tissue characteristics may be the
cause of such difficulties. All 3 participants who were scanned at this depth were female
(participants 1, 9 and 10), the remaining 4 females were scanned at depths of 5.5 cms,
whereas only 2 males were scanned at 5.5 cm. This may suggest that the nerve is more
deeply situated in females. Considerably longer periods of time were required to gain
the best images in these participants and therefore increased estimates of time were
taken into consideration for the clinical study.

The frame-by-frame cross correlation procedure identifies areas of the nerve which
match with subsequent frames based on the echogenicity of the pixels within each ROI.
This method does not always result in correct tracking of the nerve. The advantage of
the programme is the ability to visually track the moving image, and hence it was very
clear when the programme did not best track the moving nerve. In these cases, repeated
selection of different sizes and location of the ROI were required in order to establish accurate nerve excursion.

In 3 cases, differences between occasion 1 and occasion 2 were as high as 2.4mm. In these cases, the clarity of the image in occasion 1, particularly towards the end of range of knee extension was substantially poorer than occasion 2 on visual inspection, and resulted in a smaller tracked excursion in the software. The results of two of these cases can be seen as the outliers in the Bland Altman plots (figs 6.9 and 6.10). These cases highlight the importance of acquiring a clear image of the moving nerve throughout the whole target sequence.

7.1.2.4. Conclusion

The results of this study suggest that the method of frame-by-frame cross correlation for assessing longitudinal sciatic nerve motion is repeatable. The accuracy of the technique is dependent on obtaining a clear image throughout the whole movement, and observing that the tracking programme is following the moving nerve.

7.1.3 Normative sciatic nerve excursion during a modified SLR test

The data that were collected in the reliability study were utilised to assess the normative ranges of movement and any trends in normal nerve excursion during the modified side lying SLR test⁹.

7.1.3.1 Methods

The participants used, equipment and overall procedure was identical to the reliability study (section 7.1.2.1, page 152), except that on the second attendance transverse plane movement was also analysed.

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⁹ This study was published in Manual Therapy in 2014 see appendix 31
Procedure for Transverse plane movements

The sciatic nerve was located in the posterior thigh in its transverse view with the ultrasound transducer. The nerve was located on a line between the ischial tuberosity and the greater trochanter (Karmakar et al., 2007) and 10 cms distal to the gluteal fold (Bruhn et al., 2008). The best image of the nerve in its transverse view was found by moving the transducer slightly up and down along the course of the nerve. The knee was extended in 2 stages; 90 to approximately 45° of knee extension and 45 to approximately 0°. The transducer was then rotated and the longitudinal images captured in 3 stages (as described in 7.1.2.1).

Analysis
Initially the plan for the analysis of the transverse images was simply to describe the direction of movement, and therefore it was not appropriate to perform a repeatability study using this data. However, subsequent to the data collection (collected in 2011), Boyd et al., (2012) published a paper describing how to analyse the data using this technique (described below). Repeatability of the technique for the tibial nerve found by Boyd et al., (2012) was ICC (SEM) 0.97 (0.42mm), 0.98 (0.47mm) for med/lat and sup/deep respectively).

The transverse images were imported into image J (Rasband, W.S., Image J, U. S. National Institutes of Health, Bethesda, Maryland, USA, http://imagej.nih.gov/ij/, 1997-2012), and a manual outline of the borders of the nerve was made. The most central pixel (centroid) of the nerve was then identified (Alshami et al., 2009; Boyd et al., 2012). The amount of transverse plane movement (med/lat and sup/deep) was calculated by comparing the centroid value in the last frame to that in the first frame. Over or under estimation was reduced by measuring the amount of subcutaneous movement (using the same centroid method) and subtracting it from the nerve motion. This process was performed for both knee movements (90-45° and 45 to 0°), and added together to give
the overall medial/lateral and superficial movements for knee extension from 90 to 0° for the two hip positions.

The description of the analysis of the longitudinal images has been discussed in section 7.1.2.1.

Data Analysis

Descriptive statistics were used to detail the amounts and direction of nerve excursion during the modified SLR. The longitudinal excursion data were analysed for normality. A paired T test was performed to determine if there were any statistically significant differences in longitudinal nerve excursion between 30° and 60° of hip flexion. A Pearson’s correlation was performed to see if there was any relationship between participants’ height, age and longitudinal nerve excursion. All analyses were performed using SPSS version 20. Since repeatability of the transverse plane movements had not been established for the researcher, descriptive statistics only were employed for this data.

7.1.3.2. Results

Transverse Movements

The nerve moved superficially in 14/16 participants during the SLR in both 30 and 60° of hip flexion (30° hip flexion (HF) mean 4mm (SD 2.2), 60° HF mean 3.6mm (SD 2.3). For the remaining 2 participants, one had no superficial movement with 30° HF, and one participant had 0.5mm of deep movement with 60°HF. Lateral movement was the most consistent sideways movement with 10 participants moving laterally during the SLR with 30°HF, and 9 with 60° HF. However between hip positions, this was not consistent, i.e. the nerve may have moved laterally in 30° HF, but medially in 60° HF and vice versa (see fig 7.8). There was marked variation in direction of movement between individuals.
Fig 7.8 Transverse plane sciatic nerve movements

Longitudinal movements

As explained in page 147, the longitudinal excursion data were normally distributed (30° HF Shapiro Wilk p=0.2, 60° HF Shapiro Wilk p=0.78). The direction of nerve excursion in all participants was distal. Table 7.4 shows the large variability between participants in the amount of overall nerve motion. In addition it can be seen that large variability existed between the two hip positions. Overall there was a trend for a greater amount of movement at 60° HF compared to 30° HF.

The results of the paired T test found that mean nerve excursion was significantly greater when the hip was pre-positioned in 60° flexion (mean nerve excursion 30° HF=9.9mm, 60° HF =12.4mm, mean difference 2.53mm, p=0.02, 95% confidence interval (C.I.) 0.4-4.6, standard error of mean 0.99).

The Pearson’s correlation test showed non-significant correlation between participants’ height and excursion in either hip position (r= 0.23 and 0.41, p= 0.4 and 0.12 for 30° HF and 60° HF respectively), or age and excursion (r=0.06 and -0.32, p= 0.83 and 0.23 respectively).
<table>
<thead>
<tr>
<th>Subject no</th>
<th>Nerve excursion (mm)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hip 30° flexion</td>
<td>Hip 60° flexion</td>
</tr>
<tr>
<td>1</td>
<td>10.25</td>
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<td>2</td>
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</tr>
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<td>16</td>
<td>10.32</td>
<td>20.21</td>
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<tr>
<td>Mean (SD)</td>
<td>9.92 (2.20)</td>
<td>12.44 (4.42)</td>
</tr>
</tbody>
</table>

Table 7.4 Longitudinal nerve excursion. Total amount of movement is shown for the whole range of knee extension from 90 to 0° flexion. The direction of movement in all participants was distal. Minus values indicate that there was less movement with 60° hip flexion.

7.1.3.3.Discussion

The results of this study suggest that there is wide variation in longitudinal and transverse plane movement in asymptomatic individuals. Whilst transverse plane movement was measured, the technique was not considered to be accurate because of the changing shape and at times loss of outline of the nerve, and therefore the directions of movement, rather than the actual amounts of movement will be discussed further. A similar technique was used by Tagliafico et al. (2012) for measuring cross sectional area of the sciatic nerve in the mid-thigh. Relatively small measurement error (SDD= 13%) was found, however static images were obtained, and changes to the shape of the nerve during limb movements may increase measurement error. Boyd et al., (2012) found the technique to be repeatable during ankle dorsiflexion, but this was for measurements of the tibial nerve at the knee. The nerve here is more superficially located; hence the
resolution of the nerve may be enhanced compared to the sciatic nerve in the thigh. Indeed, in the present study, observation of the transverse plane images of nerves which were more superficially located (< 4 cms depth) appeared to better represent the transverse plane movements measured with the centroid method.

Most nerves (14/16) moved superficially when the knee was extended. Boyd et al., (2012) found a consistent superficial movement of the tibial nerve measured at the popliteal fossa during ankle dorsiflexion with the limb positioned in SLR. Whilst the location of the nerve and movements imposed were different to the present study, the results together suggest that mostly nerves move superficially when the nerve bed is lengthened in asymptomatic participants. It is not clear why the sciatic nerve in the thigh should move more superficially, but could be related to relative position of the nerve to the posterior femur or knee joint, or muscular effects on the nerve as the hamstrings are lengthened.

A greater proportion of nerves moved laterally, although medial movement occurred in some participants, suggesting that side to side movement during a modified side lying SLR test is variable. This may be related to the location of the sciatic nerve in the thigh compared to the tibial nerve at the knee. A more medially positioned tibial nerve compared to sciatic nerve would exert a medial pull as the knee extended. In addition, if the sciatic nerve branches closer to the knee, there may be a stronger lateral pull from the division of the common peroneal nerve. Another possible reason could be due to differences in soft tissue characteristics within the thigh; the exact effects of these are unknown. Boyd et al., (2012) also found some variation in medial and lateral movement of the common peroneal nerve at the knee during ankle movements, but not the tibial nerve. This may further support the effect of a higher or lower branching common peroneal nerve, since the direction of pull might be influenced by the region that the nerve branches. Together with the present study’s data it suggests that individual variation in side to side movements of nerve occurs during a SLR manoeuvre.
The mean longitudinal nerve excursion found at 30° of hip flexion was 9.9mm, and at 60° hip flexion was 12.4mm. A wide range of sciatic nerve excursion during SLR has been found in the literature, varying from 4 mm (Goddard and Reid, 1965) to 28mm (Coppieters et al., 2006). However such large ranges in variation are almost certainly due to participants used (cadavers), location of measurement of nerve excursion, and the order in which the joint movements occur. Likewise, Ellis et al., (2012) and Boyd et al., (2012) used the same frame-by-frame cross correlation method to measure sciatic nerve excursion (Ellis et al., 2012) during the slump test and tibial and common peroneal nerves (Boyd et al., 2012) during a modified SLR test. The differences in values found are not comparable to the present study since the location of nerve studied, combination of movements performed and nerves analysed (Boyd et al., 2012) are substantially different. Hence it is more appropriate to analyse comparable trends between studies. The sciatic nerve always moved towards the extending knee. This is consistent with a number of studies which have found that the direction of nerve movement is towards the direction of the moving joint in both upper (Erel et al., 2003) and lower limb studies (Boyd et al., 2012; 2013; Coppieters et al., 2006; Goddard and Reid, 1965).

As mentioned, variability in longitudinal excursion between individuals is large. In the present study excursion ranged between 6.42mm to 14.69 mm with the hip flexed to 30° and from 5.11mm to 20.21mm at 60°. Such variability has also been found in previous studies. Goddard and Reid (1965) found that the sciatic nerve at the pelvis varied from 4-7.5 mm during SLR. Whilst the range of movement was not given by Boyd et al. (2012), the relatively high standard deviation (e.g. in hip flexion, ankle dorsiflexion produced a mean excursion of 0.66mm, with a SD of 0.25mm) suggests a wide variation in range between individuals. It is not currently known why such large variations exist. This current study found no significant correlation between height or age and excursion. However, such a small sample size and skewed younger age group in this study may have impacted upon the robustness of such analyses and as such requires more attention in future larger scale studies. Whilst the region of the nerve analysed may have had a bearing on the amount of nerve excursion because the nerve is more compliant around the moving joint (Phillips et al. 2004), participants were measured in the same location,
and therefore the influence on distance from the joint is likely to have affected the variability between individuals. Nerves exhibit more stiffness behaviour where they branch (Millesi et al., 1995); it is possible that in some individuals where branching of the sciatic nerve into common peroneal and tibial nerves occurred more proximally, the nerve may have moved less than those whose nerve divided more distally.

Looking at differences between nerve excursion between 30 and 60 °of hip flexion, it can be seen that in 8 out of 9 male participants, there was greater nerve excursion when the hip was flexed to 60° than when it was flexed to 30°. Only subject 5 had less excursion at 60° of hip flexion than at 30°. Five out of 7 female participants also had more sciatic nerve movement at 60° compared to 30° of hip flexion. Therefore overall (in 13 participants), there was a trend to see larger amount of nerve excursion with the hip more flexed. This was not expected, as with greater range of hip flexion, it was hypothesised that more strain and less excursion of the sciatic nerve would have occurred, since increasing the nerve bed length normally has this biomechanical effect (Boyd et al., 2012; Ellis et al., 2012; Gilbert et al., 2007b; Coppieters and Butler, 2008). However, these studies looked at increasing the length of the nerve bed by adding neurodynamic components more distally or proximally, rather than comparing nerve strain and excursion in two different positions of hip flexion. In support of the present study’s findings, Dilley et al. (2003) found that during contralateral cervical flexion, proximal excursion of the median nerve in the distal upper arm was greater at 90° (greater pre-loading) than 30° shoulder abduction.

There are a few possible explanations for why this was found in the present study. Firstly, it is known that the first adaptation to movement is for the nerve above and below the moving joint to lessen their waved course by uncoiling (Millesi, 1986). Since the trunk and head were not fully flexed in the present study (as in the slump test), the nervous system was able to adapt by uncoiling proximally to the knee. With increasing range of hip flexion, the uncoiling may have fully occurred, and therefore movements of the knee resulted in a greater distal pull by the knee joint, and an increase in excursion. However, some individuals did not show this pattern of movement; for some, less
excursion occurred with the hip more flexed. This could reflect a difference in the resting slack of the nerve between individuals. If more uncoiling occurred with the hip flexed to 30°, then greater amounts of excursion would have been reached earlier, meaning that at 60° of hip flexion, the most adaptation to further movement would be by lengthening, and hence a reduction in nerve excursion would be seen compared to 30°. However, ultimately if the SLR had been performed in greater amounts of hip flexion, it is likely that a point would have been reached in all individuals, where less excursion would have been seen. Greater ranges of hip flexion were not analysed in this study since it was expected that many participants in the symptomatic study would be unable to be positioned in SLR with hip flexion greater than 60° due to pain.

**Limitations**

The limitations discussed on page 151 are relevant to the normative examination of the study’s data, but in addition some specific factors are pertinent to this section of the study. The SDD for the longitudinal nerve movements for 30 and 60° of hip flexion were 1.9mm and 2.4mm. Therefore, differences greater than these were needed to ensure a 95% chance that the differences in measurements were not due to measurement error. Since the considered differences in this current study were between the 2 hip positions, the higher of the 2 SDD measurements must be utilised. Looking at the individual differences between the 2 hip positions, 9 out of 16 participants had differences greater than 2.4mm, indicating that the differences were not attributable to error. However, differences in the remaining 5 participants were 2.4mm or less. This, together with the relatively small number of participants in this study means that caution should be taken before extrapolating to the greater population.

Difficulty in the centroid technique used for transverse plane movements were found where the outline of the nerve was less clear, or where the nerve changed shape considerably between the first and last frame in the image sequence. In the first instance, informed estimates were made on the outline. In the latter case, it is possible that errors were made in calculating the amount of movement because the centroid would be in a different part of the nerve when the nerve shape changed considerably.
7.1.3.4. Conclusion
Longitudinal sciatic nerve excursion during a modified SLR with knee extension in side lying in asymptomatic participants is variable in terms of actual amounts of nerve excursion. The direction of movement in all participants was distal, supporting previous data which has demonstrated that nerve excursion (for the nerve on the lengthened aspect of the joint) always moves in the direction of the moving joint. In some participants greater excursion occurred with the hip positioned in greater amount of flexion, suggesting differences in baseline coiling of the underlying nerves, and possibly differences between individuals in their underlying compliance. Transverse plane movement showed even greater variability, but it is not clear whether such variability is due to a true variation between individuals or due to measurement error.

The next section details the repeatability studies for the other 2 outcome measures used in the present study; vibration and pressure pain thresholds.¹⁰

7.2 Repeatability of Vibration and Pressure Pain Threshold Testing

As discussed in chapter 5, vibration thresholds (VTs) give an indication of the conduction of the large diameter afferent fibres. Pressure pain thresholds (PPTs) are a semi-objective measure of an individual’s pain response. Both have been shown to be repeatable measures (Antonacci et al., 1998; Felix and Widerström-Noga, 2009; Halonen, 1986; Hilz et al., 1998; Persson et al., 2004; Sterling et al., 2000; Vanderweeën et al., 1996), but for the purposes of the present study, it was essential to demonstrate that the current researcher was able to use these pieces of equipment repeatably, and with as small amount of error as is possible in order to ensure that any changes that occurred in the clinical study were associated with the treatment technique and not measurement error.

¹⁰ These studies were presented at IFOMPT 2012 conference in Quebec, Canada (see appendix 32 for full details)
7.2.1. Method

Participants and Recruitment

Eleven participants (6 females, mean (SD) age 37.64 years (11.4) see table 7.5 for demographics) between the ages of 18 and 65 complaining of spinally referred leg pain were recruited through University of Brighton email, and posters displayed around the University Campus at Eastbourne. Participants were asked to refrain from taking caffeine, alcohol and any over the counter analgesics for 24 hours prior to testing as this may have influenced the PPT and VT measurements.

Inclusion criteria were that their leg pain was due to referral of pain from their lumbar spine, had been present for at least three months, and that they were not currently undergoing any treatment for their pain. Exclusion criteria included any serious spinal pathology, systemic illness (such as cancer, diabetes or rheumatoid arthritis), any known neuropathy or were pregnant.

All participants were asked to read an information sheet and sign a consent form if happy to proceed (appendix 16)

Ethical approval was gained from the Faculty of Health and Social Sciences Research Ethics and Governance Committee at the University of Brighton (appendix 17).

Equipment

A Vibrameter (Somedic AB, Sweden) was used to assess the VT of each participant. The tissue displacement range was 0.1-400µm and frequency was set at 100Hz (x2 AC).

The tracker freedom wireless algometer (J Tech Medical Salt Lake City, U.S.A.) was utilised to assess pressure pain thresholds. The algometer has a 1cm² metal tip which is applied perpendicular to the testing area, and a pacer which allows the rate of pressure to be controlled at 1kg/sec. The participants press a hand plate which freezes the value at the point of change of pressure to discomfort.
Procedure

The area was screened for privacy and each participant was asked for details of their current referred leg pain problem (onset, previous episodes, previous treatment, pain levels and effect of movements on pain level and duration of pain) as well as for any previous history that may have limited them from participating in the study (as above).

Participants were asked to wear shorts and a vest top. Height and weight of each participant was measured. Participants lay supine on a plinth and neurological integrity tests were performed by testing light touch sensation, reflex and muscle power of the lower limbs. In addition a number of tests were conducted to ensure that the leg pain was referred from the lumbar spine. These consisted of lumbar spine active movements, lumbosacral passive accessory intervertebral movements, and SLR or slump test. If the subject’s symptoms were not reproduced on these tests, they were excluded from the study as the symptoms may not have been referred from the lumbar spine.

Participants then picked a piece of paper from a plastic bag which contained 10 pieces of paper with the letter V written on them and 10 with the letter P. If participants selected a letter V, then VTs were performed first and if they selected a letter P, PPTs were performed first.

Vibration testing

Participants were asked to lie prone on a plinth and a practice VT was obtained from the unaffected foot at the base of the plantar surface of the first metatarsal to familiarise each participant to the sensation. The probe was applied perpendicular to the body part and the weight of the probe rested fully on the participant. The vibration stimulus was increased until the participant first felt the stimulus and at this point the researcher was informed and the reading noted. The stimulus was elevated further, and then reduced again until the participant indicated to the researcher that they could no longer feel the stimulus. Once this was performed satisfactorily, the VT readings were taken from the affected base of the plantar surface of the first metatarsal. This process was repeated until three vibration perception (VPT) and three vibration disappearance values (VDT) were recorded. The participant was then asked to lie on their unaffected side and VT
readings taken from the lateral malleolus on their affected side. These sites represented a portion of the sensory supply of the lumbosacral plexus (Drake et al., 2005).

Participants were asked to inform the researcher if the probe was uncomfortable as Hagander et al. (2000) found that pressures over 100g were uncomfortable. Although the resting probe is 650g, no participants complained of discomfort at either of the testing sites.

*Pressure Pain Threshold Testing*

**PPT Sites**

PPTs were taken from the middle portion of deltoid on the unaffected side (this site was chosen because in the clinical study a change to this measurement may reflect a systemic pain relieving effect), the tibial nerve behind the knee and central point of gastrocnemius on the affected side (supplied by the lumbosacral plexus, predominantly sural and/or posterior cutaneous nerve of the thigh (Palastanga et al., 2012). To ensure that the same part of gastrocnemius was taken for each subject, the distance from the knee crease to the heel was measured, and a point marked one third of this distance from the knee crease.

**PPT Procedure**

Participants were asked to lie in prone and a practice PPT was taken from the unaffected leg over the gastrocnemius belly to familiarise the participant to PPT.

Participants were asked to lie on their affected side and the probe was applied perpendicular to middle portion of deltoid, and the pressure applied through the probe by the researcher at the rate indicated by the pacer. Participants were asked to push the hand plate when the sensation of pressure changed to one of discomfort. The participant was then asked to lie prone and the same procedure repeated for the tibial nerve behind the knee, before moving on to the gastrocnemius point. Two further readings were taken of each, giving a total of three for each site.
A break of 30 minutes between testing procedures then occurred, before the testing was repeated in the same way. This was to reflect the time between testing that would occur in the symptomatic study. Participants were asked to remain in the human movement laboratory for this period of time. They were offered water or juice to drink, but not caffeine as this may have affected the VT measurements.

**Analysis**

VTs were assessed by taking the three readings of VPT, the three readings of VDT and then taking a mean value of the 6 values. This is called the ‘method of limits’ and enhances the reliability of the measures (Goldberg and Lindblom, 1979; Halonen, 1986).

The PPTs were analysed by looking at the mean of all three readings for each site, the mean of the first and second reading and the mean of the second and third readings, as it has not been well established as to which method is most robust.

Repeatability of both techniques was assessed by looking at ICCs (2, 1), confidence intervals and standard error of measurements using SPSS software version 18. Smallest detectable differences (SDD) were calculated using the equation SDD = 1.96 x √2 x SEM (Schuck and Zwingmann, 2003). The results from the SPSS spread sheets can be found in appendix 29 and attached CD.
7.2.2. Results
All participants recruited were included in the study. Table 7.5 gives a breakdown of their characteristics.

<table>
<thead>
<tr>
<th>Subject number</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Height (m)</th>
<th>Weight (kg)</th>
<th>BMI</th>
<th>Leg affected</th>
<th>History of leg pain</th>
<th>VT or PPT first</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>59</td>
<td>F</td>
<td>1.6</td>
<td>64</td>
<td>25</td>
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<td>55 years</td>
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<td>2</td>
<td>46</td>
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<td>1.18</td>
<td>136</td>
<td>97.67</td>
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<td>92</td>
<td>24.19</td>
<td>L</td>
<td>2 years</td>
<td>VT</td>
</tr>
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</table>

Table 7.5 Demographic data for participants. Note participants 2, 4 and 10 have BMI over 26 kg/m²

Vibration Thresholds
The values for VTs for each subject for test 1 and test 2 are shown in table 7.6

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>VT TEST1 LM</th>
<th>VT TEST2 LM</th>
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<th>VT TEST2 IST MT</th>
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<td>1.148</td>
<td>1.229</td>
</tr>
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<td>0.190</td>
<td>1.250</td>
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</tbody>
</table>

Table 7.6 VT readings (µm) (LM = lateral malleolus, 1ST MT = plantar surface of first metatarsal)
**Statistical analysis**

Normality plots were performed on the data and it was found that the data for the lateral malleolus were normally distributed (Shapiro Wilk $p=0.33$ and $p=0.15$ for test 1 and test 2 respectively), but for the first metatarsal were not normally distributed (Shaprio Wilk $p=0.001$ and 0.000 respectively). Therefore, all VT data were log transformed which successfully normalised the data, and ICCs performed on the transformed data. ICCs for VT for lateral malleolus were 0.89 (95% C.I. 0.66-0.97) and for the first metatarsal ICC was 0.99 (C.I. 0.96-1). Since the data was log transformed, the SEM were not in the same units of measurement and would not make sense in relation to the raw data. Unfortunately it was not possible to inverse log the SEM to revert them back into meaningful measurements, and therefore they were expressed as a SEM of the mean of the log transformed data, and expressed as a percentage. SEM of the mean were 9.1% for the lateral malleolus and 5.2% for the first metatarsal. SDD were calculated from the SEM, and also expressed as the mean of the transformed data and were found to be 25.1% for the lateral malleolus site, and 14.4% for the first metatarsal site.

Bland Altman plots were undertaken to assess for any bias occurring between test 1 and test 2 (figs 7.9 and 7.10). A good spread around zero was found for both plots indicating good agreement (Rankin and Stokes, 1998). However, for the first metatarsal, a general increase in scores was found on the second reading. One of the data points (subject 7) lies outside the 95% lower limit of agreement in fig 7.9, and one of the data points lie outside the upper limit of agreement in fig 7.10 (subject 11).
Pressure Pain Thresholds
Since there was debate in the literature of a best method to ascertain the most accurate PPT readings, the data was analysed using different methods. The mean of all 3 readings, the mean of the mean of 1st and 2nd readings and the mean of 2nd and 3rd readings were all analysed and the values for each subject are shown in tables 7.7 to 7.9.

Fig 7.9. Bland Altman plot of vibration thresholds at the lateral malleolus for tests 1 and 2

Fig 7.10. Bland Altman plot of vibration thresholds at the plantar surface of the 1st metatarsal for tests 1 and 2
<table>
<thead>
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<th>SUBJECT</th>
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<th>PPT DELT TEST 2 M3</th>
<th>PPT DELT TEST 1 M1+2</th>
<th>PPT DELT TEST 2 M1+2</th>
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Table 7.7 PPT readings (Kg) for deltoid. M3= mean of all three readings, M1+2= mean of 1st and 2nd readings, M2+3= mean of 2nd and 3rd readings for test 1 and test 2

<table>
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<th>SUBJECT</th>
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<td>1.45</td>
<td>1.33</td>
<td>1.5</td>
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</table>

Table 7.8 PPT readings (Kg) for tibial nerve (TN) in the popliteal fossa. M3= mean of all three readings, M1+2= mean of 1st and 2nd readings, M2+3= mean of 2nd and 3rd readings for test 1 and test 2
Table 7.9 PPT readings (Kg) for gastrocnemius. M3 = mean of all three readings, M1+2 = mean of 1st and 2nd readings, M2+3 - mean of 2nd and 3rd readings for test 1 and test 2

Statistical analysis

All data was normally distributed (Shapiro Wilk test all greater than 0.05), and therefore ICCs (2,1) were performed on the data. Table 7.10 shows the ICCs, confidence intervals and SEM for PPTs for each method used.

Table 7.10 ICCs, C.I. and SEM for PPT readings

Different methods were best suited for different sites. Since the overall best method (considering that only one method was suitable for all sites, rather than different
methods for different sites) appeared to be the mean of the 2\textsuperscript{nd} and 3\textsuperscript{rd} measure\textsuperscript{11}. Bland Altman plots were plotted for this method (figs 7.11-7.13). The plot for deltoid (fig 7.11) shows a spread around zero, with no outliers. However for the tibial nerve whilst there are no points outside of the limits of agreement, there is a general trend for greater scores on the second test than the first test. A similar trend is shown for PPT of gastrocnemius.

\textbf{Fig 7.11 Bland Altman plot of PPTs taken from deltoid using mean of 2\textsuperscript{nd} and 3\textsuperscript{rd} readings for test 1 and test 2}

\textbf{Fig 7.12 Bland Altman plot of PPTs taken from tibial nerve using the mean of the 2\textsuperscript{nd} and 3\textsuperscript{rd} readings for test 1 and test 2}

\textsuperscript{11} Despite the slightly higher error measures for gastrocnemius, the ICC and 95\% CI were still considered sufficiently high
7.2.3 Discussion

The results of this study show that vibration threshold testing and PPTs on participants with spinal referred posterior leg pain are repeatable within a 30 minute retest period. The rest of this section will be divided specifically into discussion of the VT results and PPT results.

Vibration Threshold Testing

ICCs for VT at the first metatarsal were 0.99 and at the lateral malleolus 0.89. These values are considered to show excellent agreement (Fleiss, 1986). The percentage SEM compared to the mean were 9.1% and 5.2%, for the lateral malleolus and first metatarsal respectively, and SDD was 25.1 and 14.4 % for the 2 sites respectively. Such percentage error would reveal an SEM of around 0.04µm and 0.06µm and SDD of 0.17µm and 0.11µm for lateral malleolus and first metatarsal respectively. Therefore, relatively large changes (compared to the mean) would be required to show change (in 95% of cases) after an intervention to ensure that the difference is not related to error alone.

---

Fig 7.13 Bland Altman plot of PPTs taken from gastrocnemius using the mean of the 2nd and 3rd readings for test 1 and test 2
The findings of this study are supported by a number of studies (Felix and Widerström-Noga, 2009; Halonen, 1986; Hilz et al., 1998). Felix and Widerström-Noga (2009) found ICC values to be 0.87 and 0.9 in 8 different sites in both asymptomatic and symptomatic (individuals with spinal cord injury) participants respectively. Hilz et al. (1998) found a high short term retest reliability in 530 asymptomatic individuals (Spearman 0.87<Rs<0.99) indicating a good to excellent relationship between tests. Slightly lower correlation re-test reliability values (r=0.77) were found for 78 individuals with diabetes (Valk et al., 2000). Importantly SDD were found to be in the region of 9%, these are the same as those found for the lateral malleolus but higher than the first metatarsal.

Taken together the strength of evidence suggests that VTT is repeatable for both measuring sites, but with relatively high error measures (25% and 14% for each site respectively).

**Pressure Pain Threshold**

Since there appeared to be no superior method of establishing PPT from the literature, it was decided to establish the reliability for three separate methods; taking the mean of all 3 readings for each site, the mean of the first and second reading, and the mean of the second and third reading. The best ICC, SEM and SDD values for the deltoid site were established for the mean of 3 readings (ICC 0.87, SEM 0.52, SDD 1.44), for tibial nerve were the mean of the second and third (ICC 0.9, SEM 0.52, SDD 1.44), whilst for gastrocnemius it was the mean of the first and second readings (ICC 0.96, SEM 0.43, SDD 1.19). Such values indicate that agreement for deltoid was good, and excellent for the other two sites (Fleiss, 1986). However, using 3 different methods to assess PPT in each of the 3 sites, would not be feasible in the clinical study, and therefore a pragmatic decision was required.

The ICC values for gastrocnemius were above 0.9 for all methods, although the lowest ICC and highest SEM values were for using the second and third readings. The deltoid site also showed similarities in all three measures, but the lowest ICC and highest error
were for the first and second readings. However, for tibialis anterior ICC dropped from 0.9 for the mean of 2\textsuperscript{nd} and 3\textsuperscript{rd} to 0.78 for the mean of 3 readings, and further to 0.66 for the mean of the first and second readings. Therefore, the only acceptable measure for tibialis anterior site was the mean of the 2\textsuperscript{nd} and 3\textsuperscript{rd} readings. Since acceptable ICC and error measures were found for the other 2 sites using this method, the most acceptable method to carry over into the clinical study was the mean of the 2\textsuperscript{nd} and 3\textsuperscript{rd} readings.

Persson et al., (2004) also recommended ignoring the first of four PPT reading in a study on 27 healthy female volunteers tested on deltoid and upper fibres of trapezius. This reading was found to be significantly lower than the other readings, with no other significant differences being found on subsequent measures.

This study suggests that intra tester repeatability is good to excellent over deltoid, gastrocnemius and the tibial nerve behind the knee. High intra tester reliability of PPT testing has also been found by a number of authors (Antonaci et al., 1998; Persson et al., 2004; Sterling et al., 2000; Vanderweeën et al., 1996).

Vanderween et al., (1996) found that intra tester reliability of 14 different trigger point areas around the body ranged from ICC of 0.64-0.96, which represents moderate to excellent reliability (Fleiss, 1986), but did not indicate which sites showed moderate ICCs and which were excellent. In addition, no error or CI data was presented and so direct comparison between these results and the present study are limited. A similar spread of ICC values were found by Persson et al. (2004), (ICC 0.7-0.94), depending on whether each reading was compared with each other or a mean of 3. However, it was difficult to decipher which ICC corresponded to which comparison in measurements. In addition, the study participants were all female, and therefore the results cannot be compared precisely to the results of the present study. Almost identical intra tester ICC values to Persson et al.’s (2004) were found for PPT s around the head and shoulder region by Antonaci et al., (1998). The ICCs ranged from 0.75 to 0.91, the lowest being in masseter muscle, the highest over the greater occipital nerve.
The Bland Altman plots demonstrated that deltoid showed most even spread around zero, indicating good agreement between the first and second test (fig 7.11). Both tibial nerve and gastrocnemius plots, however showed a greater tendency for measures to be higher on the second test, indicating that in a repeated measures trial like the clinical study, any increases in PPT could be attributed to an adjustment in individual’s perception of PPT. However, taking the SDD into account when considering the effects of a rise in PPT post-intervention, would compensate for this effect.

Choosing the method of taking the mean of the second and third measurements, the SDD of this study were 1.5, 1.44 and 1.75 kg respectively. When one considers the mean values for the PPTs obtained, these error measures are relatively high (33% for deltoid and tibial nerve and 37% gastrocnemius). Hence any differences in measures before and after the SLR intervention in the clinical study needed to be greater than these figures in order that a change could be attributed to a treatment effect and not error. Compared to other studies, these values fall between those of Krouwel et al. (2010) and Willett et al. (2010) and Pentelka et al. (2012). Willett et al. (2010) found SDD values of 0.5 kg/cm² at the foot and 0.53 kg/cm² at the thigh, whilst Krouwel et al. (2010) also found low values for SDD (0.47 at a quadriceps site and 0.44 at a deltoid site). In contrast Pentelka et al. (2012) had higher SDD than the ones found in the present study (1.94 at deltoid, 2.55 in the lower leg and 2.53 in the foot). The reason for such wide variation in SDD is not clear. All participants in the 3 aforementioned studies used asymptomatic participants, but still showed marked variation in the SDD. Participants in the present study had higher BMI readings and age than participants in Krouwel et al.’s (2010) study (mean age 26.43, BMI 22.54 Krouwel et al., 2010, 37.64 years, BMI 30.61 current study). However, similar mean ages as the present study but lower BMI were found by both Willett et al., (2010) and Pentelka et al., (2012) (mean age 33.05, BMI 26.2 Willett et al., 2010, 37.63 years, BMI 23.9 Pentelka et al., 2012). This suggests that higher levels of error are not attributed to age or BMI.

As indicated in chapter 5, the consideration of BMI has been taken into account by some when measuring PPTs (Letchuman et al., 2005). Three participants had BMI greater
than 26 kg/m² (participants 2, 4 and 10), and of these, 2 had greater than 32 kg/m² (participants 2 and 4). Such small numbers of participants meant that statistical analysis of changes in PPT related to BMI was not appropriate. Subject 2 had double the mean value of PPTs for gastrocnemius, and 33% higher mean values for deltoid, whilst PPT values for tibial nerve were about average. Subject 4 had elevated deltoid PPTs of around 33%, but lower than average PPTs for the tibial nerve and average values for gastrocnemius. Subject 10 had average PPTs for gastrocnemius, very slightly higher values for tibial nerve, and lower than average values for gastrocnemius. Whilst these results cannot be considered strong evidence to support a change in PPTs with increasing BMI, subject 2 had a BMI of 97.7 and markedly higher PPTs for the two areas which have large amounts of soft tissue covering them. Subject 4 was just over Letchuman et al.’s (2005) cut off point and had considerably high deltoid values, but average values for gastrocnemius. The results in this study suggest that an elevation in BMI may cause an elevation in PPT especially in soft tissue sites. However, to exclude participants with BMI over 26 kg/m² in a spinally referred leg pain population, would possibly exclude too large a number of representative individuals. In studies where participants with increased amounts of BMI are included, BMI should be accounted for in the statistical analysis.

To summarise, this study suggests that the use of PPTs in the locations chosen for the clinical study are repeatable, but with relatively high error measurements in the region of 33-37%. Whilst each site’s repeatability was better for different methods of analysis, the mean of the 2nd and 3rd readings was acceptable for all 3 sites. Hence the mean of the second and third readings was chosen in the clinical study. BMI may increase PPT at sites where there is a greater amount of soft tissue, and should be taken into account in studies where BMI is not an exclusion criteria.
7.3 Chapter Conclusion

This chapter has provided evidence to support the use of the 3 outcome measures in the clinical study. Validity of the frame-by-frame cross correlation method for measuring nerve excursion demonstrated high levels of accuracy as compared to photography. Repeatability of the method was demonstrated for measuring longitudinal sciatic nerve excursion during a modified SLR in side lying. The repeatability of the transverse plane motion was not assessed, since the method of analysis published by Boyd et al. (2012) was not available until after data collection had taken place. However, a descriptive analysis of the results using a method where the nerve outline was drawn and movement analysed showed marked variability between asymptomatic individuals. Less variability was demonstrated for longitudinal nerve excursion, although differences were found between individuals. Some individuals had more nerve excursion with greater amounts of hip flexion, indicating that pre-tensioning the nerve does not always result in less nerve excursion. However, it is thought that if the hip had been flexed more, a point would have been reached where reduced nerve excursion (and relatively greater strain) occurred in all participants.

VTT and PPT demonstrated acceptable repeatability for all measures at all sites. However there was a tendency for greater VT after the first reading at the lateral malleolus, although the differences were small. PPT at the tibial nerve and gastrocnemius also demonstrated an increase on the repeat test, and relatively high SDD. Such error measures were required to be taken into account in the clinical study.

The next chapter details the clinical study that was undertaken as the main study for this PhD thesis.
Chapter 8 Straight Leg Raise treatment for individuals with spinally referred leg pain: exploring characteristics that influence outcome.

The overall aim of the present study was to determine what effects a 3 x 1 minute SLR tensioner treatment had on pressure pain thresholds, vibration thresholds and sciatic nerve excursion between 3 different sub-groups of individuals with spinally referred leg pain. In order for this to be achieved, individuals were first assessed by clinicians to establish suitability for the study and to appropriately sub-group. In addition, since a secondary aim was to assess if the presence of central sensitisation was different between the 3 groups and interacted with the effect of treatment, clinicians assessed participants to determine the presence of central sensitisation. By doing so, the researcher was blinded to each participant’s status. Participants then attended a second appointment where the effects of a SLR treatment were analysed using ultrasound imaging of the sciatic nerve during a side-lying SLR test, VTs to assess nerve conduction of the large diameter afferents, and PPT to assess changes to pain sensitivity. Data collection occurred from August 2012 to September 2013.

8.1 Method

Study Design

The study was an experimental, repeated measures design.

Sample Size Analysis

A power analysis was performed from the reliability nerve excursion data and indicated that a sample of 75 was required (25 in each group). This number was based on a 20% effect size with a power of 0.8 and α of 0.05. The calculation was performed in Minitab (One Way ANOVA), where the 20 % size of the effect was 1.98mm and standard deviation was 2.2, based on the mean and standard deviation data from the repeatability study (mean 9.92).
**Participants**

Participants fulfilled the inclusion criteria of referred leg pain in the posterior thigh and/or lower leg (in the lumbosacral nerve root distribution) with or without low back pain and under the age of 70 years without other medical problems such as diabetes, rheumatoid arthritis or other systemic disorders (see appendix 18 for full list of exclusion criteria). In addition, participants whose condition was considered to be severe or irritable (see appendix 26) were also excluded, to avoid exacerbating their symptoms during the study. Participants were recruited from both within and outside of the NHS to optimise numbers of participants.

**NHS participant recruitment**

Participants were recruited from the Physiotherapy waiting lists of 3 NHS trusts within Sussex, but the exact recruitment process was dependent on the trust. Two of the trust sent out letters of invitation (see appendix 20), information sheets and consent forms to potentially suitable patients alongside the standard Physiotherapy appointment letters. One trust telephoned patients directly, and if they expressed an interest in participating, the information sheet and consent form was posted or emailed out to them. Interested participants returned the signed consent form directly to the researcher. The researcher then contacted the Physiotherapists at the relevant Trust, who contacted the participants to organise their first Physiotherapy appointment.

**Non-NHS participants Recruitment**

Participants with spinally referred leg pain, who were not currently undergoing treatment for their pain, were also recruited via email within the University of Brighton, newspaper adverts in local weekly newspapers, social networking sites (Facebook and twitter) and posters displayed in various local establishments. The researcher discussed the study directly with any interested individuals and sent an information sheet and consent form for their consideration. Participants then contacted the researcher if they were still interested in participating in the study.
Ethical approval and Research Governance

Ethical approval was gained from both the University of Brighton Faculty of Health and Social Science Research Ethics and Governance Committee and NHS ethics (NRES), with research and development approval from each of the three trusts (see appendices 21 to 25). Regardless of the recruitment process, all participants were given an information sheet to read (at least 24 hours prior to consenting) and signed a consent form prior to their initial assessment by the Physiotherapist (appendices 18 and 19).

Initial Procedure: Part 1 Physiotherapy Assessment

Physiotherapists and training.
The Physiotherapists (6) who performed the examination procedures were experienced clinicians (band 6 or above), with at least 4 years clinical experience. One had a postgraduate manual therapy qualification, and 3 were close to completing their postgraduate manual therapy qualification. Prior to the commencement of the study, the researcher attended each of the trusts on 2 occasions to discuss the study with the Physiotherapists and to go through the sub-grouping procedure and assessment of central sensitisation. One Trust asked for a third visit, to ensure that all Physiotherapists were comfortable and competent with the procedure. The Physiotherapists who assessed the patients at the University were current postgraduate students on the MSc Neuromusculoskeletal Physiotherapy programme, with a minimum of 4 years clinical experience. Training was given to each of these therapists on a one to one basis.

Patient Assessment and sub-grouping
Participants were seen either in the Physiotherapy Department of one of the 3 NHS Trusts or in one of the practical teaching rooms in the School of Health Professions, University of Brighton. Screens or curtains were placed around the participant to ensure privacy during the assessment. A full subjective and physical examination of the patient was performed by the physiotherapist. The procedure was the same as if the patient was attending for a standard Physiotherapy assessment. However, if participants complained of more than 2 signs of central sensitisation (pain for longer than 6 months (O'Neill et
al., 2007), widespread areas of pain (Jensen et al., 2010), hypersensitivity to warmth or cold (Berglund et al., 2002), and hypersensitivity to touch (Jensen et al., 2010; O’Neill et al., 2007), an additional examination of painful points was also performed by the Physiotherapist (see appendix 27). The Wagner algometer was placed on each of the points, and the pressure increased up to 4kg/cm². If more than 8 of the points were painful, the participants were considered to be centrally sensitised.

The physiotherapist who assessed the patient then allocated the participants into one of the 3 groups: radiculopathy, radicular pain or somatic referred pain, based on predetermined criteria (Appendix 26). The participant was placed in the radiculopathy group if they had positive neurological integrity tests (myotomal weakness, sensory loss in a dermatomal pattern, and reduced reflex). Participants were allocated to the radicular group if they had negative neurological integrity tests, but a positive SLR or slump test (indicated by reproduction of the participant’s symptoms that was aggravated or relieved by a structural differentiation manoeuvre (e.g. ankle dorsiflexion/ release of ankle dorsiflexion)) +/- tenderness on 2 regions of nerve palpation. Individuals with somatic referred pain were identified by a negative neurological integrity test, negative SLR or slump test, and leg pain reproduced through stressing spinal structures e.g. on active movements of the spine and spinal passive accessory intervertebral movements (PAIVMS).

The therapist then informed the researcher whether the participant fulfilled all inclusion and exclusion criteria and asked if they were happy to proceed (written, informed consent had already previously been given), and gave the participant’s contact details to the researcher. A form with the individual’s main assessment details (appendix 28) was completed and coded by the physiotherapist who assessed the patient. The individual’s name and contact details were completed on a separate form with their personal code. The 2 sheets were not compared until after the laboratory part of the study and analysis of the data. In this way, the researcher was blinded to the sub-group allocation until after the analysis of each participant was completed.
Psychosocial and disability Questionnaires

Participants were given 5 questionnaires by the Physiotherapist to complete between the initial assessment and the laboratory procedure. If patients had queries or difficulties in completing the form, they were given support by the researcher when attending the laboratory for the second part of the study. The questionnaires consisted of the Fear avoidance belief questionnaire (FABQ), Tampa scale of kinesiophobia, Oswestry disability index (ODI), Depression, anxiety and stress scale (DASS), and pain catastrophising scale (PCS) (see appendices 6-10, and chapter 2.5.3 for rationale and details).

**Part 2 Laboratory study**

Participants attended the laboratory normally within one week of the initial assessment. Occasionally individuals were not able to attend for up to one month after the initial appointment, and in this case, individuals were asked to notify the researcher if there had been any change in their symptoms over the course of that time frame. All NHS patients were seen in the laboratory within a week of the initial physiotherapy appointment to ensure no disruption to their physiotherapy management. Where physiotherapists felt that participants needed to be seen again for their follow up physiotherapy appointment within one week, participants were excluded from the study. All data was collected by the researcher with help from a research assistant.

**Instruments**

*For nerve excursion measurements*

A Titan ultrasound machine (SonoSite Ltd, Hitchin, UK) with a 5-10MHz linear array transducer was used to scan the sciatic nerve in the posterior thigh. An image grabber (Global lab image with a 25f/s capture rate) was connected to the video output of the ultrasound in order to digitally save image sequences captured by the ultrasound.
A universal goniometer was used to measure the position of the knee during the modified SLR. A purpose made jig was used to enable the hip to be positioned in 30 and 60° of hip flexion, and the knee allowed to move from 90° through to 0° (see fig 7.4).

For Pressure Pain Thresholds

The tracker freedom wireless algometer (J Tech Medical Salt Lake City, U.S.A.) was utilised to assess PPTs. The algometer has a 1cm² metal tip which is applied perpendicular to the testing area, and a pacer which allows the rate of pressure to be controlled at 1kg/sec. Participants press a hand plate which freezes the value at the point of change of pressure to discomfort.

For Vibration Thresholds

A Vibrameter (Somedic AB, Sweden) was used to assess the VT of each participant. The tissue displacement range was 0.1-400µm and frequency was set at 100Hz (x2 AC).

Procedure

Participants were reminded of the full procedure and informed that the procedure would take around one and a half hours. They were asked if they had any questions about the study, and if they were happy to proceed.

Baseline measures

All participants had their height and weight measured for additional demographic data by the research assistant.

Vibration threshold Measures

Participants were asked to lie prone on a plinth and a practice VT was obtained from the unaffected side on the plantar surface of the base of the first metatarsal. The purpose of
this practice session was to familiarise each participant with the sensation. The vibrameter probe was placed perpendicular on the base of the first metatarsal so that the weight of the probe rested fully on the area. The vibration stimulus was slowly increased until the participant felt the onset of vibration. The stimulus was then increased before being reduced again until the participant could no longer feel the sensation. Once a consistent measure (within 10% of each measure) had been demonstrated, VT readings were taken from the affected side on the base of the plantar surface of the first metatarsal. Three vibration appearance values and 3 disappearance values were taken. The participant was then asked to lie on their unaffected side and VT readings were also taken from the lateral malleolus of the affected side. All VT measures were taken by the researcher, and notated by the research assistant.

Pressure pain threshold Measures

PPTs were taken from the middle portion of the deltoid muscle on the unaffected side, the tibial nerve behind the knee, and a central point of gastrocnemius on the affected side. To ensure that the same part of gastrocnemius was taken for each subject, the distance from the knee crease to the heel was measured, and a point marked one third of this distance from the knee crease.

Participants were asked to lie prone and a practice PPT was taken from the unaffected leg over the gastrocnemius belly and tibial nerve to familiarise the participant to PPT. Participants were then asked to lie on their affected side and the probe was applied perpendicular to middle portion of deltoid and the pressure applied through the probe by the researcher at the rate indicated by the pacer (1kg/sec). Participants were asked to push the hand plate when the sensation of pressure changed to one of discomfort. The participant lay prone and the same procedure was repeated for the tibial nerve behind the knee, before moving on to the gastrocnemius point. Two further readings were taken from each site, giving a total of three for each site. The researcher performed all PPT measurements.
For each subject the order in which the PPT or VT was performed was randomly allocated by asking the participant to pick a piece of paper out of a bag that contained equal numbers of papers with either a V or P written on. If V was selected, then VT was performed first.

Sciatic Nerve Excursion
The participant lay supine on the plinth and an ankle foot orthosis was placed on each foot, so that the ankle joints and rear foot were positioned in neutral. The participant lay on their unaffected side on the jig. The hip joint was positioned over the hinge of the jig so that the initial hip position was 30° of flexion and the hip was secured. The knee was passively fully extended and maintained in this position and the position marked by drawing a line on the jig posterior to the heel (in line with the AFO). The underneath leg was straightened and secured with straps, and the trunk was secured to the back plate of the jig to keep the lumbar spine in neutral flexion/extension (see fig 7.4). The head and neck were positioned in neutral flexion/side flexion. The knee was then flexed to 90° (measured by the Universal goniometer) and the position marked on the jig in pencil as described above. The knee was then extended to 45°, 20° and full extension and positions were marked on the jig again as described.

The ultrasound transducer was placed on the mid-posterior thigh (see fig 7.4), and the sciatic nerve was identified approximately 10 cms distal to the gluteal fold (Bruhn et al., 2008) on a line between the ischial tuberosity and the greater trochanter (Karmakar et al., 2007). The transducer was orientated in the transverse plane and an ultrasound image of the sciatic nerve was acquired in cross section. The knee was passively extended in two stages by the research assistant; 1) 90° to approximately 45° of knee extension, and 2) 45° to full extension.

The transducer was then rotated into the sagittal plane and an ultrasound image of the sciatic nerve in longitudinal section was acquired. The knee was passively extended by the research assistant in three separate stages; 1) 90° to approximately 45° of knee extension, 2) 45° to approximately 20° and 3) 20° to full extension. In this way, both
transverse and longitudinal movements of the sciatic nerve were captured by the ultrasound during SLR and concurrently saved digitally as image sequences by the attached image grabber. If pain was produced before full knee extension was reached, the knee movement was stopped at this point. This same terminal range of knee extension was used post-intervention, to ensure that any nerve excursion changes were not due to differences in final range of motion. All ultrasound scans were taken by the researcher.

The subject’s hip was then positioned in 60° of flexion, and the full procedure was repeated in the same way as described above.

_Treatment procedure_

The SLR treatment was undertaken by the researcher, whilst the research assistant timed each set of mobilisations. Participants lay supine on the plinth with their ankles maintained in the AFO on both sides and the affected knee extended. The affected hip was flexed to the point of a change to symptoms (onset or increase in resting symptoms), or if there was no change in symptoms, to the point where the researcher could not further increase range of hip flexion due to resistance (R2). If symptoms were still not reproduced, medial rotation and adduction were added until either symptoms occurred or resistance limited further movement. The knee was then flexed until symptoms subsided (if present) and the treatment consisted of the knee being extended to the point of symptom onset and off again repeatedly (a knee joint mobilisation in SLR position). If no symptoms were produced, the knee was flexed and extended in and out of end range resistance of the knee. A grade III- to III+ mobilisation (large amplitude into tissue resistance (Petty, 2011b) was performed. The rationale for large amplitude grades of movement was to have the most effect on proprioceptive afferents which may help to reduce pain via the pain gate mechanism or descending inhibitory pain mechanisms (Schmid et al., 2008), and also it has been proposed that theoretically these techniques could improve a number of variables including blood flow, venous return and oedema (Schmid et al., 2012; Shacklock, 2005a). In addition, mobilising soft tissue in resistance is thought to cause a temporary increase in length due to the effects of
creep and hysteresis (Lee and Evans, 1992), and creep characteristics have been demonstrated in peripheral nerve (Millesi et al., 1995; Wall et al. 1991). A treatment dose of 3 x 1 minute mobilisations were performed, with a 1 minute rest between mobilisations. The choice of treatment time has not been established to date for neurodynamic mobilisation. This choice was informed purely by routine clinical practice, and previously used by the researcher (Ridehalgh et al., 2005).

Post Treatment Measures
VT, PPT and nerve motion measures during the side lying SLR test were then repeated immediately after the treatment intervention as described above for baseline measures.

Analysis
Vibration threshold
Three appearance and 3 disappearance values were taken, as described under procedure, and the mean of these measures taken to give the final VT reading. This follows the method of limits (Goldberg and Lindblom, 1979; Halonen, 1986) previously described in 7.2.1. Repeatability was found to be excellent (see section 7.2).

Pressure pain threshold analysis
Three PPT readings were taken from each site. The first reading was discarded and the mean of the second and third measures used for the final reading of each site. This method was found to enhance the reliability of PPT measures as discussed in section 7.2.

Image analysis
The ultrasound images sequences of the nerve in cross-section were imported into Image J (Rasband, W.S., Image J, U. S. National Institutes of Health, Bethesda, Maryland, USA, http://imagej.nih.gov/ij/, 1997-2012), and the borders of the nerve were manually outlined. The programme allows identification of the location of the most central pixel (“centroid”) in the nerve (Alshami et al., 2009; Boyd et al., 2012). The location of the centroid from the first frame is then compared to the last frame of the image sequence to
calculate the amount of transverse plane motion. To prevent over- or under- estimation of movement, the amount of subcutaneous tissue movement was calculated and subtracted from the nerve motion using the frame-by-frame cross correlation programme described below (Dilley et al., 2001). This process was carried out for each of the two knee movements, and added together to produce the overall medial/lateral and superficial movements for knee extension from 90 to 0° for both hip positions. In some cases, where the borders of the nerve were not clear, the centroid method appeared to be markedly inaccurate compared to visual inspection of the image sequence. In these cases, the analysis of the transverse plane movement was done by using the cross-correlation technique described for the longitudinal images below.

The ultrasound image sequences of the nerve in longitudinal section were imported into Matlab (Mathworks Inc, Natick, MA) and analysed using frame-by-frame cross correlation as developed by Dilley et al. (2007). The detailed description of the cross-correlation procedure can be found in section 7.1, but in brief the procedure involved manual selection of three to four overlapping regions of interest within the nerve (Korstanje et al., 2010). These regions were subsequently automatically tracked throughout the image sequence, resulting in the calculation of longitudinal excursion of the nerve (see Fig 7.7). Excellent reliability of the technique was previously demonstrated (Ridehalgh et al., 2012, see appendix 31 and section 7.1).

Total longitudinal nerve excursion was calculated by adding the data from the three steps of the knee extension protocol during each hip position. Hence, for each subject, total longitudinal nerve excursion was calculated for the hip at 30° moving the knee from 90 to 0° of flexion, and for the hip at 60° moving the knee from 90 to 0°.

The scans were coded so that the researcher was blinded to participant and group allocation, and also to pre and post measures during the analysis process.

**Statistical Analysis**

The data was analysed to ensure normality using the Shapiro Wilk test. Baseline comparisons were made using Pearson’s correlation coefficients and Kendall’s tau, for
data which was not normally distributed. Baseline differences were analysed by one way ANOVA or for non-normally distributed data Kruskall Wallis, and for nominal data Chi square test was used. Differences between the 3 outcome measures, and between the 3 sub-groups were analysed using a 3 way mixed factorial ANOVA (time and site/hip position the within subject variables, and group the between subject variable) with subsequent covariate analysis to assess for any factors which influenced the outcomes. Post hoc testing was performed using Sidak corrected post hoc tests, unless indicated otherwise, and contrasts where appropriate. To minimise the chance of a type I error for the covariate analysis, assumption of homogeneity of regression slopes was tested. To compare the normative longitudinal nerve excursion data to that of the symptomatic groups, a one way ANOVA was utilised with Gabriel post hoc testing. All p values were considered significant at p<0.05 level.
**Fig 8.1 Flow chart of method**

1. **Physiotherapist - Full subjective and physical assessment**
   - Positive neurological integrity of one spinal level
     - **Radiculopathy**
   - Negative neurological integrity, positive SLR or slump +/- nerve palpation
     - **Radicular pain**
   - Negative neurological integrity and SLR/slump test. Pain reproduced on stressing lumbosacral spine
     - **Somatic pain**

2. 2 signs of central sensitisation and >8 painful points
   - **Central Sensitisation**

3. Psychosocial questionnaires completed

4. **Laboratory – height and weight measured**
   - PPT Assessment-3 measures
     i. contralateral deltoid
     ii. ipsilateral tibial nerve
     iii. ipsilateral gastrocnemius
   - VTT Assessment-3 measures
     i. plantar surface base 1st metatarsal
     ii. lateral malleolus
   - Sciatic Nerve excursion during modified SLR with real time ultrasound
     i. Hip flexed to 30°
     ii. Hip flexed to 60°

5. **SLR Treatment**
   - hip flexed to P1/R2. Knee flexion/extension grade III, 3 X 1 minute

6. **Repeat Outcome measures**
8.2 Results

Baseline data
A total of 117 participants contacted the researcher in response to letters of invitation or in response to advertisements, emails or displayed posters. Forty three of these participants were excluded due to existing conditions such as diabetes, central canal stenosis and rheumatoid arthritis, and others due to being over the age of 70. A further 6 were excluded after the Physiotherapy assessment either because their leg pain was not spinally referred, or they had symptoms suggestive of other neurological disorders which required further investigation. One participant was excluded due to their symptoms resolving between the Physiotherapy assessment and laboratory appointment. The final number of participants for the study was 67; 13 of these were recruited from Physiotherapy waiting lists, and 54 were recruited from outside of the NHS. Table 8.1 highlights the numbers in each group, and the demographic details of all participants. There were no baseline differences in any of the variables between groups except for age and pain below the knee. Post hoc testing of age using Gabriel’s pairwise test (Field, 2013, pg 458) found no significant differences between the 3 sub-groups (see below). For pain below the knee, observing the mean values of the 3 groups, it can be seen that the significance lies with the somatic group, having a marked lower percentage of individuals with pain below the knee than radicular or radiculopathy groups.
<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Somatic</th>
<th>Radicular</th>
<th>Radiculopathy</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>67</td>
<td>11</td>
<td>33</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.9 (13.3)</td>
<td>57.5 (10.6)</td>
<td>48.5 (13.2)</td>
<td>57 (13.1)</td>
<td>0.027*</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>49.3</td>
<td>54.5</td>
<td>51.5</td>
<td>43.5</td>
<td>0.78^b</td>
</tr>
<tr>
<td>Pain below knee (%)</td>
<td>70.1</td>
<td>18.2</td>
<td>75.8</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>Pain duration (years)</td>
<td>2.7 (4.9)</td>
<td>3.1 (5.9)</td>
<td>3.1 (5.7)</td>
<td>2 (2.8)</td>
<td>0.422*</td>
</tr>
<tr>
<td>NHS Patients (%)</td>
<td>19.4</td>
<td>25</td>
<td>21.2</td>
<td>13.04</td>
<td>0.58^b</td>
</tr>
<tr>
<td>BMI</td>
<td>27.1 (4.6)</td>
<td>25.4 (3.6)</td>
<td>27.2 (4.9)</td>
<td>27.8 (4.6)</td>
<td>0.36^a</td>
</tr>
<tr>
<td>Disability (ODI)</td>
<td>17.3 (10.1)</td>
<td>16.3 (7.9)</td>
<td>17.5 (8.1)</td>
<td>17.4 (13.5)</td>
<td>0.94^a</td>
</tr>
<tr>
<td>Fear avoidance physical activity (FABQ)</td>
<td>10.4 (4.9)</td>
<td>11.6 (4.2)</td>
<td>10.3 (4.8)</td>
<td>10.2 (5.5)</td>
<td>0.79^a</td>
</tr>
<tr>
<td>Fear avoidance work (FABQW)</td>
<td>9.2 (8.4)</td>
<td>5.7 (7.2)</td>
<td>9.2 (9)</td>
<td>10.8 (7.9)</td>
<td>0.26^a</td>
</tr>
<tr>
<td>Pain Catastrophising (PCS) Total</td>
<td>8.7 (8.9)</td>
<td>5.8 (3.8)</td>
<td>9.2 (8.9)</td>
<td>9.4 (10.5)</td>
<td>0.5^a</td>
</tr>
<tr>
<td>PCS Ruminations</td>
<td>1 (5)</td>
<td>1 (4)</td>
<td>1 (5)</td>
<td>2 (6)</td>
<td>0.5^c</td>
</tr>
<tr>
<td>PCS Magnification</td>
<td>2 (3)</td>
<td>2 (2)</td>
<td>2 (3)</td>
<td>2 (2)</td>
<td>0.46^c</td>
</tr>
<tr>
<td>PCS Helplessness</td>
<td>2 (3)</td>
<td>2 (2)</td>
<td>2 (5)</td>
<td>2 (4)</td>
<td>0.71^c</td>
</tr>
<tr>
<td>Depression (DASS21)</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>1 (6)</td>
<td>0.72^c</td>
</tr>
<tr>
<td>Anxiety (DASS21)</td>
<td>1 (3)</td>
<td>1 (2)</td>
<td>2 (3)</td>
<td>1 (3)</td>
<td>0.69^c</td>
</tr>
<tr>
<td>Stress (DASS21)</td>
<td>4.8 (3.8)</td>
<td>3.9 (3.2)</td>
<td>5.3 (3.7)</td>
<td>4.5 (4.2)</td>
<td>0.54^a</td>
</tr>
<tr>
<td>Kinesiophobia (Tampa)</td>
<td>33 (10)</td>
<td>34 (10)</td>
<td>33 (10)</td>
<td>35 (11)</td>
<td>0.59^c</td>
</tr>
</tbody>
</table>

**Table 8.1 Baseline characteristics for the study participants**

^aOne Way ANOVA, data given is means and standard deviations  * post hoc testing revealed no sig diffs between groups (somatic v radicular $p = 0.114$, somatic v radiculopathy $p = 0.999$, radicular v radiculopathy $p = 0.051$).

^bChi Square Test

\*Kruskall Wallis, data not normally distributed and data given is median and interquartile ranges

Key: BMI body mass index, ODI Oswestry disability scale, DASS disability anxiety and stress scale.
8.2.1 Correlations within the data

The data were explored to assess any significant relationships between the 3 outcome measures (PPT, VT and sciatic nerve excursion) and all other variables. The strong, significant correlations were found for the PPT and VT readings, but not the longitudinal nerve excursion and can be found in table 8.2. Details of all other significant, but weak correlations and non-significant correlations can be found in attached CD.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Type</th>
<th>Correlation coefficient</th>
<th>P value</th>
<th>Confidence interval</th>
<th>r²</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTLM pre : age</td>
<td>Pearsons</td>
<td>0.554</td>
<td>0.000</td>
<td>0.37-0.71</td>
<td>0.307</td>
</tr>
<tr>
<td>VTLM post: age</td>
<td>Pearsons</td>
<td>0.501</td>
<td>0.000</td>
<td>0.31-0.67</td>
<td>0.25</td>
</tr>
<tr>
<td>VT1MT pre: age</td>
<td>Pearsons</td>
<td>0.467</td>
<td>0.000</td>
<td>0.27-0.63</td>
<td>0.22</td>
</tr>
<tr>
<td>VT1MT post: age</td>
<td>Pearsons</td>
<td>0.446</td>
<td>0.001</td>
<td>0.22-0.63</td>
<td>0.199</td>
</tr>
<tr>
<td>PPT deltoid pre: BMI</td>
<td>Pearsons</td>
<td>0.403</td>
<td>0.003</td>
<td>0.14-0.63</td>
<td>0.16</td>
</tr>
<tr>
<td>PPT gastrocnemius pre: BMI</td>
<td>Pearsons</td>
<td>0.45</td>
<td>0.001</td>
<td>0.19-0.66</td>
<td>0.203</td>
</tr>
<tr>
<td>PPT gastrocnemius post: BMI</td>
<td>Pearsons</td>
<td>0.423</td>
<td>0.001</td>
<td>0.19-0.63</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Table 8.2 Correlations between outcome measures and other factors

Key: VTLM vibration threshold from lateral malleolus, VT1MT vibration thresholds 1st metatarsal.

Main Analyses

Pressure Pain Thresholds

Mean (SD) pre and post SLR treatment PPT readings and mean differences (SD) can be found in table 8.3. Very small differences in PPT can be seen for all sites and subgroups. It can also be seen that there are large standard deviations, suggesting marked variation in response to SLR treatment between individuals. Looking at the individual differences (attached CD), some individuals demonstrated an increase in PPT post treatment, and others a decrease in PPT. It has been suggested that this represents
responders and non-responders to treatment (Farrar et al., 2006), and to analyse this further a cumulative proportion of responders analysis was performed (Fig 8.2 to 8.4).

<table>
<thead>
<tr>
<th>Site</th>
<th>Deltoid</th>
<th>Tibial Nerve</th>
<th>Gastrocnemius</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
<td><strong>Pre Rx</strong></td>
<td><strong>Post Rx</strong></td>
<td><strong>Mean Diffs</strong></td>
</tr>
<tr>
<td>Somatic</td>
<td>5.69 (2.19)</td>
<td>6.27 (2.73)</td>
<td>0.58 (2.45)</td>
</tr>
<tr>
<td>Radicular</td>
<td>4.59 (2.33)</td>
<td>4.4 (2.08)</td>
<td>-0.19 (0.97)</td>
</tr>
<tr>
<td>Radiculopathy</td>
<td>4.58 (1.54)</td>
<td>4.96 (1.98)</td>
<td>0.38 (0.95)</td>
</tr>
</tbody>
</table>

**Table 8.3 Mean (SD) PPT for each site and for each sub-group of individuals with spinally referred leg pain. Key: Rx treatment**

**Fig 8.2 Cumulative proportion of responders PPT at deltoid site for each group**

Figure (8.2) shows that a greater proportion of individuals with somatic referred pain, positively responded to the SLR treatment than the other 2 sub-groups. The proportion of individuals who responded in the radicular and radiculopathy groups is similar. More than 50% of individuals in all 3 groups had an increase in PPT after the SLR treatment.
Fig 8.3 Cumulative proportion of responders PPT at tibial nerve site for each group

Fig 8.3 Demonstrates that a greater proportion of individuals (>80%) in the somatic group positively responded to the SLR treatment at the tibial nerve site. The other 2 groups had a smaller proportion of individuals who responded compared to the somatic group, but still had more than 50% responding (increased PPT) post treatment.

Fig 8.4 Cumulative proportion of responders PPT at gastrocnemius site for each group

At the gastrocnemius site, both the radicular and somatic group had a larger proportion of responders than non-responders; with over 70% of individuals in the somatic group with increased PPT post treatment, and over 60% of individuals in the radicular group. However, only just over 30% of individuals with radiculopathy showed an increase in PPT.
**Statistical Analysis**

All data were normally distributed (Shapiro Wilk $p > 0.05$), apart from the tibial nerve pre-readings in the radicular group ($p = 0.009$) suggesting that for all other data at the 95% significance level, there is not enough evidence to reject the null hypothesis that the variable is normally distributed. Since only one out of the 18 readings reached statistical difference on the Shapiro Wilk test, and ANOVA is robust to alterations in normal distribution (Field, 2013 pg 444), no transformations were carried out, and the 3 way mixed factorial ANOVA was carried out on the data (see appendix 30).

Mauchly’s test of sphericity was not significant therefore sphericity was assumed. There was no main significant effect ($p > 0.05$) of group ($F (2, 64) = 2.77, p = 0.07$). There were no significant main effects of time or site, and no significant interaction effects for time v site, or time v group (appendix 30 and attached CD gives the full results of the statistical analysis), but a statistically significant interaction effect between site v time v group ($F (4, 128) = 2.47, p = 0.048$) was found. Planned contrasts revealed a statistical difference between deltoid and gastrocnemius, before and after treatment ($p = 0.022$). Fig 8.5 shows the mean difference (pre to post treatment) in PPT for all sites in the 3 groups. In the somatic group, both sites showed a similar mean increase in PPT after treatment, but in the radicular group there is a trend for a reduction in PPT post treatment in the deltoid site, but a slight mean increase in PPT post treatment at the gastrocnemius site. In the radiculopathy group, however, an opposite effect is seen, with a mean increase in PPT at the deltoid site, but a decrease at the gastrocnemius site.

Controlling for the effects of body mass index, demonstrated a significant main effect of group ($F (2, 64) = 4.279, p = 0.018$). Sidak corrected post hoc tests showed significantly higher PPT readings for the somatic group compared to the radicular group ($p = 0.016$). A significant main effect of site ($F (2, 126) = 3.96, p = 0.021$) and a significant interaction effect between time v site v group was also found ($F (4, 126) = 2.634, p = 0.037$). Planned contrasts revealed that the difference for site alone was between the tibial nerve and gastrocnemius sites ($F (1, 63) = 6.17 p = 0.016$), and the 3 way interaction (time v site v
group) lay between the tibial nerve and gastrocnemius site, before and after treatment (F (2, 63) = 4.45, p = 0.016).

In addition, there was a significant interaction effect for BMI and site (F (2, 126) = 3.16, p = 0.046). Planned contrasts revealed the difference lay between tibial nerve site and the gastrocnemius site (p = 0.028).

Tests for the assumption of homogeneity were significant for group and BMI (F (1, 63) = 5, p = 0.01), and for site v time v group and BMI (F (4, 126) = 2.72, p = 0.033), but not for site and BMI (F (2, 126) = 2.74, p = 0.068). Therefore the main effect for group and interaction effect for site v time v group found in the covariate analysis cannot be accepted as the assumption of homogeneity is not tenable (Field, 2013 pg 499), however the interaction effect for site and BMI can be accepted.

![Fig 8.5 Mean differences PPT (Kg) (before and after Rx) at the 3 sites.](image)

Since no main effect for sub-group had been found, further analysis of pre-readings with the 3 groups’ data combined was performed to assess if there was a difference in baseline readings for each site related to BMI. A one way ANOVA for each site revealed no significant difference for BMI (over or under 26 kg/m²) for deltoid (F
(1,66)= 3.16, P=0.08) and the tibial nerve sites (F (1,66) =0.92, P=0.34), but a significantly higher PPT reading for individuals with BMI over 26 kg/m² at the gastrocnemius site (F (1,66) = 5, p=0.029). Figs 8.6 to 8.8 show the overall mean PPTs between the 2 BMI groups for all participants. It can be seen that all readings showed a higher trend for BMI over 26 kg/m².

**Fig 8.6 Mean PPT (Kg) readings pre Rx for all 3 groups combined at the deltoid site**

**Fig 8.7 Mean PPT (Kg) readings pre Rx for all 3 groups combined at the tibial nerve site**
Controlling for pain below the knee resulted in a similar result to the PPT analysis alone, in that the only significance was an interaction effect between time, site and group (F (4, 126)= 2.54, p=0.043), and planned contrasts showed a significance between deltoid and gastrocnemius sites, before and after treatment (p=0.033). Testing the assumption of homogeneity resulted in non-significant results between time, site, group and pain below the knee (F (4, 122) = 2.74, p= 0.117), therefore we can assume the relationship and accept these results. Fig 8.9 demonstrates that the response to treatment was different in individuals with pain above and below the knee. At the somatic site individuals with pain below the knee showed a mean decrease in PPT after treatment, but individuals with pain above the knee increased at both sites. In the radicular group, individuals with pain below the knee showed a mean decrease in PPT at the deltoid site, but an increase at the gastrocnemius site, whereas the mean PPT decreased at both sites in individuals with pain above the knee. Minimal mean differences were seen at either site for individuals with pain above the knee in the radiculopathy group, but an increase in PPT at deltoid and a decrease at gastrocnemius was noted.
Fig 8.9 Mean difference in PPT (Kg) readings in individuals with pain above and below the knee at the deltoid and gastrocnemius sites (note no confidence interval bars are included as only 2 participants in the somatic group had pain below the knee).

However, caution must be taken when analysing these results since only 3 participants had pain that was above the knee in the radiculopathy group, and only 8 (out of 33) in the radicular group. Conversely only 2 (out of 11) participants in the somatic group had pain below the knee.

Whilst gender was not statistically different between the groups, and no significant correlations had been found, it has been suggested that females have lower PPT than males, and so this was added as a covariate into the analysis. A main effect was found for group (F (2, 63) = 3.6, p= 0.033), with planned contrasts showing the significant difference was between somatic and radiculopathy groups. There were no main effects for time or site, but an interaction effect of time, group and site was found (F (4, 126) = 2.59, P=0.04) with planned contrasts showing the significant difference between the deltoid and gastrocnemius sites. Testing for the assumption of homogeneity revealed a significant difference between gender and groups (F (3, 63) =5.84, p=0.001), and between time, group, site (F (6,126) = 2.25, P=0.043) therefore the assumption of homogeneity of regression slopes has been broken, and the results of the covariate analysis cannot be accepted.
As there were no significant differences between the groups, the data for the 3 groups were combined, and an additional analysis was performed to assess the effect of gender on baseline PPT readings. A one way ANOVA found a significantly greater PPT at the deltoïd site \( (F(1,66)=15.74, \ p=0.000) \) and the gastrocnemius site \( (F(1,66)=15.05, \ p=0.000) \) in men compared to women, but no significant difference at the tibial nerve site \( (F(1,66)=3.11, \ p=0.08) \). Figs 8.10- 8.12 show the baseline PPT readings at all 3 sites.

**Fig 8.10** Mean PPT (Kg) readings for men and women from the deltoïd site.

**Fig 8.11** Mean PPT (Kg) readings for men and women from the tibial nerve site.
No other covariate analyses were explored as there were no other strong correlations or baseline significant differences.

**Vibration Thresholds**

At the start of the data collection, the vibrameter was unexpectedly damaged and needed to be repaired, but participants were already booked into the laboratory, and as they were NHS patients who were unable to receive their next Physiotherapy appointment until after the laboratory session, the session could not be delayed. Two participants therefore had missing VT data, one from the somatic group, and the other from the radiculopathy group. In addition, 3 participants had VT readings which were too high to be recorded from the vibrameter for the 1st metatarsal site (one from each group), and an additional participant from the radicular group had VT readings too high from both sites. Therefore 9 participants in the somatic group had VT from both sites, and one from the lateral malleolus site only, 30 participants in the radicular group had VT readings from both sites, and one from the lateral malleolus site only, and 22 participants from the radiculopathy group had VT readings from both sites, and 1 from the lateral malleolus site only. In the case of the missing data due to elevated VT readings, all participants were male and 64 years of age or over (64-69).
Mean (SD) and mean differences (SD) can be found in table 8.4. From these differences it can be seen that there was a tendency for a decrease in VT to occur in both the radiculopathy and somatic groups after treatment, but a slight increase in VT in the radicular group. However the large standard deviations show the marked variability in the data. Fig 8.13 shows the mean differences (before and after) measures for each site in the 3 sub-groups, with 95% confidence intervals demonstrating the large variability in readings especially for the somatic and radiculopathy groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Lateral Malleolus</th>
<th>1st Metatarsal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre Rx</td>
<td>Post Rx</td>
</tr>
<tr>
<td>Somatic</td>
<td>2.27 (4.08)</td>
<td>1.75 (2.94)</td>
</tr>
<tr>
<td>Radicular</td>
<td>0.68 (0.48)</td>
<td>0.75 (0.74)</td>
</tr>
<tr>
<td>Radiculopathy</td>
<td>3.00 (4.43)</td>
<td>2.50 (3.26)</td>
</tr>
</tbody>
</table>

Table 8.4 Mean Vibration threshold (VT) (µm) for each site and for each sub-group of individuals with spinally referred leg pain

Fig 8.13 Mean VT measures (µm) before and after treatment at the lateral malleolus and first metatarsal sites.
Table 8.5 shows the numbers of individual in each group who had differences in measurements greater than the SDD (25.1% and 14.4 % lateral malleolus and 1st metatarsal respectively) found in chapter 7.

<table>
<thead>
<tr>
<th></th>
<th>Lateral Malleolus</th>
<th>1st Metatarsal</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT ↑&gt;SDD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VT↓&gt;SDD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic</td>
<td>0/10 (0%)</td>
<td>3/9 (33.3%)</td>
</tr>
<tr>
<td>Radicular</td>
<td>7/31 (22.6%)</td>
<td>8/30 (26.7%)</td>
</tr>
<tr>
<td>Radiculopathy</td>
<td>3/22 (13.6%)</td>
<td>7/21 (31.8%)</td>
</tr>
</tbody>
</table>

Table 8.5 Numbers (percentage) of individuals with differences in VT greater than SDD in the three leg pain groups

Statistical Analysis

Normality

All data were not normally distributed, (Shapiro Wilk test<0.05), and an outlier was found in the radicular group. After removal of the outlier, the data remained not normally distributed, and therefore a number of transformations were attempted. A box-cox transformation (VT^a)-1/a (where a=0.1) successfully normalised all but one of the readings (the post treatment measures for the radicular group at the lateral malleolus) (see appendix 30). Since ANOVA is robust to minor violations of normality, this transformation was considered successful.

Mauchly’s test of sphericity was not relevant as there were only 2 levels of within subject variables, therefore sphericity is assumed (Field, 2013 pg 561). There was a main effect for group (F (2, 57) = 4.79, p= 0.012). Sidak corrected post hoc tests indicated significantly higher VT for the radiculopathy compared to radicular group (p=0.01). There was a main significant effect for site (F (1, 57) = 38.17, p=0.00), but no other significant within subject effects (see appendix 30 and attached CD).
As age was strongly correlated with vibration thresholds, this interaction was entered into the analysis. No significant differences were seen for any within or between subjects analyses, indicating that the differences found in the first analysis, were strongly related to age. However, further testing for the assumption of homogeneity of regression slopes revealed a significant difference for age and group, indicating that the assumption of homogeneity of the regression slope has been broken \( F(3, 54) = 7.28, P=0.000 \). Therefore the results from the 3 way mixed factorial ANOVA without age entered as a covariate are accepted.

Since pain below the knee was significantly different between groups at baseline, this was entered into the analysis to assess any interaction effect. There was a significant main effect for site \( F(1, 56) = 4.07, p=0.048 \), but no other main effects of within subject variables or any interaction effects (see appendix 30 and attached CD). A significant main effect was found for group \( F(2,56) = 5.27, p=0.008 \). However testing the assumption of homogeneity found a significant difference between group and pain below the knee \( F(3,56) = 4.7, p=0.005 \) and therefore the assumption is not tenable. Therefore, the significant group effect found after entering pain below knee as a covariate was not accepted.

Since there were no other baseline differences between groups, no further covariate analyses were performed.

**Sciatic Nerve excursion during modified SLR test**

Of the 67 images sequences, 60 were of sufficient quality to track. Of the 7 that were not, 4 were in the radicular group and 3 in the radiculopathy group. Of these 5 were women, 3 had BMI over 26kg/m², and one had a BMI over 35kg/m², and 2 were men both with BMI over 36kg/m². Hence longitudinal sciatic nerve excursion data is given for 11 participants in the somatic group, 29 participants in the radicular group and 20 participants in the radiculopathy group.
Longitudinal Nerve Excursion

The mean values (SD) of the nerve excursion can be seen in table 8.6.

<table>
<thead>
<tr>
<th>Group</th>
<th>Hip flexed to 30°</th>
<th>Hip flexed to 60°</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre Rx</td>
<td>Post Rx</td>
</tr>
<tr>
<td>Somatic</td>
<td>10.26 (2.85)</td>
<td>10.08 (2.51)</td>
</tr>
<tr>
<td>Radicular</td>
<td>8.85 (3.15)</td>
<td>9.07 (3.01)</td>
</tr>
<tr>
<td>Radiculopathy</td>
<td>9.44 (4.22)</td>
<td>8.7 (2.73)</td>
</tr>
</tbody>
</table>

Table 8.6 Mean (SD) pre and post treatment and differences in longitudinal sciatic nerve excursion (mm) for the 3 sub-groups.

The table demonstrates the very small mean differences that were found after treatment, although the direction (increased or decreased) plus amount of excursion was varied. The greatest mean difference found was for the radiculopathy group at 30° hip flexion, this represented a mean decrease of 8.2%. Fig 8.14 and 8.15 show the proportion of participants whose nerve excursion increased in the 3 groups with the hip flexed to 30° and 60° hip flexion.

![Proportion of individuals with increased sciatic nerve excursion after treatment with hip flexed to 30°](image)

Fig 8.14 Proportion of individuals with increased sciatic nerve excursion after treatment with hip flexed to 30°
It can be seen that the somatic group had a greater proportion of individuals whose nerve excursion increased after treatment in both hip positions. Both radicular and radiculopathy groups had similar proportion of individuals with increased nerve excursion at 60° hip flexion (around 50%), but a smaller proportion (40-45%) with the hip flexed to 30°. A small proportion of individuals had nerve excursion greater than 50% in all 3 groups with the hip flexed to 30°, but a smaller proportion with the hip flexed to 60°.

**Statistical Analysis**

**Normality**

All data were normally distributed (Shapiro Wilk p >0.05), apart from the pre-treatment readings at 30° hip flexion for the radicular group (p=0.047), and post treatment readings at 60° hip flexion in the radiculopathy group (p=0.027). Hence for all data apart from these 2 readings, at the 95% significance level there is not enough evidence to reject the null hypothesis that the variable is normally distributed. Since only 2 out of the 12 readings reached statistical difference on the Shapiro Wilk test and ANOVA is robust to alterations in normal distribution, no transformations were carried out, and the 3 way mixed factorial ANOVA was carried out on the data.
There were no significant main effects for group (F (2, 57) = 0.014, p= 0.986 ), or within subject analyses (see appendix 30 and attached CD).

There were no baseline differences for any measures except pain below the knee, and age. Covariate analysis was performed using age, and no significant main or interaction effects were found.

Covariate analysis using pain below the knee resulted in a significant main effect for hip position (F (1, 56) =6.98, p=0.01), but no other main or interaction effects. The assumption of homogeneity was performed and there was no significant difference between the covariate and hip position (F (1, 58) = 0.00, p=0.998), therefore the assumption of homogeneity is established, and the result of the covariate analysis can be accepted.

Since individuals with somatic referred leg pain alone did not show any signs of neurological compromise or mechanosensitivity, and it was of interest to see how the 2 groups with neuropathic pain behaved, the data was combined for these 2 groups and analysed descriptively to assess how the factor of pain below the knee impacted the ultrasound readings. Two analyses were performed, the first to look at baseline mean values for each hip position in individuals with pain below and above the knee (Fig 8.16), and the second to assess the mean difference scores (before and after treatment) in individuals with pain below and above the knee in the 2 neuropathic pain groups (Fig 8.17). It can be seen in Fig 8.16 when the hip is flexed to 30°, that a similar mean sciatic nerve excursion is seen, regardless of whether pain is below or above the knee, but with the hip flexed to 60° individuals with pain below the knee had greater sciatic nerve excursion than those with pain above the knee. Fig 8.17 demonstrates that in individuals with pain below the knee in the 2 neuropathic groups, there was a trend for a reduction in nerve excursion after the SLR treatment at both hip positions. In individuals with pain above the knee, there was a tendency for an increase in nerve excursion with the hip flexed to 30°, but minimal mean differences with the hip flexed to 60°.
Fig 8.16 Mean (pre-treatment) longitudinal sciatic nerve excursion (mm) for individuals with pain below and above the knee at the 2 hip positions (radicular and radiculopathy groups).

Fig 8.17 Difference (pre-post treatment) longitudinal sciatic nerve excursion (mm) for individuals with pain below and above the knee at the 2 hip positions (radicular and radiculopathy groups).
Comparison with asymptomatic data from chapter 7
The mean pre-treatment measures for each group were compared to the mean excursion values obtained in the reliability study for asymptomatic participants. Figs 8.18 and 8.19 show the mean values for each group.

**Fig 8.18 Longitudinal sciatic nerve excursion (mm) for all groups (pre-treatment readings for symptomatic groups) with the hip flexed to 30 degrees.**

**Fig 8.19 Longitudinal sciatic nerve excursion (mm) for all groups (pre-treatment readings for symptomatic groups) with the hip flexed to 60 degrees.**
One way ANOVA was performed for each hip position to assess if any differences arose between the asymptomatic and symptomatic groups. A statistically significant difference was found with the hip at 60° flexion (F (3, 75) = 3.7, p= 0.016). Gabriel corrected post hoc tests revealed a significantly greater amount of nerve excursion in the asymptomatic group compared to the somatic group (p=0.012). Since there was a marked difference in age for the asymptomatic group compared to the symptomatic groups (mean asymptomatic group = 28.9 years), age adjustment with covariate analysis was performed. No statistical significance was found between groups (with 60° hip flexion) after age adjustment (F (3,71) = 1.28, p= 0.288), indicating that age predicted the outcome between groups. However, tests for the assumption of homogeneity were significant for age and group (F (3,71) =2.72, p=0.036), indicating that a violation has occurred, and therefore the analysis without adjustment for age is accepted.

**Transverse plane nerve excursion**

The method of analysis for transverse movements is also affected by image quality and therefore some images were not of sufficient quality for the methods to adequately analyse nerve excursion. Therefore data was missing for one participant from the somatic group, 8 from the radicular group, and 3 from the radiculopathy group, resulting in data from 10 somatic participants, 25 radicular participants and 20 radiculopathy participants.

There was marked variability in the direction and total amount of nerve excursion between individuals. Figs 8.20 and 8.21 demonstrate the mean values before and after treatment for each group and each hip position. Note the large confidence intervals indicating the wide spread of excursion values between individuals, particularly in the somatic group.
Fig 8.20 Mean medial and lateral sciatic nerve excursion (mm) for the 3 groups at 30° hip flexion (left) and 60° hip flexion (right). Note –ve numbers indicate lateral movement, +ve numbers indicate medial movement.

Fig 8.21 Mean superficial and deep sciatic nerve excursion (mm) for the 3 groups at 30° hip flexion (left) and 60° hip flexion (right). Note –ve numbers indicate deep movement, +ve numbers indicate superficial movement.

Before treatment at both hip positions, the somatic group showed a different pattern of nerve movement to the other 2 groups, with a tendency to move laterally during the SLR, whereas the other 2 groups predominantly moved medially. After treatment, with the hip at 30° the nerve excursion in the somatic group moved medially, and at 60° of flexion moved laterally but to a lesser degree. At 30° hip flexion, both radicular and radiculopathy groups tended to move less medially than prior to treatment. However, at
60° there was little difference in medial/lateral excursion after treatment compared to before.

At 30° hip flexion, all groups showed a tendency for the nerve to move more superficially before and after treatment. The somatic and radicular group tended to have less superficial excursion after treatment, whereas the radiculopathy group had a tendency to have slightly greater superficial movement after treatment. With 60° hip flexion, sciatic nerve excursion was superficial in the somatic and radicular groups, but deep in the radiculopathy group. After treatment, the nerve moved less superficially in the somatic and radicular groups, and much deeper in the radiculopathy group.

**Presence of Central Sensitisation**
Only 2 participants were found to have central sensitisation using the method described in appendix 26. The baseline data for each of these participants is shown in table 8.7, and mean values for each of the outcome measures in table 8.8.
<table>
<thead>
<tr>
<th>Participant</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-group</td>
<td>Radiculopathy</td>
<td>Radicular</td>
</tr>
<tr>
<td>Age</td>
<td>56</td>
<td>36</td>
</tr>
<tr>
<td>Gender</td>
<td>F</td>
<td>F</td>
</tr>
<tr>
<td>Pain below knee</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pain duration (years)</td>
<td>35</td>
<td>10</td>
</tr>
<tr>
<td>NHS Patients</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>BMI</td>
<td>28.96</td>
<td>17.96</td>
</tr>
<tr>
<td>Disability (ODI)</td>
<td>58</td>
<td>26</td>
</tr>
<tr>
<td>Fear avoidance physical activity (FABQP)</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Fear avoidance work (FABQW)</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>Pain Catastrophising (PCS) Total</td>
<td>14</td>
<td>35</td>
</tr>
<tr>
<td>PCS Rumination</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>PCS Magnification</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>PCS Helplessness</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Depression (DASS21)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anxiety (DASS21)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Stress (DASS21)</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Kinesiophobia (Tampa)</td>
<td>30</td>
<td>44</td>
</tr>
</tbody>
</table>

**Table 8.7 Baseline data for the two participants with central sensitisation.**

From the table it can be seen that both participants had a long duration of symptoms, much greater than the average of the participants (2.7 years). Participant 1 had a greater BMI than the average, but participant 2 had a much lower BMI than average (27.1 kg/m²). Both had a greater score for ODI than the mean score of the group (17.3). Participant 1 had higher scores than the average score for all psychosocial scores except for FABQ (work), PCS (magnification), depression and stress (for average scores please refer to table 7.1). Participant 2 had higher scores than the average values for all other psychosocial scores, except for depression.
Table 8.8 demonstrates the effects of the SLR treatment on the 3 outcome measures in the 2 participants with CS. It can be seen that these 2 participants had considerably lower PPTs than the mean of participants in each of the associated sub-groups (see table 8.3 for details).

<table>
<thead>
<tr>
<th>Participant</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre Rx</td>
<td>Post Rx</td>
</tr>
<tr>
<td>PPT (Kg) deltoid</td>
<td>2.2</td>
<td>2.45</td>
</tr>
<tr>
<td>PPT (Kg) tibial Nerve</td>
<td>1.85</td>
<td>2.25</td>
</tr>
<tr>
<td>PPT (Kg) gastrocnemius</td>
<td>2.1</td>
<td>2.35</td>
</tr>
<tr>
<td>VT(µm) lateral malleolus</td>
<td>0.99</td>
<td>1.35</td>
</tr>
<tr>
<td>VT 1ST (µm) metatarsal</td>
<td>1.64</td>
<td>1.08</td>
</tr>
<tr>
<td>Long nerve exc H30°</td>
<td>7.73</td>
<td>9.02</td>
</tr>
<tr>
<td>Long nerve exc H60°</td>
<td>7.29</td>
<td>9.34</td>
</tr>
<tr>
<td>M/L nerve exc H30°</td>
<td>2.36</td>
<td>-1.64</td>
</tr>
<tr>
<td>Sup/deep nerve exc H30°</td>
<td>2.87</td>
<td>3.95</td>
</tr>
<tr>
<td>M/L nerve exc H60°</td>
<td>-1.51</td>
<td>-7.15</td>
</tr>
<tr>
<td>Sup/deep nerve exc H60°</td>
<td>1.14</td>
<td>-0.35</td>
</tr>
</tbody>
</table>

Table 8.8 Outcome measures- before and after treatment, with differences for the two participants with central sensitisation. Note for medial and lateral movement, -ve means the nerve moved in a lateral direction, and for superficial and deep, -ve means nerve moved deeply. All nerve excursion measurements in mm.

VT were also considerably lower in both of the participants than the mean of the participants in the respective sub-group (see table 8.5). Participant 2 had a larger longitudinal excursion at 30° but smaller excursion at 60° than the group mean, whereas participant 1 had lower longitudinal excursion than the group mean in both hip positions (see table 8.6). With regards to transverse movement, participant 2 moved medially and superficially in both hip positions which matched the mean direction of movement for
the sub-group. Participant 1’s nerve moved medially and superficially with the hip at 30° (matching the group mean directions), but then moved laterally and superficially at 60°, in contrast to the group mean which demonstrated medial and deep movement.

**Psychosocial Factors**
Correlation analyses were done between psychosocial factors and disability to assess the relationship between them. The significant, strong correlations can be found in table 8.9. All other correlations were weak or not significant (see attached CD). In addition, since pain below the knee had been associated with higher psychosocial factors, or higher levels of disability, correlations were performed between pain below the knee and the ODI and psychosocial scales. No significant correlations were found between pain below the knee or any of the scales.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Type</th>
<th>Correlation coefficient</th>
<th>P value</th>
<th>Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODI and PCS (total)</td>
<td>Pearsons</td>
<td>0.43</td>
<td>0.001</td>
<td>0.22-0.64</td>
</tr>
<tr>
<td>ODI and PCS rumination</td>
<td>Pearsons</td>
<td>0.41</td>
<td>0.001</td>
<td>0.16-0.6</td>
</tr>
<tr>
<td>PCS (total) and rumination</td>
<td>Spearmans</td>
<td>0.86</td>
<td>0.000</td>
<td>0.77-0.92</td>
</tr>
<tr>
<td>PCS (total) and helplessness</td>
<td>Spearmans</td>
<td>0.90</td>
<td>0.000</td>
<td>0.83-0.94</td>
</tr>
<tr>
<td>PCS (total) and magnification</td>
<td>Spearmans</td>
<td>0.73</td>
<td>0.000</td>
<td>0.57-0.83</td>
</tr>
<tr>
<td>PCS (total) and tampa</td>
<td>Spearmans</td>
<td>0.49</td>
<td>0.000</td>
<td>0.28-0.66</td>
</tr>
<tr>
<td>PCS (total) and anxiety</td>
<td>Spearmans</td>
<td>0.53</td>
<td>0.000</td>
<td>0.311-0.69</td>
</tr>
<tr>
<td>Rumination and anxiety</td>
<td>Spearmans</td>
<td>0.40</td>
<td>0.001</td>
<td>0.18-0.60</td>
</tr>
<tr>
<td>Rumination and helplessness</td>
<td>Spearmans</td>
<td>0.79</td>
<td>0.000</td>
<td>0.67-0.88</td>
</tr>
<tr>
<td>Magnification and helplessness</td>
<td>Spearmans</td>
<td>0.52</td>
<td>0.000</td>
<td>0.29-0.71</td>
</tr>
<tr>
<td>Magnification and anxiety</td>
<td>Spearmans</td>
<td>0.55</td>
<td>0.000</td>
<td>0.32-0.71</td>
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*Table 8.9 Correlation analyses of disability and psychosocial factors*
8.3 Discussion

The main aim of the study was to determine if a 3 x 1 minute SLR tensioner treatment had an immediate effect on pressure pain thresholds, vibration thresholds and sciatic nerve excursion in 3 different sub-groups of individuals with spinally referred leg pain. In addition, it aimed to assess if the presence of central sensitisation, disability and psychosocial factors were different between the 3 groups and interacted with the effect of treatment. A smaller aim was to assess how well the psychosocial factors and levels of disability were related to each other. The first and second aims will be discussed under each outcome measure in turn. A separate section will be given to the third aim, as it relates less directly to the 2 main aims.

8.3.1 Pressure Pain Thresholds

Overall Findings
There was no main effect for group or time and site. A significant interaction effect was found for time, group and site (between deltoid and gastrocnemius). However, when adjusting for BMI, a significant difference was found between the tibial and gastrocnemius sites and BMI, and an interaction effect was found between group, before and after treatment and between sites. However the interaction effect could not be accepted because the assumption of homogeneity was not demonstrated. Therefore, 2 main findings emerged.

The first finding was a significant interaction effect between group, time and between gastrocnemius and deltoid. Analysis of Fig 8.5 revealed that the radicular group showed a decrease in PPT at the deltoid site after treatment, but a slight increase at the gastrocnemius site, and the radiculopathy group showing a marked increase at the deltoid site, and a marked decrease at the gastrocnemius site. The cumulative responders analysis was performed because it has been suggested that the use of such analysis allows for a more comprehensive analysis of the response to treatment between groups (Farrar et al., 2006). Figs 8.2-8.4 demonstrate some interesting trends for each site and between the groups. For the deltoid sites, over 60% of participants in the somatic group
showed improvement in PPTs, whereas in the radicular and radiculopathy groups, this was just over 50%. At the tibial nerve site, over 80% of the somatic group showed improvement in PPTs, whereas in the radicular and radiculopathy groups, over 50% improved. However, for the gastrocnemius site over 70% of somatic participants and over 60% of radicular participants showed improvement in PPT, but only around 30% of participants in the radiculopathy group improved after treatment. It has been suggested that a change in PPT over 15% may be clinically significant (Moss et al., 2007). It can also be seen in Figs 8.2 to 8.4 that at the deltoid site, over 40% of individuals in the somatic and radiculopathy groups showed an increase in PPT over 15%, but only around 25% in the radicular group. This trend reversed at the tibial nerve site with around 35% of individuals in the radicular group having increases of over 20%, whereas in the somatic and radiculopathy groups this fell to around 20% of participants. At gastrocnemius, less than 10% of participants in the radiculopathy group improved over 15%, whereas 30% of participants in the radicular group and over 50% in the somatic group improved by over 15%.

The different sites tested were used to determine if any beneficial effects were segmentally or systemically mediated. Improvements at the deltoid site would indicate a descending, systemic inhibitory effect, possibly activated from the dorsal periaqueductal gray matter (Moss et al., 2007; Schmid et al., 2008; Skyba et al., 2003; Sluka and Wright, 2001) since the area was distant from the site of treatment. Any improvements at the tibial nerve site could indicate a more segmental effect since the nerve was being directly influenced, or a systemic effect. Gastrocnemius site changes could also reflect segmental or systemically mediated pain inhibition. Whilst there was no main significant effect at this site there was a significant interaction effect between the deltoid and the gastrocnemius site between the radicular and radiculopathy groups, and this relates to the cumulative responders analysis. Greater proportions of individuals in the radicular group had a clinically relevant improvement in symptoms at the gastrocnemius site than in the radiculopathy group, but the opposite response was seen at the deltoid site. This may indicate that for individuals with radiculopathy, a SLR treatment may be less effective at improving the site of pain, but still has an effect on descending
inhibitory pathways. The literature does not specifically support this assertion since blockage of the descending inhibitory systems have been postulated to occur in individuals with CS and neuropathic pain (Zusman, 2008; Yunnus, 2007), whilst descending excitatory systems operating via the rostroventromedial medulla, have been considered to exacerbate pain (Fields, 2004). This may explain the smaller proportion of individuals with a positive response to treatment in the radiculopathy group. However, descending excitation and loss of descending inhibition, may have been expected to markedly increase PPT at tibial nerve and gastrocnemius sites; this was not seen (no individuals had PPT greater than SDD at the gastrocnemius site in the radiculopathy group- see below). Whilst more individuals responded positively at the gastrocnemius site in the radicular group compared to the radiculopathy group, only around 30% had clinically significant changes, therefore no overall claim can be made of effectiveness of treatment at this site in this group.

It is also of importance when interpreting these results to examine the individual differences in comparison to the SDD found in the repeatability study in chapter 7.2. The SDD found for each site were 1.55 for deltoid, 1.44 at the tibial nerve and 1.75 for gastrocnemius. Since the interaction effect was at the deltoid and gastrocnemius sites, and between the radicular and radiculopathy groups only, the SDD will be considered for these sites and groups only. For the radicular group at the deltoid site, only 1 participant had increased PPT above the SDD, and only 3 participants had reduced PPT above the SDD. For gastrocnemius site, no participants had changes to the PPT readings after treatment that were above SDD. In the radiculopathy group, no participants had a reduction in PPT greater than the SDD, and only 2 had increased PPT above the SDD at the deltoid site, and no participants had scores greater than the SDD at the gastrocnemius site. Therefore this suggests overall that there was no overall effect on PPT of the treatment in any of the 3 groups.

This lack of improvement in PPT differs from research which has looked at changes in PPT after spinal mobilisations in asymptomatic participants (Krouwel et al., 2010; Pentelka et al., 2012; Willett et al., 2010), spinal mobilisation in symptomatic
participants (Moss et al., 2007; Sterling et al., 2001; Vincenzino et al., 1996),
n eurodynamic mobilisation in symptomatic participants (De Le LLave Rincon et al.,
2012; Silva et al., 2013), and after neurodynamic mobilisations in symptomatic patients
with degenerative pain (Villafane et al., 2011; 2012). Only one study was found where
no significant differences in PPT were found after mobilisations, but this was in
asymptomatic participants (Soon et al., 2010).

However, statistical significance alone does not determine the effectiveness of the
treatment. Both SDD, and clinical significance must be taken into account when
considering these studies. Moss et al. (2007) proposed that a change greater than 15% is
suggestive of a clinically significant effect. De Le LLave Rincon et al., (2012) found a
small significant improvement in PPT after a slider median nerve treatment measured at
C5/6, but no other sites (including over nerve sites) one week after treatment, but not
immediately after treatment in individuals with carpal tunnel syndrome. However, the
percentage difference at this site was only 13.5%. In addition, 30 minutes of soft tissue
mobilisations were applied to the neck and arm prior to the slider treatment, therefore it
is not known if the small findings were influenced more by the soft tissue treatment than
the neurodynamic treatment.

Using a median nerve slider technique to treat individuals with osteoarthritis of the
thumb improved the immediate PPTs at the trapeziometatarsal joint (TMJ), but not other
tested sites in the hand (Villafane et al., 2011). Whilst a radial nerve slider improved
PPT immediately in all 3 tested sites in the hand (Villafene et al., 2012). The mean
change at the TMJ was only 0.84 kg/cm² (Villafane et al., 2011), and whilst small, such
a change was over 15%, making it clinically significant according to Moss et al., (2007).
Whilst error measures were not revealed in this study, the authors’ 2012 study revealed
the SEM as 3.07kg/cm², with resultant SDD of 8.51 kg/cm². Assuming that the error
measure was as high for the 2011 study, it is unlikely that the differences found between
measures could be considered to be due to the treatment alone. Greater mean changes to
PPT (3.33 kg/cm²) were found in the 2012 study after a radial nerve slider technique,
although it is unlikely that the individual differences after treatment were as high as the
required SDD of 8.51kg/cm². Such high error measures render the results of these 2 studies inconclusive.

More relevant to the present study, Silva et al., (2013) demonstrated a significant change in PPT in individuals with sciatica compared to control participants after a SLR mobilisation. However, only 15 participants were recruited to each group and these were further divided into 4 sub-groups who underwent different lengths of time of treatment, resulting in only 4 participants in 3 of the time groups, and 4 in the fourth. Whilst the crossover design improved the power of the study, such low participants overall make the extrapolation of the results less convincing. In addition, the statistical analysis could be questioned since separate between and within subject analyses were performed. Baseline differences between the groups were not accounted for, despite individuals in the sciatica group having significantly smaller mean baseline differences to the control group at 3 time points. Such limited and inappropriate statistical testing limits the findings of Silva et al., (2013). One final limitation is the lack of detail on the diagnosis, or even definition of sciatica. Not only is the term outdated, but the omission of how the diagnosis was made means that a potentially heterogeneous group of individuals were studied, making the extrapolation of these results untenable.

Other joint mobilisation studies have also demonstrated statistically significant increases to PPT in symptomatic participants after knee joint mobilisations in individuals with Osteoarthritis (OA) of the knee (Moss et al., 2007), and cervical mobilisations in individuals with lower cervical spine pain (Sterling et al., 2001) and lateral epicondyalgia (Vincenzino et al., 1996). All studies showed mean increases in PPT over 20% of baseline levels. However, all 3 studies analysed the data using percentage differences instead of the raw data. Bonate (2000) suggested that percentage change scores should be avoided because the score is a biased estimator of the population change. Bonate (2000) advocated that if such percentage change scores are used, they should be carefully assessed to ensure that they do not violate the assumptions of the statistical test being used. None of the above researchers described such analysis, although Moss et al., (2007) used the baseline scores as a covariate to minimise bias.
Hence the results of Sterling et al., (2001) and Vincenzino et al., (1996), may be questioned. Whilst Moss et al.’s (2007) results may be more robust, it is not clear whether the values were greater than error measures despite the authors performing a repeatability study, because the raw PPT values were not revealed.

The limitations of the studies discussed above may suggest that the significant differences found in their studies either may have been incorrectly analysed, or irrelevant since values may have been less than error measures or clinical significance. This may suggest that the lack of statistical differences in PPT found in the present study is not at odds with other published research. Another reason for the lack of statistically significant differences in the present study may be related to duration of symptoms. Duration of symptoms for individuals in the 3 groups was quite varied, and ranged from 3 months to 20 years. It is possible such long duration of the recent episode may have meant that one treatment session may not have been sufficient to have an effect, although in Moss et al.’s (2007) study, 47% of individuals had complained of knee OA for greater than 5 years, demonstrating that this factor alone may not be sufficient to account for the lack of significant differences in PPT found in the present study.

Further rationale for the non-significant findings in the present study may be related to only retesting immediately after treatment, which may have limited the body’s response to treatment. De Le LLave Rincon et al., (2012), only found significant changes to PPT one week after treatment, although the lack of a comparison group means that other variables could be responsible for the changes found after one week. Finally, the present study used a 3 x 1 minute treatment dose. There appears to be no clear optimal treatment dose, and this dose was chosen to reflect current clinical practice (this was decided not only on the researcher’s own practice, but also from discussions with colleagues and postgraduate students). Whilst Silva et al., (2013) did not look at the difference in outcome between their 3 treatment durations (3, 5 and 15 minutes), all doses produced statistically significant improvements compared to control groups and placebo. This indicated that 3 minutes may be an appropriate treatment dose, although this was done
over one set, rather than 3 sets. However, Pentelka et al. (2012) found that a 4th set of mobilisations (for either 30 or 60 seconds) resulted in a statistically significant elevation in PPT compared to 3 sets or less, however this was for spinal accessory mobilisations in asymptomatic individuals. In addition, Sluka and Wright (2001) found that 9 but not 3 minutes of knee joint mobilisations lead to a hypoalgesic effect in rats after ankle joint irritation. More research is needed to establish the optimal neurodynamic treatment times in symptomatic individuals.

Whilst there is no definitive explanation for the differences found between the present study and other studies showing statistical significance, the limitations discussed in the studies using symptomatic participants suggest that changes to PPT after manual techniques are not sufficiently proven, and more research is required to corroborate or refute such findings. Studies which have used asymptomatic participants may not reflect the changes that occur in symptomatic participants.

Effect of BMI
The second main finding from this analysis was the significant difference between PPT sites and BMI. Therefore, descriptive analysis was performed to look at baseline PPT values for individuals with BMI under 26 kg/m², and those over 26 kg/m² since this was the value that had been suggested as a cut off point for exclusion, as it may lead to a rise in PPT (Defrin et al., 2003; Krouwel et al., 2010). Whilst the mean PPTs were higher at all sites in individuals with BMI over 26 kg/m², statistically significant increases were only found at the gastrocnemius site. The results at this site are explicable, since PPT tests the sensory receptors in both the superficial and deep tissue (Defrin et al., 2003), hence greater adipose tissue may cushion the tested site more than in individuals with less cushioning. These results were in contrast to the results for the deltoid and tibial nerve groups. The tibial nerve may be less influenced by BMI since there is little adipose tissue behind the knee. Whilst the deltoid site may be more prone to adipose tissue, changes to PPT were not demonstrated in this study, and the rationale for this is not clear. Men have been demonstrated to have less adipose tissue in their upper limbs than women (Durnin and Womersled, 1974), and there were greater numbers of men
than women (20:16) with BMI over 26 Kg/m². Therefore if more women had presented with BMI over 26 Kg/m², PPT may have been more greatly affected at the deltoid site.

Defrin et al. (2003) found no difference in PPT related to BMI. However the three sites chosen were the upper back, the hand and the foot, where less adipose tissue is situated. It may be that sites that have greater amounts of subcutaneous tissue may require additional pressure in individuals with greater BMI. However, more research is required to establish this trend.

**Effect of pain below knee and PPT**

Adjusting for pain below the knee did not change the main analysis. Only 2 individuals had pain below the knee in the somatic group, and each had opposite responses to it (i.e. one participant had greater PPT at both sites after treatment, and one had reduced PPT), therefore reporting of trends are inappropriate in this group. Some trends were seen for the radicular and radiculopathy groups. At the gastrocnemius site, individuals with pain below the knee showed a mean decrease in PPT, whereas minimal mean change was seen in individuals with pain above the knee. The radicular group showed a slightly different trend with a mean increase at deltoid site, but a mean increase at the gastrocnemius site. The results of the radicular group are difficult to justify, as if a systemic effect had occurred, as shown by the deltoid site change, then it would be expected that an improvement in PPT would also be found at the gastrocnemius site. Therefore, it is possible that the trend here is due to measurement error. For the radiculopathy group, it is possible that a segmental effect was seen, since only the gastrocnemius site showed a change, and not the deltoid site. As the tibial nerve site was not found to be significant in contrast testing, this suggests that any change related to the effect of pain below the knee was not apparent at the tibial nerve site. The reason for this is difficult to explain, since a segmental effect would also have been expected to have shown changes to the tibial nerve, as well as to the skin over the gastrocnemius. This again may suggest that such changes were related to measurement error. Since the SDD found in this study at the gastrocnemius site was 1.75, and decreased PPT at this site in individuals with pain below the knee was around 0.25, it is highly likely that this is not a
genuine effect. In addition, only 3 participants in the radiculopathy group had pain above the knee, reducing the strength of the finding.

Effects of gender
The results for the main analysis, adjusting for gender, could not be accepted because of the loss of homogeneity. Further analysis of gender on PPT was performed, to assess if baseline differences in PPT postulated to occur between men and women (Chesterton et al., 2003; Manning and Fillingim, 2002; Sterling et al., 2000; Vanderweeën et al., 1996), also occurred in individuals with spinally referred leg pain. Statistically higher PPTs were found in men compared to women at both deltoid and gastrocnemius sites, and a trend was seen at the tibial nerve site, which did not reach statistical significance. These higher PPT at deltoid and gastrocnemius nerve sites are in agreement with a number of authors (Chesterton et al., 2003; Manning and Fillingim, 2002; Sterling et al., 2000; Vanderweeën et al., 1996). Overall the current study suggests that in individuals with spinally referred leg pain, the trend for men to have higher PPT than women is retained.

8.3.2 Vibration Thresholds
There were no significant differences found before and after treatment between groups. However, there was a significant difference for VT readings between groups, with the radiculopathy group showing higher VT readings than the radicular group. However, age is known to increase VT readings, and individuals in the somatic and radiculopathy groups had a greater mean age than the radicular group (table 8.1). Whilst this did not reach statistical significance with post hoc testing, a strong significant correlation was seen between the VT readings and age, and therefore age was entered as a covariate into the analysis. The significant difference between groups found without age adjustment, was accepted because the assumption of homogeneity for the age adjusted analysis had been breached.

The findings of a significant difference between the radicular and radiculopathy group with regards to VT may be explained by the pathological processes occurring. Generally most animal and human studies have demonstrated greater losses to nerve conduction
with greater nerve insult, be this at the nerve root level (Hou et al. 2003; Omarker and Myers, 1998; Pedowitz et al, 1992; Rydevik et al., 1991; Takahashi et al., 2003) or in other compression neuropathies like carpal tunnel syndrome (Atroshi et al., 2003; Finsen and Russworm, 2001). Since individuals in the radiculopathy group were identified as having an objective conduction loss on manual examination, the findings of greater elevations in VT in this group compared to the radicular groups may not be unexpected. However, it was not significantly different from the somatic group, who did not display any signs of neuropathy on examination.

This could be explained by 2 factors, the first because of small numbers in the somatic group, leading to a type II error. However, whilst VT at both sites was higher in the radiculopathy group than the somatic group, the difference was not as large as between the radicular and radiculopathy group; therefore the results may be genuine. Another second factor could be related to age.

As explained, the results of the analysis with age adjustment could not be accepted because of the breach of homogeneity. Whilst this may seem appropriate from a statistical perspective, a pragmatic approach must be taken when determining the results, because age is such an important factor when considering VT readings, particularly in men over the age of 40 (Goldberg and Lindblom, 1979; Halonen et al., 1986; Hilz et al., 1998). In the radiculopathy group 50% of participants were men over the age of 40 (one of whom had such high VT readings that the vibrameter reached its maximum reading without the participant reporting vibration at the 1st metatarsal site). In the radicular group, men over the age of 40 represented 35% of individuals, and in the somatic group represented 40%. Therefore, the lack of statistical significance between the neuropathic and somatic groups could be related to the high proportion of men over 40 in the somatic group as well as the small numbers in this group. Overall, it is not possible to conclusively state that individuals with radiculopathy in this study had higher VT, because of a skew in the data with greater age.
There was also a main significant effect between sites, with VT being higher at the 1\textsuperscript{st} metatarsal than the lateral malleolus in all 3 groups. In some individuals the measure was so high at this site that the reading was too high to be captured by the vibrameter. More distal sites are known to have an increase in VT than proximal sites possibly because of the distance with which the stimulus has to travel (Hiltz et al., 1998), but also in this case possibly because the plantar surface of the foot bears the weight of the body, and may therefore be less sensitive to the stimuli. In some individuals, hard callus on the base of the 1\textsuperscript{st} metatarsal made the stimulus difficult to feel, in these cases the probe was moved around to attempt to test the skin in a region where less hard skin occurred. There was no significant difference between groups at this site, suggesting that this increase in not related to pathology of the lumbosacral nerve roots.

\textit{Effect of Treatment}

No significant differences were found in VT for any of the groups before and after treatment. Whilst a trend was seen, which suggested that individuals in the radiculopathy and somatic groups decreased VT after treatment, and those in the radicular group increased VT, these were mean differences, and individual variation meant that there were no significant differences overall.

Hence no beneficial effects of a 3 x 1 minute treatment can be claimed, but also of importance, no detrimental effects can be claimed, even in individuals with altered neurological integrity. It has been suggested that applying tensioner techniques in individuals with neuropathy may be detrimental to nerve function (Dilley et al., 2005, Boyd et al., 2005). The results of this study do not support such conclusions. Whilst it could be argued that the risk of accepting the results of the study may be due to the sample size and a type II error, it is important to consider the large variation in the effect of SLR treatment on VT between individuals, some showing decreases and others increases in VT post treatment, which may have washed out the effect of the treatment. In addition, the change in VT values related to the SDD, showed that in the somatic and radicular groups there was little difference in the proportion of individuals whose VT
increased after treatment above the SDD, and those who decreased. In the radiculopathy group, a much greater proportion of individuals showed a decrease in VT after treatment, than an increase above the SDD at both sites (see table 8.6). This indicates that if greater numbers had been recruited, either no effect would have been found, or it is possible that a significant improvement may have been found in the radiculopathy group. Also of importance the repeatability study (chapter 7) noted a trend for higher VT on the second reading compared to the first, therefore small elevation in VT could be related to this trend in the absence of a true deterioration in nerve conduction.

To the author’s knowledge, only one study has looked at the effects of a neural mobilisation on VT (Ridehalgh et al., 2005). The findings of this study revealed no significant differences in asymptomatic participants, and a sub-group of participants who were runners. Runners have been considered to be more at risk of neuropathy due to incidence of injuries such as ankle inversion sprains and compartment syndrome (Leach and Purnell, 1989; Fabre et al., 1998; McCrory et al., 2002). Whilst the study did not show any significant changes after treatment, it did show a trend for a rise in VT to occur after treatment, with a possible risk of a type II error due to small numbers of participants. Nee et al., (2012) analysed the occurrence of adverse effects in individuals treated with upper quadrant neural treatments. A risk ratio was calculated to assess whether any adverse effects reported during the study resulted in a poorer outcome at follow up. Adverse effects included unpleasant sensation during the treatments, such as aggravation of neck or arm pain, arm weakness and nausea. It was found that there was no difference in improvement between those who reported an adverse event and those who did not. Whilst this study did not analyse changes to nerve conduction, it does suggest that adverse effects from neural mobilisation are short lived and not harmful.

The results of the present study suggest that even in participants with objective signs of neuropathy, no detrimental changes to VT, and therefore nerve conduction were found. This is an important clinical finding as it reduces the concern that such techniques are detrimental to nerve function.
Sciatic Nerve Excursion

Longitudinal Excursion

The results of the study found no significant difference after treatment between groups, in either of the 2 hip positions that the SLR was performed. An analysis of the proportion of individuals with increased excursion after treatment (Figs 8.14 and 8.15) showed that at 30° hip flexion, over 55% of individuals in the somatic group increased, but less than 50% of the other 2 groups increased. A slight difference was seen at 60° hip flexion, with over 60% of individuals in the somatic group showing an increase, around 50% in the radiculopathy group, and less than 50% in the radicular group. However such differences between groups were not significant. It is possible that the use of a 3 x 1 minute treatment dose is not sufficient to cause biomechanical changes to the nerve in some individuals, however literature which has examined the effects of mobilisations on other soft tissues have found a creep effect to occur between 30 and 60 seconds (Bandy and Irion, 1994; Bandy et al., 1997; Lee and Evans, 1994), and optimal changes to tissue length between the 1st and 2nd repetition (Lee and Evans, 1994). Therefore, there may be other explanations for why such differences were found between individuals. The theories are complex and speculative, and are presented below.

It is known that most nerve excursion and nerve strain occurs close to the moving joint (Boyd et al., 2013, Coppieters et al., 2006). In the present study, the knee was extended and flexed in the SLR position, and therefore the greatest effect may have occurred at the nerve around the knee joint. For some individuals by doing this, a reduction in nerve excursion occurred. This may be explained by the predominant biomechanical change (i.e. lengthening through creep and hysteresis) occurring at the knee, resulting in greater compliance, and therefore less reliance on convergence occurring from the proximal segments. An explanation for an increase in nerve excursion seen may be the location of where the nerve divided. It is known that where nerves divide, they exhibit greater stiffness (Millesi, 1995). Hence, the effect of the mobilisation may be greater at these points of division, resulting in greater nerve excursion in the posterior thigh in those whose nerve divided closer to the scanned region. In addition nerves which had generally less compliance throughout, may have had a point of limited movement at the
posterior thigh, where nerve excursion occurred just proximal and distal to it. This point of restriction, may have incurred a greater mobilisation effect.

An explanation for minimal change in excursion seen in some participants could be related to baseline compliance of the proximal nervous tissues. It is possible in an individual who had greater compliance of nervous tissue from above the knee (i.e. at the hip, lumbosacral plexus, or nerve root level), that as the knee was mobilised, most of the effects of extending the knee were unfolding of undulations from the more proximal areas. In such cases, there may be minimal changes to nerve excursion, because a point has not been reached where sufficient levels of strain are reached, resulting in a smaller biomechanical effect on the tissue due to creep or hysteresis. In individuals who have less compliance (either due to hypermobility, or because there is a restriction at the nerve root for example), then applying the SLR treatment may have caused more of a potential lengthening effect (either at the knee, or possibly at the point of restriction) due to creep and hysteresis. Less excursion at the posterior thigh may then be seen after treatment, because the greater compliance from the proximal regions, or around the knee allows more nerve borrowing from these regions during knee extension.

Whilst there are minimal data which can directly support or refute these hypotheses, it is known that nerves take an undulating course through the nerve bed, and start to straighten out as the first adaptation of limb movement (Millesi, 1986; Millesi et al., 1995; Sunderland, 1989a). Convergence, where nerves proximal and distal to the site of joint movement move towards the moving joint, has been demonstrated in numerous studies (Boyd et al., 2013, Breig and Marions, 1963; Coppieters et al., 2006; O’Connell, 1946). Dilley et al., (2007) found that excursion of the ulnar nerve in the forearm was minimal during shoulder abduction, even with the elbow flexed, when it would be expected that excursion would increase as a result of increasing the length of the nerve bed. The authors suggest that compliance at the shoulder and around the elbow accounted for such lack of change to nerve excursion in the forearm. Taken together they help to add some credence to the theoretical concept proposed above. In addition,
considering the results of individuals with pain below the knee may add further credence to the consideration of effects at the nerve root.

Covariate analysis using pain below the knee resulted in a significant main effect for hip position and pain below the knee. Comparing the baseline readings of individuals with pain below the knee and pain above the knee, there was a tendency for individuals with pain below the knee to have greater nerve movement with the hip flexed at 60° than with the hip flexed to 30°. It has been postulated that the incidence of pain below the knee is more prominent in individuals with neuropathic referred leg pain than somatic referred leg pain (Beith et al., 2011; Freynhagen et al., 2008). Indeed, in the present study, only 2 (out of 11) participants had pain that was below the knee in the somatic group, with 25 out of 33 in the radicular group, and 20 out of 23 in the radiculopathy group. It may be that pain below the knee suggests greater disruption to the nerve root, particularly the lower lumbosacral roots (Murphy et al., 2009), since most individuals in the radiculopathy groups had pain below the knee, and all had objective signs of neurological loss. It is possible that greater compression or irritation of the nerve root results in greater restriction to movement at this location. Marked restriction of L5 and S1 nerve roots (mean 0.5mm and 0.3mm L5 and S1 respectively) was found during SLR, which markedly improved after discectomy (3.8mm at L5 and 4.1mm at S1) in individuals with lumbosacral disc herniation (Kobayashi et al., 2003). The data was collected before and after the micro discectomy, suggesting that symptoms were severe enough in these individuals to warrant surgery, and hence represents findings of a more affected group. In addition, nerve excursion has been demonstrated to be reduced in another nerve entrapment disorder, carpal tunnel syndrome (Hough et al., 2007; Korstanje et al., 2012).

If the nerve root has less ability to move, this may reduce the ability of these proximal nerve segments to accommodate to movement of the nervous tract lower down. Therefore, with more hip flexion, as the knee is extended and more accommodation of the nervous tissue is required, greater amounts of nerve excursion would be seen at the posterior thigh. This may explain the findings of the current study, where individuals
with pain below the knee had greater amounts of nerve excursion with the hip flexed to 60°, than at 30°. In addition, differences before and after the treatment may also be influenced by greater changes at the nerve root. In individuals in the radicular and radiculopathy groups, mean nerve excursion decreased after treatment in those with pain below the knee, but increased or showed minimal change in the individuals with pain above the knee. This may suggest that in individuals with pain below the knee, the nerve root was more influenced than in individuals with pain above the knee (and possibly where the nerve root was better able to move) because a greater mobilisation effect at the nerve root may have occurred during the SLR treatment. This mobilisation effect could have occurred due to creep or hysteresis, leading to greater compliance at the nerve root, or helped to reduce or disperse oedema (Brown et al., 2011; Schmid et al., 2013). In this case, the reduced amount of nerve excursion seen after treatment at the posterior thigh can be explained by the ability of the more proximal tissues to accommodate to the SLR movement.

As mentioned, all of these theories are speculative, and in addition the results should be taken into consideration with the smallest detectable differences found from the repeatability study (chapter 7). More individuals had differences after treatment greater than the SDD with the hip flexed to 30° (6/11 in the somatic group, 14/29 radicular and 10/20 radiculopathy). For all 3 groups combined, this resulted in 50% of individuals with sufficient change to have a genuine treatment effect. This reduced to 25% when the hip was flexed to 60°. This was related to the fact that the SDD was greater when the hip was flexed to 60° (2.4mm compared to 1.9mm with hip flexed to 30°). Overall this suggests that the effects of mobilisation at 30° may be accepted more readily than those at 60°, and more research is required to investigate this further.

Effect of age on longitudinal nerve excursion
No significant correlation with age was found for either of the hip positions, which may suggest that there is no change to nerve excursion during neurodynamic testing with increasing age. This was a surprising finding, since the sciatic nerve shows dramatic changes to its structure during the aging process, with greater amounts of adipose and
fatty tissue, and general loss of myelinated fibres (Sladjana et al., 2008). Such increases in adipose tissue, and the general effects of ageing on connective tissue characteristics (Osakabe et al., 2001) might suggest less extensibility, and therefore differences may have been expected between the older and younger participants. This was not the case, but may be related to the fact that age was not found to be statistically different on post hoc testing between the groups, SLR was not taken to the extremes of the individual’s range of movement, and was measured at the posterior thigh, rather than the knee.

**Poorly tracked images**
The images of 7 participants were of poor quality, meaning that the cross-correlation software could not adequately track the images. As mentioned in chapter 7, the software relies on a clear image of the nerve in order that it can match the grey scale pattern in each of the ROI to the next ROI. One explanation for the poor images in 6 of the participants was the high BMI found in these individuals. The propagated ultrasound wave had to pass through greater amounts of adipose tissue, which may have attenuated the ultrasound beam more, and also may mean that the nerve is more deeply situated. For the final participant, it is not clear why a poor image was obtained, although her age (58 years) may have resulted in a poorer image due to the larger amount of adipose tissue found within the nerve of older individuals (Osakabe et al., 2001).

**Normative v symptomatic**
Significantly less sciatic nerve excursion was found with the hip flexed to 60° between the somatic group in this study and the asymptomatic groups in the normative study in this thesis. This was not expected, since it was considered that participants with somatic pain have no nerve involvement, and therefore nerve excursion during the SLR test would have been similar to a group of asymptomatic individuals. However, with age adjustment, this became non-significant, but since the assumption of homogeneity was broken, this result could not be accepted. The marked difference in age between the somatic group and asymptomatic group (mean age 57.5 years somatic and 28.9 years asymptomatic) however, indicates that age may have impacted upon the significant finding between these 2 groups. Whilst age was not considered to be of significance in
the clinical study, this may be because of similar ages within the 3 groups. It is of interest to note that the other 2 groups also had less nerve excursion at 60° compared to the asymptomatic group, but this did not reach significance.

Boyd et al., (2012) found a reduction in mean tibial nerve excursion in both a neutral SLR position and hip flexed to the point of discomfort, during ankle dorsiflexion, in individuals with diabetes than asymptomatic individuals. However, the mean age of the asymptomatic group were markedly less than the group with diabetes (40 years compared to 57 years), hence changes to nerve excursion could have been attributed to age. The small numbers of participants recruited by Boyd et al., (2012) (5 in each group), also diminishes the conclusions of their study.

Transverse plane movement
Medial/lateral excursion
No statistical analysis was performed on this data due to lack of evidence for reliability, and difficulty found when analysing the nerves in this plane. Before treatment at both hip positions, the somatic group had a tendency to move laterally during the SLR, whereas the other 2 groups predominantly moved medially. It is not clear why this might have happened. In the normative study in chapter 7, whilst marked variations were found in individuals in the amount of medial and lateral movement, the majority of individuals moved more laterally with the hip flexed to 30°. This may suggest that the somatic group moved similarly to individuals without spinally referred leg pain. Medial sciatic nerve movement may have occurred in the 2 neuropathic pain groups because this would be the shortest pathway that the nerve could follow. There was greater variation in the asymptomatic group at 60° of hip flexion, whereas variation was high in both hip positions in the clinical study. After treatment, with the hip at 30°, the nerve excursion in the somatic group moved medially, and at 60° of flexion moved laterally but to a lesser degree. At 30° hip flexion, both radicular and radiculopathy groups tended to move less medially than prior to treatment, possibly indicating that the nerve was moving similarly to asymptomatic participants. However, at 60° there was little difference in medial/lateral excursion after treatment compared to before. This suggests
that there are changes to the medial and lateral nerve movements after treatment at 30°, but with the hip flexed further, where greater nerve bed length changes would occur, no consistent response is seen. Linking these findings with the longitudinal data, at 30° hip flexion, the ROM tended to decrease after treatment, and therefore the nerve was not pulled medially to the same extent as prior to treatment. At 60°, such variation between individuals before treatment, makes the understanding of changes afterwards more complex, and at this time not feasible.

The increased variability in medial/lateral nerve movement in individuals with neuropathy has also been found by Boyd et al. (2012), but at the common peroneal site, not the tibial nerve site during ankle dorsiflexion. In addition, despite the ROM of hip flexion being similar to the final hip position used in this study, individuals with and without diabetes showed a more consistent medial pattern of movement at the tibial nerve site. However, the tibial nerve at the ankle sits medial to the medial malleolus, and the direction of pull therefore from the posterior knee to the ankle must be in a medial direction, in order for the nerve to continue its course. Since the sciatic nerve may divide anywhere between the ischial tuberosity and the posterior aspect of the knee, its direction of pull towards the middle of the knee may vary during knee extension as its position in the upper leg is less predictable. In addition, the position of the nerve in relation to medial or lateral hamstrings may also affect the medial or lateral excursion (see fig 8.22 below). However, another reason for such difference could be attributed to error of the measurements. Whilst Tagliafico et al., (2012) found smaller measurement error for cross sectional area of the sciatic compared to tibial nerve; this was for static, rather than moving images. The marked change in shape of the outline of the sciatic nerve during the SLR makes this method of analysis challenging. Whilst Boyd et al., (2012) found the technique to be reliable at the tibial nerve, only small amounts of longitudinal nerve excursion movement occurred as the ankle was dorsiflexed (mean 0.6mm). Such small movements are likely to have less of an effect on the changing shape of the nerve, and may explain the high reliability found in their study (ICC= 0.97). More research is required to assess the repeatability of transverse plane movement at the posterior thigh site.
Superficial/deep excursion

At 30° hip flexion all groups showed a tendency for the nerve to move more superficially before and after treatment. Somatic and radicular groups tended to have less superficial excursion after treatment, whereas the radiculopathy group had a greater tendency to have slightly greater superficial movement after treatment. This concurs with the findings in the asymptomatic participants, where the majority of participants showed a superficial movement during the SLR test. In addition, Boyd et al. (2012) also found a consistent pattern of superficial movement of the tibial nerve during ankle dorsiflexion in individuals with and without diabetes. However at 60° hip flexion, sciatic nerve excursion was superficial in the somatic and radicular groups prior to treatment, but deep for the radiculopathy group. Hence the somatic and radicular group behaved like the asymptomatic participants, but not the radiculopathy group.

It is possible that the individuals in the radiculopathy group, with greater nerve root dysfunction may have more protective muscle contraction of the hamstrings during the SLR test (Boyd et al., 2009). Since the sciatic nerve sits between semimembranosus and the short head of biceps, it is possible that if the muscles contracted, they could limit the amount of superficial movement (see fig 8.22). In addition, Boyd et al., (2009) found that if the ankle was dorsiflexed prior to SLR that semitendinosus contracted greater than biceps femoris. Whilst semimembranosus and short head of biceps femoris were not analysed, it is possible that they may show similar activation patterns as their medially and laterally placed counterparts. Since the ankle was placed and held in plantargrade in the present study, this may support the effect of muscle activation on this direction of nerve movement. In addition, Goeken et al., (1993) suggest that semimembranosus is the first hamstring muscle to become activated during the SLR. It is possible that a greater force was exerted anteriorly to the nerve resulting in a deep movement.

After treatment, the somatic and radicular groups moved less superficially but the radiculopathy group moved even deeper. This may suggest that muscle activation did not improve after treatment. However, this is speculative and further research analysing
muscle activation during the SLR, whilst scanning the sciatic nerve would be needed to substantiate this.

Fig 8.22 Cross section through the mid-thigh (adapted from Bickels and Malawar, 2009)

Central sensitisation
The presence of CS occurred in only 2 participants. The proportion of individuals with CS in people with spinally referred leg pain is not clear within the literature, however it is considered to be prevalent in individuals with chronic low back pain (Giesbrecht and Battie, 2005; Giesecke et al., 2004; Jensen et al., 2010; Schmidt-Wilcke et al., 2006; Smart et al., 2012). The small numbers found in this study perhaps suggests that CS may not be so prevalent in this group of individuals, but may also reflect a lack of willingness of individuals with CS to participate in the study. It is not known how many individuals saw the recruitment posters or emails, or were sent the information sheets and decided not to participate in the study.

Another consideration is the method of ascertaining the presence of CS used in this study. No validated method of testing CS has been developed, therefore presence was assessed by subjective and physical factors which suggested a heightened nociceptive system. Such factors included subjective reporting of widespread allodynia,
hyperalgesia, and the presence of painful regions when tested with an algometer, which are commonly used to support a diagnosis of fibromyalgia. These points were used by Jensen et al. (2010) and found to be heightened in individuals with chronic LBP.

The results of the 2 individuals with CS can be seen in section 8.2. Since such small numbers meant that no statistical analysis was appropriate, only descriptive analyses was performed. The relevance of some of the measures is not possible to comment on with such low numbers, however some points of interest will be briefly discussed. Both individuals had a long duration of symptoms, and had a higher ODI score than the mean of each of their respective group allocations (radicular and radiculopathy). Both participants had higher psychosocial scores than the group means for most scales. However, both participants scored zero for depression, and anxiety levels were also low in both participants. This finding may suggest that depression and anxiety sub-traits are not inextricably linked with greater levels of pain. In addition, they indicate that in these 2 individuals they are not linked to higher levels of disability, which has been postulated in individuals with LBP (Wand et al., 2010). Both PPT and VT were lower than the group mean for each individual. A lower PPT was expected because these individuals had had pain on tender point assessment, which was an important indicator of CS in this study. Lowered VT levels may indicate a heightened sensitivity to the vibration stimulus, although this may have been expected to be reported as pain, since such heightened responses to non-nociceptive stimuli are considered to be a feature of individuals with CS. Neither individual reported the stimulus as painful.

Pain below the knee
The proportion of participants with pain below the knee varied markedly between the 3 groups, with both the radicular and radiculopathy groups having a much greater proportion of individuals with pain below the knee (76% and 87% respectively) than the somatic group (18%). Schafer et al. (2011) found no significant difference in the presence of pain below the knee between 4 sub-groups of individual with spinally referred leg pain. It is not clear why the 2 studies found such different presentations of pain below the knee. Despite the differences in the way that the patients were sub-
grouped (see chapter 2), individuals with neuropathic pain had a similar proportion of pain below the knee to the somatic sub-group in Schafer et al.’s (2011). However, it is possible that the small numbers of individuals with somatic referred pain in the present study, could have led to a false representation of location of referred leg pain in a larger population.

It has been postulated that people with pain below the knee have a poorer prognosis than those with pain above the knee (Hill et al., 2011). This was not demonstrated in the current study, since minimal changes to PPT occurred in any of the 3 groups and individuals in the radiculopathy group showed a decrease in VT, although this trend did not reach statistical significance. However, the difference in this study compared to Hill et al. (2011) is that the present study only assessed the immediate effects of one treatment, rather than a longitudinal observation of outcomes after 6 months. In addition, the individuals in Hill et al.’s (2011) study were not all treated in the same way, some receiving advice only, whereas other received medication or a course of physiotherapy. In agreement with the present study, Kongsted et al., (2013) found that the location of symptoms did not affect prognosis in individuals with spinally referred leg pain.

Greater levels of disability (Kongsted et al., 2012), depression and anxiety (Hill et al., 2011) have been found in individuals with pain below the knee. The current study does not concur with these findings, since there was no correlation between pain below the knee and higher levels of psychosocial or disability factors.

Psychosocial Factors
There were no significant differences in the psychosocial factors or level of disability between the 3 groups. This is in contrast to Walsh and Hall (2009a) who found higher disability and fear avoidance for individuals in a peripheral nerve sensitisation group (similar classification to the radicular group in the present study) than the denervated group (radiculopathy in the present study) and individuals with central sensitisation. However, the somatic group did not differ significantly from the peripheral nerve
sensitisation group, which is similar to the present study’s findings. Schafer et al.,
(2009) using the same sub-classification system as Walsh and Hall (2009a), only found
a difference in anxiety in individuals with central sensitisation, and not between the
other groups. Since only 2 participants in the present study were classified as having CS,
it is not possible to fully compare the findings with Schafer et al., (2011), but of interest
anxiety was low in both of the participants with CS found in the present study.
Since no differences were found in the baseline scores between the 3 sub-groups, further
analysis was not carried out into the effects of psychosocial factors on the outcome of
treatment.

The correlation of certain psychosocial scales to each other have been described in the
literature. In the present study, strong correlations were found between sub-scales of the
same questionnaire (e.g. different elements of the pain catastrophising scale, and
between depression, anxiety and stress on the DASS scale). More interestingly, pain
catastrophising (and all of its sub-scales) was found to correlate moderately with anxiety
and kinesiophobia, and anxiety was found to correlate moderately with kinesiophobia.
French et al. (2007) also found that pain catastrophising correlated with kinesiophobia,
and Osman et al. (1997) found concurrent validity of the PCS as measured against
anxiety.

Fear avoidance beliefs (FAB) about work or physical activity did not show significant
strong correlations with any of the other scales. This may be surprising, since fear about
physical activity would be expected to correlate with fear of movement (kinesiophobia),
however the correlation of these 2 subscales in the present study were only 0.35,
suggesting a weak correlation (Taylor et al., 1990). This is in contrast to Crombez et al.
(1999) who found that the FABQ correlated strongly to the Tampa scale (r= 0.57 and
0.56 (physical activity and work respectively), in 35 individuals with chronic LBP. It is
not clear why such differences were found compared to Crombez et al.’s (1999) study.
The main difference between the 2 sub-scales is that FABQ asks questions which are
mainly related to fear of movement due to pain, whereas the Tampa scale suggest more
fear of causing more harm rather than more pain. With regards to median scores,
individuals with spinally referred leg pain had slightly higher Tampa scores than the FABQ physical activity scores (33/64 Tampa compared to 10.4/24 FABQ). It is possible therefore that individuals with spinally referred leg pain were more fearful of causing greater harm than pain. However, more research is required to establish if this trend is replicated in a larger cohort, and with comparison to individuals with LBP only.

8.4 Summary of the Findings

- Pressure pain thresholds, vibration thresholds and sciatic nerve excursion during the SLR test were not significantly different between the 3 sub-groups of individuals with spinally referred leg pain after a 3 x 1 minute SLR treatment.

- Such findings may relate to the fact that individuals with these symptoms had a long history of the current problem, were only given one treatment session lasting for 3 minutes in total, and were only assessed immediately after treatment.

- VTT found no difference between groups, and in individuals with radiculopathy (where an objective sign of conduction loss was found), there was a mean trend for an improvement in VT after treatment. Whilst this did not reach statistical significance, it suggests that even in individuals with conduction loss, further losses to nerve conduction are not seen after a neural mobilisation. This is a key finding which may influence clinical practice, where tensioner techniques have previously been considered as a more aggressive form of treatment.

- Changes to sciatic nerve excursion in the posterior thigh after a 3 x 1 minute SLR mobilisation were variable. This may be due to individual differences in biomechanical compliance of the nerve along its length, and possibly restriction of the nerve root. However, the limited ability to view the nerve root, and the fact that it is only possible to measure one nerve site at one time, means that this is speculative at the current time.
• A greater proportion of individuals with pain referred below the knee were found in the radicular and radiculopathy groups, particularly in the radiculopathy group. This may suggest that location of symptoms may help to identify the mechanism of pain. However, since only 11 participants were recruited to the somatic group, more research is required to verify these findings.

• Disability and psychological characteristics were not found to be significantly different between the 3 sub-groups in this study.

8.5 Limitations of the study

Sub-grouping

At present there are limited methods of sub-grouping individuals with spinally referred leg pain. Quantitative sensory testing would differentiate between neuropathic and non-neuropathic pain, but is costly and time consuming. Pain questionnaires such as painDETECT and the LANSS scale do not distinguish between neuropathic pain with and without conduction loss. This study aimed to use a pragmatic sub-grouping system which is currently used in clinical practice. As such, the relevance of these findings may be more readily applied to clinical practice, since clinicians already use the sub-grouping system. However, the use of neurological integrity tests has been debated, with often poor validity for the identification of specific levels. In addition, recently, deterioration in small calibre sensory fibres has been found in entrapment neuropathies (Rehm et al., 2008), and these may have not been identified by light touch assessment. It is possible therefore that some individuals were not correctly identified, and some of the individuals sub-grouped as having radicular pain may have had a radiculopathy. Since no differences were found between these 2 sub-groups, it may be that these 2 groups do not behave differently to a SLR treatment, and may be considered as one group.

Sample Size

The sample size calculation suggested that 25 participants were required in each group. Sixty seven participants were recruited overall, and only 11 participants were allocated
to the somatic group. Whilst the main risk of low numbers is a type II error, the results overall suggest that an increase in numbers may not have altered the findings. This is due to the fact that for all 3 outcome measures, many individuals showed an increase in the measure, whilst large proportions of individuals decreased. Such a wash out effect has been considered to be related to responders and non-responders in individuals, and in some cases the rationale for the introduction of clinical prediction rules (Tseng et al., 2006). The use of psychosocial factors aimed, in part, to identify if such factors resulted in differences in the response to treatment. As these factors did not differ significantly between the sub-groups, it indicates that any change in the outcome measures were unlikely to be related to the psychosocial factors or disability. Therefore more research is needed to find out why some individuals responded to treatment more than others.

Location of ultrasound imaging

Whilst ultrasound imaging offers exciting opportunities to assess in vivo nerve excursion, there are limitations to this technique in the current study. The most useful area to have scanned would have been at the level of the nerve root, since individuals in the 2 neuropathic pain groups had pain referring from the nerve root. Any changes to nerve excursion or differences in nerve excursion prior to treatment between the groups may have been better analysed at this level. Unfortunately, ultrasound cannot penetrate through bone, and therefore obtaining a clear longitudinal view of the nerve roots in the lumbosacral region would be extremely challenging. The sciatic nerve can be easily visualised in the posterior thigh, and has been used to demonstrate nerve mechanics during slump test (Ellis et al., 2012). As it extends from the lumbosacral nerve roots via the lumbosacral plexus, any effects of the nerve treatment may be seen along the course of the nerve. Hence extrapolation for what may have been happening at the nerve root was attempted in the present study, utilising supportive research which has investigated normal mechanics of nervous tissue. Future possibilities to corroborate such assertions may be possible with dynamic MRI.
Transverse plane measurements

New methods of analysing transverse plane nerve excursion emerged after the data collection for the reliability study. Since these measures had only ever been planned to be descriptively analysed, it was decided to use the new method of analysis that had been shown to be reliable by Boyd et al. (2012), but to continue to describe, rather than statically analyse the data. Ideally, if there had been more time, this method of analysis would have been more thoroughly investigated. It is not known therefore, if the large variability in readings is due to measurement error, or is indeed a true finding in both asymptomatic and symptomatic groups.

Maintaining same final position of leg post treatment

Whilst greater changes to nerve excursion would have been seen if the final SLR position had been allowed to change post treatment, this would have led to an inability to explain whether such changes were simply due to alteration in the nerve bed length, due to a greater joint range of motion (either due to changes to pain or muscle/joint increased range), or changes to the nervous tissue itself. Since it is known that overall nerve movement is a consequence of a complex series of events, including undulation, excursion and strain, regional alterations in overall excursion occur without altering the overall joint range of motion.

Age of participants

The mean age of participants in this study was 52.9 years. This reflected the problems with recruitment that were not anticipated at the start of the study. Since the majority of participants were not recruited from the NHS, many individuals who responded to the adverts in the local newspapers or radio were retired. This also reflects the local geographical area to where the study was located, where there is a large proportion of retired individuals (23% compared to 10% in the London borough of Wandsworth (Royal Geographical society, n.d.). Age adjustments were made to the final analysis, but the higher mean age may affect the extrapolation of the results.
In addition FABQ for work was more difficult for participants to apply when they were not currently working. Participants were asked to consider their activities of daily living as work, but the responses may be different from individuals in paid employment.
Chapter 9 Summary, Contribution to knowledge and suggestions for future work

9.1 Overall Summary of findings

The overall aim of this thesis was to determine what effects a 3 x 1 minute SLR tensioner treatment had on pressure pain thresholds, vibration thresholds and sciatic nerve excursion between 3 different sub-groups of individuals with spinally referred leg pain. Three outcome measures were identified which gave an indication of the impact of the treatment on pain, nerve conduction and sciatic nerve excursion. Prior to the start of the clinical study, validity of the nerve excursion measurement and repeatability of the outcome measures were undertaken, to ensure that the measures were acceptable. In addition, since the participants in the nerve excursion repeatability study were asymptomatic, normative movement was ascertained during the SLR.

The method of analysing nerve excursion with frame-by-frame cross correlation was found to be valid. The findings of the 3 repeatability studies suggested that all 3 outcome measures were highly repeatable. Error measures were identified for each outcome, and these were considered in light of the clinical study. Transverse plane (medial/lateral, and superficial and deep) nerve movement was captured, initially to simply describe trends, but as new methods of analysis emerged during the course of the PhD journey, it was decided to try to measure this movement. However, this occurred subsequent to the reliability study data collection, and therefore no repeatability measures were available for analysis. Some difficulties in the use of this method were found, particularly where the nerve changed shape considerably during the SLR, or where the outline of the nerve was less clear.

Normative findings in the nerve excursion study produced new literature on in vivo sciatic nerve excursion, and supported some of the work done in the upper limb. These findings were that some individuals showed an increase in longitudinal nerve excursion with greater range of hip flexion, whilst others showed a decrease. Since greater strain is
known to occur with combinations of joint movements which result in greater lengthening of the nerve bed (a tensioner manoeuvre), it was considered that knee extension performed with the hip more flexed would result in less nerve excursion measured at the posterior thigh. It was postulated that where (counterintuitively) greater nerve excursion occurred with knee extension at 60° hip flexion compared to 30° occurred, this could be explained by the participants having higher resting levels of nerve compliance. At 30° hip flexion, the accommodation to joint movement would mainly be through nerve undulation, but as the hip was flexed further into range, the undulations were taken out, resulting in greater nerve strain and nerve excursion from the observed, posterior thigh region. Transverse plane movement was more variable, but in general the nerve moved superficially and medially during knee extension.

Overall there were no significant differences between the sub-groups, before and after the 3 x 1 minute treatment for any of the 3 outcome measures. In addition, for the PPT, few individuals showed changes after treatment which were above the SDD calculated from the repeatability study. Whilst the proportion of individuals who showed a clinically significant change was different between the 3 groups, such small changes after treatment in comparison to SDD, mean that some of the observed differences could be attributed to error. With regards to VT, whilst no significant improvements were found, an important finding of this study was that no significant deterioration was found even in participants with conduction loss. Indeed, in these participants a trend for a reduction in VT (suggesting an improvement in conduction) was found, with larger proportions of individuals showing a decrease in VT of levels greater than the SDD, than those showing an increase. These findings suggest that a SLR tensioner applied to the point of onset of symptoms for 3 x for 1 minute duration in non-severe and non-irritable individuals with radiculopathy, is not harmful.

There were two main considerations for longitudinal nerve excursion in this study. Firstly, that nerve excursion increased in the posterior thigh after treatment in some individuals, but decreased in others. It was postulated that individuals who moved less after treatment at the measured site may have had less compliance from the proximal or
distal structures, either due to predisposed stiffer connective tissue, or due to a restriction in compliance proximally due to changes at the nerve root for example. Therefore, the SLR technique may have caused a greater change in the length of the tissue which then allowed adaptive change to occur through creep and hysteresis. Such altered compliance may then have allowed greater adaptation from the previously restricted structures, resulting in less excursion closer to the moving joint (the knee). This was further supported by the fact that individuals with pain below the knee showed a decrease in excursion, and the majority of these individuals were in the radicular or radiculopathy groups.

The second consideration was that in individuals with pain below the knee, greater nerve excursion was seen with the hip flexed to 60° than 30°. This again may suggest changes to nerve mechanics proximally, since an inability to accommodate to the movement of the knee due to a restriction more proximally (e.g. at the nerve root), would result in greater excursion as the sciatic nerve in the posterior thigh is pulled towards the moving knee joint.

Transverse plane movement in the somatic group was similar to asymptomatic individuals with a superficial and lateral excursion during the SLR. In the neuropathic pain groups, the nerve moved medially, and in the radiculopathy group there was a tendency for the nerve to move more deeply. These differences may reflect the attempt to shorten the nerve path during SLR in the neuropathic pain group, and also the possible contribution of protective muscular responses in the thigh to SLR.

The prevalence of central sensitisation in individuals with spinally referred leg pain is not known, although it has been postulated to be high. This study did not support such a high proportion since only 2 participants were identified, however 2 main factors could account for this. Firstly, individuals with CS may have greater amounts of pain, higher disability levels and greater levels of psychosocial attributes. Such factors may have meant that people with CS were less likely to volunteer for a study where they had to tolerate being moved around, or be given questionnaires assessing their levels of...
psychosocial distress. In addition, no validated measures of CS have been developed; therefore this study used the presence of recognised signs and symptoms of CS, and the presence of widespread hyperalgesia to pressure. It is possible that this method did not adequately identify the presence of CS. The 2 individuals in this study had higher levels of disability than the cohort average, and many of the psychosocial factors. However, since only 2 participants were identified with CS, no further conclusion can be drawn.

The presence of pain below the knee was highest in the radiculopathy group, but was also high in the radicular group. This may suggest that pain below the knee is a good indicator of neuropathic spinally referred leg pain. However, the somatic sub-group consisted of only 11 participants, and therefore further research is required to substantiate this.

9.2 Original Contribution to Knowledge

There has been a growth in neurodynamic research in the last 5 years, which have increased the body of knowledge about the effects and effectiveness of such treatments. At the start of this PhD thesis in 2005, relatively little research had been published on lower limb neurodynamic treatments. The opportunity to find out more about what happened after such a treatment was exciting and pioneering at that time. However, even with the recent increasing body of knowledge, there remain gaps regarding the basic underlying effects of such treatment in symptomatic groups.

Recent research has demonstrated that these treatments may be effective in combination with other physiotherapeutic modalities, and animal studies have uncovered some physiological rationale for improvements. This study aimed to assess the effects of a single dose of neurodynamic treatment between sub-groups of individuals with spinally referred leg pain, and establish differences between the 3 groups on pressure pain thresholds, vibration thresholds and sciatic nerve excursion. Whilst overall no significant differences were found, some important findings provide some original and valuable points for practice or research.
1. A 3 x 1 minute SLR tensioner is not harmful even in non-severe, non-irritable individuals with neurological impairment.
2. In individuals with spinally referred leg pain, the presence of neuropathic pain does not appear to determine the response to treatment.
3. The frame-by-frame cross correlation technique for analysing longitudinal sciatic nerve excursion is repeatable even where large amounts of nerve excursion occur.
4. Variations in amounts and direction of nerve excursion during SLR occur between individuals. These variations may depend on a number of factors, including predisposed physiological characteristics (e.g. connective tissue compliance), age and pathology.

9.3 Suggestions for future work

Changes to nerve mechanics, both in pathological groups and after treatment, are complex and difficult to clearly establish. Limitations of ultrasound scanning exist, because of the restricted field of view and inability to view structures through bone. In addition only nerve excursion, not strain was explored in the present study, which does not allow for the full exploration of changes to nerve mechanics. Whilst strain measures using a similar technique to the present study have been attempted for 2D B mode images of supraspinatus tendon (Kim et al., 2011), limitations of the technique threaten its validity (Slagmolen et al., 2012). The development of elastography for analysing tissue mechanics (Drakanoni et al., 2009; Lalitha et al., 2011) and 3D USI offers new opportunities for nerve excursion studies, so that exploration of the relationship of both nerve excursion and strain may be feasible in the future. The use of dynamic MRI may allow for better exploration of changes to tissue mechanics at the nerve root and along the course of the nerve after nerve treatment.

Only immediate changes were analysed in the present study due to the length of time that participants were expected to devote to the study. Two sessions consisting of an hour, and an hour and a half were considered acceptable for the present study, since no
on-going treatment was offered to participants (although NHS participants commenced
treatment after the laboratory part of the study). Even repeating the outcome measures
after 15 minutes would have resulted in extending the laboratory session for an extra 50
minutes, resulting in participants giving up almost 2 ½ hours of their time. However, by
not including repeated measures after treatment, it is not known if an effect may have
been established subsequent to the treatment. Therefore, future studies may consist of
additional measures post treatment, but it may be that additional treatment sessions
would need to be added to justify this additional time commitment for participants. In
addition, only one treatment dose was explored. Currently the researcher is supervising
groups of postgraduate students assessing the effects of different neurodynamic
treatment doses in asymptomatic participants. It is planned that further development of
this work will continue on symptomatic groups of participants.

Vibration threshold testing has been considered an important measure of changes to
nerve conduction for individuals with minor peripheral nerve disorders. However,
changes to small diameter afferent nerve activity have also been documented, and it is
unknown what the effects of neurodynamic treatments might have to these fibres.
Measures such as hot or cold pain thresholds, and temporal summation may give an
indication of changes to small diameter afferent activity.

Some individuals in the study commented that they felt much better after the SLR
treatment, and some were surprised that it hadn’t made them feel worse. It is unknown
from the present study whether some of the individuals who improved after treatment
fell into these groups. The effect of coming to the University to participate in the study
may have had an impact on the pain measures, but perhaps less to the vibration
thresholds (although since VT are a semi-objective measures of nerve conduction,
relying on the individual to report the onset and disappearance of VT, some subjective
element could have altered VT). However, overall there was no obvious Hawthorne
effect seen, since a variation in measures was apparent between individuals, even within
the same sub-group. The limitations of solely quantitative studies are that the
individual’s experience, understanding and beliefs about the study (or their condition)
are not known or taken into account. Additional research which investigates these factors is essential to try to understand how individual attributes impact on outcome.

Finally, the investigation of one form of physiotherapy intervention alone is useful in that it allows a detailed exploration of the effects of that one treatment. However, this does not replicate clinical practice, since a combination of treatment modalities is normally required. Whilst studies have looked at combining treatment modalities, often these have been pre-determined by the researchers regardless of the patient presentation. In these instances, this removes the clinician’s role in ascertaining the best treatment for the individual patient based on high levels of clinical reasoning. Pragmatic trials (Roland and Torgerson, 1998) which allow for more active decision making by the clinician are needed to justify Physiotherapy management, but do detract from the justification of specific treatment modalities. Further work is needed in the future to establish best ways of establishing efficacy of treatment in individuals with spinally referred leg pain.

9.4 Conclusion

The use of frame-by-frame cross correlation analysis of B mode ultrasound images is repeatable for measuring sciatic nerve excursion during a modified side-lying SLR test. Vibration thresholds and pressure pain thresholds are reliable techniques for assessing pain response and conduction of the large diameter afferent nerves in individuals with spinally referred leg pain.

There is no difference in the outcome of a single 3 x 1 minute SLR tensioner treatment between sub-groups of individuals with spinally referred leg pain of greater than 3 months duration. The results suggest that this treatment dose of SLR is not effective in changing pressure pain thresholds or vibration thresholds in these individuals. However, the results importantly suggest that there are no detrimental effects for this form of treatment, even in individuals with non-severe, non-irritable radiculopathy. In addition, a varied response to longitudinal nerve excursion was observed in the posterior thigh, with some individuals demonstrating an increase, and others a decrease in longitudinal
nerve excursion after treatment. However, there was a trend for individuals with pain referred below the knee in the radicular and radiculopathy groups, to show a decrease in excursion at the posterior thigh, which may reflect changes to the compliance of the nerve after treatment.
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### Results

**Minor compression DR**
- Minor firing of Aβ fibres for 1-20 stimuli compared to 5 minutes of repetitive firing for the DRG.
- Aδ fibres only discharged for 15-25 secs after acute DR compression, but up to 25 minutes for DRG acute compression.

**Chronic NR compression**
- Caused similar changes as acute DRG.

**Groups 2 and 3**
- Motor paresis 2/52 post op, group 3 not recovered by 6/52.
- Thermal hyperalgesia from day 4 to day 10 (group 2) and from day 2 to day 14 (group 3).
- MWT in groups 2 and 3 - hypoalgesia up to week2 and then hyperalgesia (remained at 6/52).

**NP group**
- Decreased MWT 1+2/52 post op.

**NP+AF group**
- Mechanical hypoalgesia for NP+AF 1/52 post op, normal by 2/52.
- Increased TWL for NP+AF only at 1 and 2/52, normal by 4/52.

**All animals**
- Decreased PWMT post op.
- Combination group stat sig to sham at 2,4 and 16 days, medial displacement sig diff to sham at18 days. PWTL only sig for combined group, normal by day 14.

### Outcome measures

- Electrophysiological studies - 3 different methods used to assess discharge of sensory nerve fibres; microelectrode technique (Aβ fibres), microfilament technique (Aβ and Aδ fibres), a collision technique (C fibre activity).

### Method of application of material to nerve root

**Acute compression of lumbar DRs.** Method not detailed. Chronic compression model with chromic gut ligature. Applied to lumbar DRs.

**Four groups:**
- Sham - surgery alone (laminectomy), Surgery and exposure of L4 and L5 NR and DRG, L4 and L5 DRG loose ligated with CGS, control rats.

**Five groups:**
- Control, sham, adipose tissue in Lx epidural space, NP in epidural space, NP+AF on post dura mater

**Four groups:**
- Sham, disc punctured and NP applied to L4 NR and DRG, L4 NR displaced medially, combination of the 2.

### Authors

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<th>Outcome measures</th>
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<tbody>
<tr>
<td>Howe et al. 1977</td>
<td>25 cats and 8 rabbits</td>
<td>Acute compression of lumbar DRs. Method not detailed. Chronic compression model with chromic gut ligature. Applied to lumbar DRs.</td>
<td>Electrophysiological studies - 3 different methods used to assess discharge of sensory nerve fibres; microelectrode technique (Aβ fibres), microfilament technique (Aβ and Aδ fibres), a collision technique (C fibre activity).</td>
<td>Minor compression DR- minor firing of Aβ fibres for 1-20 stimuli compared to 5 minutes of repetitive firing for the DRG. Aδ fibres only discharged for 15-25 secs after acute DR compression, but up to 25 minutes for DRG acute compression. Chronic NR compression caused similar changes as acute DRG.</td>
</tr>
<tr>
<td>Chatani et al. 1995</td>
<td>71 Sprague-Dawley rats</td>
<td>Four groups: Sham - surgery alone (laminectomy), Surgery and exposure of L4 and L5 NR and DRG, L4 and L5 DRG loose ligated with CGS, control rats.</td>
<td>Motor paresis, PWL noxious thermal (heat), MWT (von Frey) - pre –op, 2, 4, 7, 10,14, 17, 21, 28, 35, 42 days post op.</td>
<td>Groups 2 and 3 motor paresis 2/52 post op, group 3 not recovered by 6/52. Thermal hyperalgesia from day 4 to day 10 (group 2) and from day 2 to day 14 (group 3). MWT in groups 2 and 3 - hypoalgesia up to week2 and then hyperalgesia (remained at 6/52).</td>
</tr>
<tr>
<td>Kawakami et al. 1996</td>
<td>82 Sprague-Dawley rats</td>
<td>Five groups: control, sham, adipose tissue in Lx epidural space, NP in epidural space, NP+AF on post dura mater</td>
<td>Tail flick mechanical withdrawal threshold (MWT) and tail in hot water thermal withdrawal latency (TWL) 1,2,4 and 6/52 post surgery.</td>
<td>No motor changes. No sig diff MWT between adipose, sham and control groups. NP group decreased MWT 1+2/52 post op. Mechanical hypoalgesia for NP+AF group 1/52 post op, normal by 2/52. Increased TWL for NP+AF only at 1 and 2/52, normal by 4/52.</td>
</tr>
<tr>
<td>Omarker and Myers 1998</td>
<td>40 Sprague-Dawley rats</td>
<td>4 groups.: sham, disc punctured and NP applied to L4 NR and DRG, L4 NR displaced medially, combination of the 2.</td>
<td>PWMT and PWTL 2 days post op and every 2 days for 18 days.</td>
<td>All animals decreased PWMT post op. Combination group stat sig to sham at 2,4 and 16 days, medial displacement sig diff to sham at18 days. PWTL only sig for combined group, normal by day 14.</td>
</tr>
<tr>
<td>Authors</td>
<td>Subjects</td>
<td>Method of application of material to nerve root</td>
<td>Outcome measures</td>
<td>Results</td>
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<tr>
<td>Hu and Xing 1998</td>
<td>24 Sprague-Dawley rats</td>
<td>4 groups: sham, compression with steel rod in IV foramen to compress DRG L5, compression with rod for 20 secs and removed, inflammation through carrageenan injection.</td>
<td>PWTL and electrophysiological measures in situ and after hanging a 5g weight from the nerve 5-10 days post-surgery. Observation of the nerve.</td>
<td>No change to PWTL for 30 sec compressed group. Both comp and inflamed groups sig diff PWTL but most severe in compressed group. Spontaneous activity in chronic compressed group in 21.5% fibres compared to 1.8% in control rats. The weight evoked a greater and more prolonged ectopic response.</td>
</tr>
<tr>
<td>Kawakami et al. 2000</td>
<td>56 Sprague-Dawley rats</td>
<td>NP from excised coccygeal NR AA. 4 groups; sham, NP applied to L5 NR, silk applied to NR, silk and NP to NR.</td>
<td>PWMT and PWTL 3, 7, 14, 21, 28, 35 days post-op. Motor patterns observed. Histology on 4 rats from each group.</td>
<td>Both silk groups had paresis 3 days post op and hypoalgesia. NP decreased PWMT for 21 days. Only combined silk and NP had decreased PWTL. Histological findings showed constriction of nerve for both silk groups but only slight adhesions in NP group.</td>
</tr>
<tr>
<td>Obata et al. 2002</td>
<td>111 Sprague-Dawley rats</td>
<td>NP and AF from excised coccygeal NR (AA) and applied to L4 and L5 NR. Sham and control animals</td>
<td>PWMT and PWTL AT 1, 3, 5 and 7 days post-surgery. L4/5 DRG dissected and processed for NGF and BDNF at these time points.</td>
<td>Reduced PWMT 1 day post-surgery but normal by day 5. No change to PWTL. No motor loss. Statistically significant greater number of NGF immuno-receptive cells (compared to sham) at 1 day, normalised by day 5. BDNF sig greater than naïve rats at 3 and 5 days.</td>
</tr>
<tr>
<td>Hou et al. 2003</td>
<td>51 Sprague-Dawley rats</td>
<td>Tail excised and disc material taken from coccygeal IV discs. 6 groups: sham, L5 DNR compression with disc, DNR compression with bone fragment, disc material applied no compression, NP alone, AF alone.</td>
<td>PWMT and PWTL % change from baseline. Motor function observed 1, 2, 3, 5 days and then weekly for 6 weeks.</td>
<td>All groups (except sham) sig reduced PWMT. Worst group combined disc and comp peak at 3/52 almost recovered at 6/52. PWTL sig only at certain time frames in certain groups, but only around 80% diff from baseline compared to 20% for PWMT. No motor loss.</td>
</tr>
<tr>
<td>Authors</td>
<td>Subjects</td>
<td>Method of application of material to nerve root</td>
<td>Outcome measures</td>
<td>Results</td>
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<tr>
<td>Rothman and Winkelstein 2007</td>
<td>37 Sprague-Dawley rats</td>
<td>Four groups: Sham exposure of C7 NR, Chromic gut suture (CGS) to C7 NR, 10gf compression dip to NR, combined comp and CGS.</td>
<td>PWMT measured at 1,3,5 and 7 days post-op. Presence of glial fibrillary acidic protein (GFAP) and CR3/CD11b analysed for astrocyte and microglial activation respectively on day 1 and 7.</td>
<td>All groups (except sham) sig decrease in PWMT. CGS only sig day 1, normal day 5. Comp and CGS most affected but not sig diff between comp alone and comp + CGS. Contralateral effects for combined group. GFAP sig increased at day 1 and 7 in comp and comp/CGS. CGS only sig day 7 compared to normal. CR3/CD11b not sig diff any group day 1, day 7 no sig diff for CGS alone, sig diff combined and</td>
</tr>
<tr>
<td>Hubbard and Winkelstein 2008</td>
<td>36 Sprague-Dawley rats</td>
<td>3 groups: C7 NR compressed between micro-compression plates for 15 mins range of loads (6.9-93.4 Nm) loads above and below previous behavioural changes day 1) compression above and below these levels day 7 (5.3-97.9), sham.</td>
<td>PWMT and macrophage infiltration and axonal degeneration from histology. Macrophage infiltration and neurofilament immunoreactivity assessed by CD68 and NF200 immunoreactivity respectively.</td>
<td>Day 1 only loads above 26.3Nm sig decreased PWMT, day 7 loads above 38.2 Nm. No macrophage infiltration at day 1. At day 7 evidence of macrophage infiltration in 7/8 nerves above 38.2, but also in 4/6 below this load. Axonal swelling and Wallerian degeneration at day 7 in 7/8 rats. Day 1 no changes to either CD68 or NF200. Marked decrease to NF200 on day 7 in loads greater than 38.2Nm. CD68 presence at all loads at day 7.</td>
</tr>
</tbody>
</table>
### Appendix 2: Effects of nerve root compression and irritation on inflammation, nerve conduction and structure

<table>
<thead>
<tr>
<th>Authors</th>
<th>Subjects</th>
<th>Method of application of material to nerve root</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olmarker and Rydevik 1989</td>
<td>39 pigs</td>
<td>A balloon inserted in the cauda equina and pressure applied to the nerve roots of 50 or 200 mm Hg. Pressure applied both rapidly (0.05-0.1 seconds) and slowly (15 to 20 seconds). Compression held from 2 mins to 2 hours.</td>
<td>Post compression EBA injected intravenously and allowed to circulate for 30 mins.</td>
<td>With rapid compression, more pronounced oedema found following 2 hours of compression regardless of level of pressure. With slower rate, minimal oedema only at edges of compressed segments after 2 hours.</td>
</tr>
<tr>
<td>Rydevik et al 1991</td>
<td>25 pigs</td>
<td>Silicone balloon to the cauda equina. Comp 0 up to 200 mmHg applied over 2 hours.</td>
<td>Sensory (CNAP) and motor nerve conduction (EMG) monitored every 5 minutes over 2 hours. Histological assessment.</td>
<td>No changes to CNAP or EMG &lt;75 mm Hg. Marked deterioration &gt;75 mm Hg, esp at 200 mmHg. Recovery after 2 hours at 75 mmHg complete after 40 mins, but at 200 mm Hg incomplete after 1/12 hrs with CNAP slightly less recovered than EMG. Histology: min changes 50 mmHg, 100 mm Hg widespread oedema in the nerve roots, 200 mm Hg injury to myelin sheaths and haemorrhage of nerve fibres.</td>
</tr>
<tr>
<td>Pedowitz et al. 1992</td>
<td>20 Yorkshire minipigs (5 animals in each group)</td>
<td>An inflatable plastic bag placed between a plate inserted into lamina and the nerve roots in the cauda equina. Bag connected to tubing and inflated 0-200 mmHg for 2 or 4 hours. Recovery over 1 1/2 hours.</td>
<td>Motor (CMAP) and sensory (CNAP) measured. Histological assessment.</td>
<td>No changes to conduction at 0 or 50 mmHg even after 4 hours. 100 and 200 mm Hg sig deterioration in CNAP and CMAP. Recovery above baseline levels after 1 1/2 hours. 200mmHg complete block CNAP after 2 hours, near complete block CMAP after 3 hours. Partial recovery CMAP, but min recovery in 1 animal (4.7% of baseline) and no recovery in 4 animals of CNAP. Mild to mod oedema at 100mmHg. Mod to severe oedema at 200mmHg. Sig diff in recovery between CNAP and CMAP.</td>
</tr>
<tr>
<td>Olmarker et al. 1993</td>
<td>30 pigs</td>
<td>Cauda equina exposed, NP placed epidurally in close contact with nerve roots. Control group - same procedure but retroperitoneal fat placed close to NR.</td>
<td>Histological analysis and nerve conduction velocity (NCV) at 1,3, and 7 days.</td>
<td>NCV stat sig lower in exp group at 1,3 and 7 days than control animals. Epidural hyperaemia and bleeding in most animals in both groups. Little endoneurial bleeding or hyperaemia in either group. Greater Schwann cell oedema in exp group than control group.</td>
</tr>
<tr>
<td>Authors</td>
<td>Subjects</td>
<td>Method of application of material</td>
<td>Outcome measures</td>
<td>Results</td>
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<tr>
<td>Kobayashi et al. 1993</td>
<td>65 dogs</td>
<td>Compressed the 7th spinal nerve roots for 1 hour with a microvascular clip at 7.5, 15, 30 and 60 gf (7.5gf equivalent to 50 mm Hg Kobayashi et al., 2004a).</td>
<td>Trace proteins (EBA and HRP) injected into subarachnoid space and intravenously. Examined presence with and without compression in NR and DRG in dogs.</td>
<td>In non-compressed dogs post sub-arachnoid injections, proteins in-between nerve fibres in endoneurial space (hence poor nerve root sheath barrier). With intravenous injection, proteins in DRG, but not the NR, suggesting minimal nerve-blood barrier in DRG. 30 and 60gf, proteins in endoneurial space of the nerve root, none at 7.5gf.</td>
</tr>
<tr>
<td>Kawakami et al. 1994</td>
<td>22 male Sprague-Dawley rats</td>
<td>Left L4-NR and DRG exposed. 3 groups - sham (surgery only), loose silk ligatures around L4-L6 NR just prox to DRG, CGS around NR L4-L6</td>
<td>Histological assessment</td>
<td>Silk and CGS had similar and sig changes in fibre composition at level of NR and DRG- loss of large and increase in small diameter fibres.</td>
</tr>
<tr>
<td>Chatani et al. 2005</td>
<td>71 Sprague-Dawley rats</td>
<td>Four groups: Sham -surgery alone (laminectomy), Surgery and exposure of L4 and L5 NR and DRG, L4 and L5 DRG loose ligated with CGS, control rats.</td>
<td>Histological analysis day 5 and week 6</td>
<td>Day 5 grps 2 and 3 swelling of the L DRG. Week 6 scarring around DRG- sl worse in grp 3. Enlargement of endoneurial spaces and axonal vacuolization. Decrease in nos of large myelinated fibres and increase in smaller ones in DRG and adjacent spinal nerve and nerve roots.</td>
</tr>
<tr>
<td>Yoshizawa et al. 1995</td>
<td>48 dogs</td>
<td>Silicone tube placed around the 7th lumbar nerve root. Left in situ for 24 hours up to 12 months.</td>
<td>Protein markers (HRP and EBA) injected intravenously to assess blood-nerve barrier. Microscopic changes. Sensory amplitude and conduction velocity of nerve root.</td>
<td>3/12 NR compressed by scarring and swelling either end of tube, &gt; changes 6/12. Dura and arachnoid thickened 1/12. 3/12 ↓ myelinated and ↑ thin myelinated fibres, in endoneurium vacuoles (ingestion myelin) and macrophages in endoneurial spaces. After 1 year more regeneration than degeneration. Tracers in endoneurial space after 1/12, but arachnoid mater barrier function maintained. Both amplitude and CV deteriorated at 1 year, but only amplitude deteriorated at 3/12</td>
</tr>
<tr>
<td>Omarker and Myers 1998</td>
<td>40 Sprague-Dawley rats</td>
<td>4 groups: 1. sham, 2. disc punctured and NP applied to L4 NR and DRG, 3. L4 NR displaced medially, 4. combination of the 2.</td>
<td>Histological assessment from segments of DRG and nerve root 2, 5, 10 and 21 days post op.</td>
<td>NP group- oedema in DRG within 5 days which remained at end of study. Displacement similar to above but more severe. Combination group – more severe oedema and fibrosis in endoneurial space which separated nerve fibres, axonal demyelination seen, Schwann cell hypertrophy.</td>
</tr>
</tbody>
</table>
### Results

No change immediately after compression. After 1/52, NP group CEAP decreased to 50% of baseline measures. Combination group, both CEAP and SNCV stat reduced after 1/52. Stat diff after 1/52 for SNCV between combined and compression, and combined and NP group but not between NP and compression. More severe changes to intraneural and Schwann cell oedema and nerve fibre injury in the combined group than the other groups.

7.5gf no changes EBA compared to C/L side. 15gf EBA site of compression only, 30 and 60gf EBA central DRG. Intercellular space widened due to oedema in 15, 30 and 60 gf. HRP similar findings- no diff at 7.5gf, greater at 15, but most sig at 30 and 60 gf with HRP staining whole DRG in the latter 2 groups. No Leakage of HRP to epineurium indicating that perineurial barrier intact.

1/52, EBA in DNR proximal to compression, VNR distally. At 3/52, EBA found further towards SC. At 1/52 signs of Wallerian degeneration in DNR prox to comp and distal in VNR. At 3/52 large areas fibrosed and myelin sheath with no axons. On electron microscopy discontinuity in the capillaries and breakdown of the blood-nerve barrier.

Chromatolysis was found one week after compression. Suggesting nerve degeneration and regeneration. A marked decrease found in the neurotransmitters. It has been demonstrated that chromatolysis inhibits the production of neurotransmitters, so this finding supports the histological findings.

### Method of Application of Material to Nerve Root

- **Sham group**, compression group using plastic balloon, NP group- NP taken from same dog and applied to sacrococcygeal NR, combined group (comp and NP)
- 7th Lx DRG compressed using vascular clip at 60,30, 15 or 7.5gf for 1 hour in 8 animals each. C/L DRG as control.
- Compressed the 7th spinal nerve roots for 1 to 3 weeks with a microvascular clip at 7.5gf
- Compression of 7.5gf (~50 mm Hg) of the 7th lumbar dorsal nerve root. The NR compressed for 24 hours and up to 3/52.

### Outcome Measures

- Ascending cauda equina action potentials (CEAP), sensory nerve CV (SNCV) before, after and 1/52 after and histological analysis
- EBA and HRP injected intravenously. Animals killed 1 hour later.
- Intravenous injection of EBA. Histological analysis of nerve fibres.
- Histological analysis and immunostaining for calcitonin gene-related peptide (CGRP), substance P and somatostatin in the DRG.

### Authors

- Takahashi et al. 2003
- Kobayashi and Yoshizawa 2002
- Kobayashi et al. 2004a
- Kobayashi et al. 2004b

### Subjects

- 18 dogs
- 32 dogs
- 12 dogs
- 18 dogs

### Key

- DNR/VNR dorsal/ventral nerve roots, DRG dorsal root ganglion, NR nerve root, NP nucleus pulposus, AF annulus fibrosus, CV conduction velocity, CMAP compound motor action potential, CGS chromic gut suture, EBA Evans blue albumin, HRP horseradish peroxidase, EMG electromyography, CNAP compound nerve action potential, SNCV sensory nerve conduction velocity, EBA Evans blue albumin, HRP horseradish peroxidase
Appendix 3 Recent studies investigating somatic referral of leg pain

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<tr>
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<th>Diagnosis of condition</th>
<th>Results</th>
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<tr>
<td>Fukui et al. 1997</td>
<td>48 patients with suspected Z jt pain.</td>
<td>Injected with contrast medium under fluoroscopic guidance. When pain occurred anaesthetic given. In addition electrical stimulation of medial branch of dorsal ramus</td>
<td>Controlled double block technique., if temporary relief only, electrical stimulation of medial branch</td>
<td>Marked overlap of pain referral. No pain below thigh</td>
</tr>
<tr>
<td>Ohnmeiss et al. 1997</td>
<td>187 patients with suspected lumbar disc dysfunction.</td>
<td>Pain drawings prior to discography. Discs injected and pain reported areas of pain.</td>
<td>CT discography</td>
<td>Grade 1 annular disruption pain to buttock and thigh, grades 2 and 3 similar distribution; pain mostly thigh and lower leg.</td>
</tr>
<tr>
<td>O’Neill et al. 2002</td>
<td>25 patients with suspected lumbar disc dysfunction</td>
<td>Patients identified current pain on body chart. Posterior annulus heated by IDET incrementally until patient had a VAS score &gt;6/10</td>
<td>Positive discogram at one level</td>
<td>Pain in back, thigh and lower leg. Same distribution as original pain pain drawing.</td>
</tr>
<tr>
<td>Jung et al. 2007</td>
<td>200 patients initial study confirmed diagnosis (facet and SIJ). 419 patients next part of study.</td>
<td>Initial study patients made pain drawings. Subsequent study patients shown diagrams and asked to compare their areas of pain to previous drawings.</td>
<td>&gt;50% relief of pain after nerve blocks. If pain not relieved &gt;50% relief on radiofrequency neurotomies.</td>
<td>Diagnostic reliability best for LB and LB + post thigh for Z joint and for SIJ bilateral buttock.</td>
</tr>
<tr>
<td>Laplante et al. 2012</td>
<td>157 cases from 153 patients with non-resolving LBP</td>
<td>Patients indicated if pain was in hip girdle, thigh or lower leg.</td>
<td>Discography, double facet block, or double SIJ block. Provocative discography had to increase the pain&gt;6/10, the blocks had to decrease the pain by 75%</td>
<td>Difference in areas of symptoms not stat different between different pathology groups.</td>
</tr>
</tbody>
</table>
### Appendix 4: Studies on dermatome mapping

<table>
<thead>
<tr>
<th>Authors</th>
<th>Participants</th>
<th>Methods of ascertaining dermatome</th>
<th>Major Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sherrington, 1894</td>
<td>Monkeys</td>
<td>Remaining sensibility. Divided the nerve root above and below the level to be tested.</td>
<td>Marked overlapping of dermatomes suggesting more than one nerve root responsible for supplying each area of skin.</td>
</tr>
<tr>
<td>Bolk, 1898</td>
<td>Humans</td>
<td>Dissecting from one nerve root and following through the plexus and cutaneous nerves.</td>
<td>No overlap of dermatomes (but unable to follow finest cutaneous nerve into periphery)</td>
</tr>
<tr>
<td>Head and Campbell, 1900</td>
<td>Humans</td>
<td>A combination of location of rash in individuals with Herpes Zoster, outlining hyperaesthesia of skin in visceral diseases compared to spinal cord injured patients</td>
<td>Some overlap of dermatomes. Some missing levels from this method. Herpes eruptions can extend over several DRG, so method inaccurate.</td>
</tr>
<tr>
<td>Foerster, 1933</td>
<td>Humans</td>
<td>1. Resection of nerve roots above and below and testing skin sensation of remaining nerve root. 2. Resected each nerve root and tested for anaesthesia. 3. Electrical stimulation of nerve roots and observing area of skin vasodilation.</td>
<td>Dermatomes may vary between individuals, overlap of dermatomes. No clinical sensory loss if only 1 nerve root sectioned.</td>
</tr>
<tr>
<td>Keegan and Garrett, 1948</td>
<td>Humans</td>
<td>Light pin scratch on individuals with diagnosis of disc herniation.</td>
<td>Dermatomes in neat longitudinal bands with no overlap.</td>
</tr>
<tr>
<td>Davis et al., 1952</td>
<td>Humans</td>
<td>Light pin scratch and pin prick on individuals with disc herniation.</td>
<td>Not able to reproduce bands like Keegan and Garrett (1948), most had loss in lower leg and foot only. Most variability being related to extent and location of disc herniation, and variable NR compression.</td>
</tr>
<tr>
<td>Nitta et al., 1993</td>
<td>Humans</td>
<td>Patients with radicular pain going for nerve blocks.</td>
<td>Variability and overlap of dermatomes. S1 extended into buttocks in 92% of cases.</td>
</tr>
<tr>
<td>Lee et al., 2008</td>
<td>Amalgamated findings of dermatomal studies</td>
<td>Overlapped Foerster’s and Head and Campbell’s maps and the modified from a number of other sources.</td>
<td>No autonomous zones of sensory innervation due to adjacent overlapping of dermatomes. S1 may extend up the back of the leg and overlap with S2</td>
</tr>
</tbody>
</table>
### Appendix 5: Studies for Psychosocial factors and disability in individuals with LBP

<table>
<thead>
<tr>
<th>Author</th>
<th>Participants</th>
<th>Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Picavet et al. 2002</td>
<td>Questionnaires sent to 8000 Dutch inhabitants. Follow up questionnaire sent out to 2,338 individuals who fitted inclusion criteria. 1571 participated in the follow up at 6 months</td>
<td>Initial and follow up questionnaires included details about the LBP: presence of, length of time, severity, disability (Quebec back pain disability questionnaire (QBDQ)), pain catastrophising scale (PCS), Tampa scale of Kinesiophobia (TSK).</td>
<td>High levels on the PCS and TSK predicted low back pain (in those who did not have it at the first questionnaire), and chronicity (in those who had it at initial questionnaire) and severe low back pain and disability.</td>
</tr>
<tr>
<td>Burton et al., 2004</td>
<td>252 patients with low back pain attending a private osteopathic clinic</td>
<td>Detailed history of low back pain, clinical examination, verbal rating pain scale (VRPS), Roland Morris disability questionnaire (RDQ), depression, fear avoidance belief (FAB), somatic concern. Treatment with osteopathic techniques (not standardised), and advice to remain active. Follow up with questionnaire at 1 year and around 4 years (range 3.5-5).</td>
<td>186 and 151 participants responded at 1 year and 4 years respectively. RDQ sig diff between baseline and 1 year, but not 1 and 4 years. 43% deteriorated between 1 and 4 years. 73% and 59% had pain at 1 and 4 years respectively. Predictors of recurrence: length of time of pain, presence of leg pain, high FAB and high somatic concern. Poor outcome at 4 years was predicted by higher levels of depression.</td>
</tr>
<tr>
<td>Woby et al., 2004</td>
<td>54 individuals with chronic LBP</td>
<td>Disability measured by RDQ, VAS, FABQ, catastrophising sub scale of coping strategies (CSQ), were given to participants before and after a cognitive behavioural therapy, educational and exercise programme.</td>
<td>Significant improvements occurred on all measures except pain intensity and FAB about work. Reductions in pain intensity were strongly related to reductions in disability. Reductions in FAB work and physical activity increased perceptions of control over pain. Changes in catastrophising strongly related to control over pain.</td>
</tr>
<tr>
<td>Walsh and Hall, 2009a</td>
<td>45 individuals with low back related leg pain</td>
<td>Participants completed the Oswestry disability index (ODI), Hospital anxiety and depression scale (HADS) and FABQ, The Leeds assessment of neuropathic symptoms and signs questionnaire (LANSS) was completed, and VAS used. Physical examination performed. Sub-groups as detailed in chapter 2 used: central sensitisation (CS) (n=15), denervated (D)[n=7], Musculoskeletal (MS)[n=12] and peripheral nerve sensitisation (PNS) (n=11).</td>
<td>Statistically higher disability (ODI) and FAB for physical activity in PNS group than the other groups, except for MS. All groups had anxiety levels considered to be borderline abnormal and moderately high levels of FAB for activity.</td>
</tr>
<tr>
<td>Author</td>
<td>Participants</td>
<td>Method</td>
<td>Results</td>
</tr>
<tr>
<td>----------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Benecuij et al.,</td>
<td>62 healthy participants</td>
<td>Questionnaires given: PCS, Fear of pain questionnaire (FPQ-9), TSK, State-trait Anxiety questionnaire (STAI). Upper limit neurodynamic test 1 for the median nerve (ULNT1). ROM, sensory descriptors, VAS for pain and sensation.</td>
<td>PCS and FPQ-9 strongly associated, as were TSK and FPQ-9 and STAI. PCS predictor of pain intensity during the ULNT1. However, no psychological factors were predictors of non-painful stimuli (e.g. pins and needles).</td>
</tr>
<tr>
<td>Jensen et al.,</td>
<td>351 employed but (currently signed off work) LBP patients with or without S and S of neurological involvement recruited to a RCT. Sub- -grouped as non-specific LBP or radiculopathy</td>
<td>Participants randomised to an evaluation and advice group or in addition coaching from a social worker and occupational therapist. Measures: LBP rating scale, RDQ, common mental disorders questionnaire (stress, depression and anxiety), fear avoidance about physical activity, work related questions, general health. Disc height on X-ray, MRI where indicated (75% participants)</td>
<td>231 responded to follow up questionnaire at 1 year. Higher fear avoidance negatively associated with change in disability at one year (linear regression). Predictors for disability and back and leg pain at 1 year: intensity of back and leg pain, worrying and health anxiety, little exercise. No particular diffs between radiculopathy and non-specific LBP.</td>
</tr>
<tr>
<td>Schäfer et al.,</td>
<td>74 patients with unilateral back and leg pain &gt;6/52 duration</td>
<td>4 sub-groups: 1. Neuropathic sensitised (NS), 2. Denervation (D) (+ve neuro integrity), 3. Peripheral nerve sensitised (PNS), 4. Musculoskeletal (M) (somatic), Rx-2 neurodynamic interventions (7 sessions, 2 x weekly). Pain NRS, RDQ, global perceived change scale (GPC). Covariates- HADS, FABQ.</td>
<td>group (56%) than other groups (NS 11%, D 15%, M 11%). Significant improvements in all outcome measures in the PNS group than all other groups, although pain measures not stat diff between PNS and NS (P=0.052). No sig diff between groups for depression or FAB, but sig for anxiety (NS greater than PNS or D, but not M). However no sig interaction effect for anxiety in main analysis.</td>
</tr>
<tr>
<td>Kongsted et al.,</td>
<td>2673 patients with LBP +/- leg pain: 437 LBP only patients, 398 LBP and pain above knee, 807 LBP and pain below knee, 1031 LBP and nerve involvement (+NI) (+ve neuro integrity or SLR test)</td>
<td>Data collected from spine data database (routine clinical data collected at time of assessment) from a spine centre in Denmark. Patients seen from Dec 2008-Nov 2011. Pain intensity numerical rating scale (NRS), RDQ, work participation, depression (PRIME-MD), FABQ, general health (Euroqol health thermometer)</td>
<td>Most disabled (from RDQ) in LBP + NI (sig diff all comparisons). Most sick days in LBP and NI (least in LBP alone) (sig diff between LBP+NI and all groups). Depression and fear of movt greatest in LBP+NI and least in LBP alone (sig diff between LBP and LBP+NI). No real diffs in health between groups.</td>
</tr>
<tr>
<td>Author</td>
<td>Participants</td>
<td>Method</td>
<td>Results</td>
</tr>
<tr>
<td>-------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Haugen et al., 2012</td>
<td>466 patients with referred leg pain below the knee and lumbar disc herniation on MRI or CT scan in Norway.</td>
<td>Baseline data day 1: socio-demographic factors, VAS pain in back and leg, TSK, emotional distress (Hopkins symptoms check list 25 (HSCL-25). Neuro integrity and SLR performed. Patients then received usual intervention e.g. advice, physical therapy, pain medication. Surgery in severe cases. Questionnaires sent at 3,6,12 and 24 months. Outcomes: Maine-Seattle back Q (MSBQ), Sciatica bothersome index (SBI)</td>
<td>88% and 82% response rate at 1 year and 2 years. First episode 45% of patients. Non-success (MSBQ ≥ 5) 178 (44%) patients at 1 year and 145 (39%) at 2 years. Using SBI (≥7), non-success at 1 year = 194 (47%), and 159 (42%) at 2 years. Slight better success surgical V non-surgical at 1 year, but similar at 2 years MSBQ. Prognostic factors: 1 and 2 years comorbid health, at 1 year, male, &gt; LBP intensity and abnormal reflexes, at 2 years, high TSK, longer duration pain.</td>
</tr>
<tr>
<td>Kongsted et al., 2013</td>
<td>264 LBP only patients, 204 LBP and pain above knee, 344 LBP and pain below knee, 940 LBP and nerve involvement (+NI) (+ve neuro integrity or SLR test)</td>
<td>Data collected from spine data database from a spine centre in Denmark. Same baseline data as for 2012 paper above, but more restricted time frame (i.e. patients seen between October 2010-October 2011). Outcome measures RDQ after 3 and 12 months, Global perceived effect (GPE) 3 months, sick leave 3 months. Not clear what, if any interventions patients underwent.</td>
<td>76% and 70% responded at 3 and 12 months, but data re work only received from 46%. Baseline and improvement in disability greatest in the LBP+NI group. GPE- LBP+NI higher odds for being better than the other groups, but when adjusted for duration was not significant. A larger proportion of LBP+NI were on sick leave after 3 months than other groups. Location of leg pain (no neurological signs) did not appear to have any effects on prognosis.</td>
</tr>
</tbody>
</table>
Appendix 6 Oswestry Disability Scale (Fairbank et al., 1980)

Oswestry Disability Questionnaire

This questionnaire has been designed to give us information as to how your back or leg pain is affecting your ability to manage in everyday life. Please answer by checking one box in each section for the statement which best applies to you. We realise you may consider that two or more statements in any one section apply but please just shade out the spot that indicates the statement which most clearly describes your problem.

Section 1: Pain Intensity

☐ I have no pain at the moment
☐ The pain is very mild at the moment
☐ The pain is moderate at the moment
☐ The pain is fairly severe at the moment
☐ The pain is very severe at the moment
☐ The pain is the worst imaginable at the moment

Section 2: Personal Care (eg. washing, dressing)

☐ 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 can 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 me extra pain
☐ Pain prevents me lifting heavy weights off the floor but I can manage if they are conveniently placed e.g. on a table
☐ Pain prevents me lifting heavy weights but I can manage light to medium weights if they are conveniently positioned
☐ I can only lift very light weights
☐ I cannot lift or carry anything

Section 4: Walking*

☐ Pain does not prevent me walking any distance
☐ Pain prevents me from walking more than 2 kilometres
☐ Pain prevents me from walking more than 1 kilometre
☐ Pain prevents me from walking more than 500 metres
☐ I can only walk using a stick or crutches
☐ I am in bed most of the time

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 sitting more than one hour
☐ Pain prevents me from sitting more than 30 minutes
☐ 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 30 minutes
☐ Pain prevents me from standing for more than 10 minutes
☐ Pain prevents me from standing at all

Section 7: Sleeping

☐ My sleep is never disturbed by pain
☐ My sleep is occasionally disturbed by pain
☐ Because of pain I have less than 6 hours sleep
☐ Because of pain I have less than 4 hours sleep
☐ Because of pain I have less than 2 hours sleep
☐ Pain prevents me from sleeping at all

Section 8: Sex Life (If applicable)

☐ 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. sport
☐ Pain has restricted my 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 pain
☐ I can travel anywhere but it gives me extra pain
☐ Pain restricts me to journeys of less than one hour
☐ Pain restricts me to short necessary journeys under 30 minutes
☐ Pain prevents me from travelling except to receive treatment
Appendix 7 Fear Avoidance Beliefs Questionnaire (Waddell et al., 1993)

Fear Avoidance Beliefs Questionnaire (FABQ) for patients with Back Pain

Instructions: Here are some of the things which other patients have told us about their pain. For each statement please circle the number from 0 to 6 to say how much physical activities such as bending, lifting, walking and driving affect or would affect your back or leg pain.

<table>
<thead>
<tr>
<th>Rating</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meaning</td>
<td>Completely disagree</td>
<td>Unsure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Completely agree</td>
</tr>
</tbody>
</table>

Statements

1) My pain is caused by physical activity
2) Physical activity makes my pain worse
3) Physical activity might harm my back
4) I should not do physical activity which (might) make my pain worse
5) I cannot do physical activities which (might) make my pain worse

The following statements are about how your normal work affects or would affect your back or leg pain.

6) My pain was caused by my work or by an accident at work
7) My work aggravated my pain
8) I have a claim for compensation for my pain
9) My work is too heavy for me
10) My work makes or would make my pain worse
11) My work might harm my back
12) I should not do my normal work with my present pain
13) I cannot do my normal work with my present pain
14) I cannot do my normal work till my pain is treated
15) I do not think that I will be back to normal in 3 months
16) I do not think that I will ever be able to go back to work
# Appendix 8 Tampa Scale of Kinesiophobia

## Tampa Scale for Kinesiophobia

*(Miller, Kori and Todd 1991)*

1 = strongly disagree  
2 = disagree  
3 = agree  
4 = strongly agree

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>I’m afraid that I might injury myself if I exercise</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2.</td>
<td>If I were to try to overcome it, my pain would increase</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3.</td>
<td>My body is telling me I have something dangerously wrong</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4.</td>
<td>My pain would probably be relieved if I were to exercise</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5.</td>
<td>People aren’t taking my medical condition seriously enough</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6.</td>
<td>My accident has put my body at risk for the rest of my life</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7.</td>
<td>Pain always means I have injured my body</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8.</td>
<td>Just because something aggravates my pain does not mean it is dangerous</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9.</td>
<td>I am afraid that I might injure myself accidentally</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>10.</td>
<td>Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>11.</td>
<td>I wouldn’t have this much pain if there weren’t something potentially dangerous going on in my body</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>12.</td>
<td>Although my condition is painful, I would be better off if I were physically active</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>13.</td>
<td>Pain lets me know when to stop exercising so that I don’t injure myself</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>14.</td>
<td>It’s really not safe for a person with a condition like mine to be physically active</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>15.</td>
<td>I can’t do all the things normal people do because it’s too easy for me to get injured</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>16.</td>
<td>Even though something is causing me a lot of pain, I don’t think it’s actually dangerous</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>17.</td>
<td>No one should have to exercise when he/she is in pain</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
Appendix 9 Pain Catastrophising Scale

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

0 – not at all   1 – to a slight degree   2 – to a moderate degree   3 – to a great degree   4 – all the time

When I’m in pain …

☐ I worry all the time about whether the pain will end.
☐ I feel I can’t go on.
☐ It’s terrible and I think it’s never going to get any better.
☐ It’s awful and I feel that it overwhelms me.
☐ I feel I can’t stand it anymore.
☐ I become afraid that the pain will get worse.
☐ I keep thinking of other painful events.
☐ I anxiously want the pain to go away.
☐ I can’t seem to keep it out of my mind.
☐ I keep thinking about how much it hurts.
☐ I keep thinking about how badly I want the pain to stop.
☐ There’s nothing I can do to reduce the intensity of the pain.
☐ I wonder whether something serious may happen.

...Total
<table>
<thead>
<tr>
<th>Statement</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I found it hard to wind down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. I was aware of dryness of my mouth</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. I couldn’t seem to experience any positive feeling at all</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. I found it difficult to work up the initiative to do things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. I tended to over-react to situations</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. I experienced trembling (eg, in the hands)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. I felt that I was using a lot of nervous energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. I was worried about situations in which I might panic and make a fool of myself</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>10. I felt that I had nothing to look forward to</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>11. I found myself getting agitated</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>12. I found it difficult to relax</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>13. I felt down-hearted and blue</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>14. I was intolerant of anything that kept me from getting on with what I was doing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>15. I felt I was close to panic</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>16. I was unable to become enthusiastic about anything</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>17. I felt I wasn’t worth much as a person</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>18. I felt that I was rather touchy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>19. I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>20. I felt scared without any good reason</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>21. I felt that life was meaningless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Author</td>
<td>Participants</td>
<td>Movements and region/s of nerve studied</td>
<td>Method of measurement</td>
<td>Results</td>
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<tr>
<td>O’Connell (1946)</td>
<td>4 cadavers aged 44-73</td>
<td>1. Cervical flexion. Duramater and spinal cord in cervical region, mid-thoracic region and conus.</td>
<td>Marker placed on surface of duramater or spinal cord (incision or white thread), scalpel blade inserted into vertebral lamina. Amount of movement between scalpel and marker.</td>
<td>1. Cervical flexion: cephalad movement of all regions, 5mm cervical region, 4mm mid thoracic and 1mm at the conus. 2. SLR: caudad movement of duramater. Bilateral movement up to 10mm of dura, around the cauda equina.</td>
</tr>
<tr>
<td>Falconer et al. (1948)</td>
<td>3 fresh cadavers, ages not disclosed.</td>
<td>SLR L5 and S1 nerve roots</td>
<td>Observational methods, details not disclosed.</td>
<td>Distally ranging from 2-6 mm. Movement started at around 35° SLR with maximum amounts at 60-90°.</td>
</tr>
<tr>
<td>Smith (1956)</td>
<td>4 Rhesus monkeys</td>
<td>1. From full extension to full cervical and trunk flexion. Markers along the spine</td>
<td>Sawed monkeys in half, hemilaminectomy performed. Pins inserted into spinal cord, dorsal nerve roots and different parts of the sciatic and tibial nerve. Nails into bony landmarks. Lateral roentgenogram to analyse movement.</td>
<td>1. Trunk and neck flexion: caudad movement of spinal cord above C4, cephalad movement of spinal cord below C4. Greatest movement 5.9mm around T7. Strain 16% C0-1, 24% C6-C7, 4% L3-4. 2. SLR: LX sacral plexus at pelvic rim distal mvt 4mm, sciatic nerve posterior thigh distal mvt 11mm, 21mm distal popliteal fossa, tibial nerve upper calf, proximal 9mm.</td>
</tr>
<tr>
<td>Reid et al. (1960)</td>
<td>18 fresh cadavers aged 15-75 years</td>
<td>All measures from C5 through to T12. 1. Flexion head and neck. 2. Flexion neck and trunk.</td>
<td>Pins inserted through dura into cord and pedicles.</td>
<td>1. Flexion head and neck: cephalad mvt, least at T12 (mean 0.8mm), greatest at T1 (mean 6.8mm), C5 mean 1.5mm. 2. Flexion neck and trunk: cephalad C8 to T5. No mvt C6. C5, T10 and 12 varied, some cephalad, some caudal. Greatest mvt T1 (mean 6.6mm).</td>
</tr>
<tr>
<td>Breig (1960)</td>
<td>143 cadavers aged 23-84.</td>
<td>1. Cervical, thoracic and lumbar spinal cord from full trunk and neck extension to full flexion.</td>
<td>1. Paper markers anchored on cord during extension - separation of strips during flexion. 2. Silver pin markers and wire indicators- X ray in extension and flexion.</td>
<td>Difference in length from extension to flexion: Cervical cord- 18-28 mm Thoracic cord- 9-13 mm Lumbar cord- 10-20 mm Dura and NRs move around 2mm cephalad during flexion- not shown which region.</td>
</tr>
<tr>
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<tr>
<td>Breig and Marions</td>
<td>9 cadavers, ages not disclosed</td>
<td>Cervical flexion and extension sacral cone and nerves of cauda equina</td>
<td>1. Tension 2/9 cadavers laminectomy, thread around cauda equina at L4 level attached to spring balance. Tension of 20g applied prior to mvt to gently lift cauda equina. 2. 2/9 Observation of deformation of NRs. 3. 3/9 cadavers Recording of deformation by myelography.</td>
<td>1. Increased tension in cauda equina with Cx flexion. System too crude to give measurements. 2. Dura and NRs moved cephalad by 1-2mm. Reduction in cross section of dura and sacral cone. 3. Dura, NRs and root sleeves stretched in Cx flexion and NRs in contact with pedicles and superficially to root sleeves.</td>
</tr>
<tr>
<td>Goddard and Reid</td>
<td>30 unembalmed cadavers aged &lt;35 to &gt;75.</td>
<td>SLR L4, 5 and S1 (just above formation of nerve root and in intervertebral (IV) foramen), lumbosacral cord and sacral nerve (1cm proximal to sciatic notch).</td>
<td>Anterior dissection of soft tissue and bone. Pins inserted into perineurium and paper markers into adjoining bone.</td>
<td>Min distal mvt L4 NR, most distal movement at sciatic nerve mean; range from 4 (&gt;75 years) to 7.5mm (&lt;35 years). L5 and S1 NR min mvt proximal to formation of NR, greater at level of IV foramen (1.5-3mm mean range L5, 2-5mm mean range S1).</td>
</tr>
<tr>
<td>Breig and Troup</td>
<td>6 fresh cadavers, 5 aged 51-83, 1 age unknown.</td>
<td>1. Medial rotation (MR) hip 2. SLR 3. Hip adduction. Sacral plexus</td>
<td>Paper markers inserted into S2 and S3 NRs. Photographic recordings in 4/6 cadavers. No other details of method given.</td>
<td>On MR increase in resistance to pressure over sacral plexus and increased tension in all 6 cadavers. Hip MR mvt of markers from 2-10mm into greater sciatic foramen (GSF) (in 4 cadavers). SLR mvt 6-10 mm towards GSF (in 3 cadavers), Hip adduction mvt 3mm towards GSF (in 1 cadaver).</td>
</tr>
<tr>
<td>Sugiura et al.</td>
<td>5 fresh cadavers, ages not disclosed</td>
<td>SLR L3-S1 regions</td>
<td>Rubber tube inserted between nerve roots and lumbar disc. Tube filled with water and connected to a pressure transducer.</td>
<td>Increased pressure after 30 ° SLR, greatest pressures at L5-S1 level, pressure at L3-4 &lt;1/10th at L5-S1. Hip adduction increased pressure, hip abduction decreased the pressure.</td>
</tr>
<tr>
<td>Smith et al.</td>
<td>10 fresh cadavers aged 55-77.</td>
<td>SLR L4-S1 NRs</td>
<td>Metal screws pedicles and transverse processes L4-S1. Ink dots on each NR at 4mm intervals between cauda equina and DRG. Photographs taken, projected transparencies onto paper and nerve motion compared in relation to the pedicle. Strain measured comparing length of nerve segment at 0° SLR to 60°</td>
<td>Minimal motion &lt;30° SLR. 2 directions of mvt- in line with direction of nerve and perpendicular to nerve. Mean mvt's DRG at L4 = 1.4mm, L5 = 2.1mm, S1 = 2.5mm but varied considerably between cadavers. Less mvt more proximally. Strain 3.2% L4, 2.8% L5, 3.4% S1.</td>
</tr>
</tbody>
</table>
Results

Overall max strain of cervical cord between 6.8% and 13.6% posterior surface and 3.7% to 8.7% anterior surface (p<0.01 ant: post).

Caudad movt C2-3 (mean post cord 2.7mm), cephalad movt C6-7 (mean post cord 6.7 mm, C7 2.7 mm). Little displacement C4-5.

In neutral hip position, knee extension mean increased strain to 14% (range 10-19%). Hip 45° flexion mean increased strain 26% (range 19-30%).

DF had greatest effect on change in tibial nerve (TN) strain at the ankle (3.28%), and least at the sciatic nerve (SN) at the hip (-0.02). HF greatest effect on SN strain (6.61%) and least on TN at the ankle (-2.5%).

Direction of excursion always towards moving joint. DF - distal excursion TN ankle 9.5 mm, TN knee 3.1 mm, SN 0, HF proximal excursion SN of 28 mm, 12.7 TN knee, 6.4 TN ankle.

Distal excursion parallel to NR axis was 0.53, 0.48, and 0.51 mm for L4, L5, S1. Perpendicular to NR axis was 0.17, 0.04 and 0.15 mm.

Strain increased to 0.56%, 0.68% and 1.89% L4-S1.

With dorsiflexion and SLR, distal excursion parallel to NR axis was 0.06, 0.04 and 0.2 mm for L4, L5, S1. Perpendicular strain was -0.23, -0.02 and 0.15 mm. Strain increased to 0.56%, 0.68% and 1.89% L4-S1.

Method of measurement

Motion tracking MRI scans. Mid-sagittal images. 3 or 4 markers drawn onto epineurium of sciatic nerve. Video-extensometry used to calculate strain. Strain measured with linear displacement transducers. Excursion using digital vernier calipers - fixed markers into cortical bone, mobile markers suture around nerve close to fixed markers.

Locations - tibial nerve prox to ankle and at the knee, sciatic nerve distal to greater trochanter.

Implantation of helical metal markers into L4, L5 and S1 NRs at 3 locations: extraforaminal, intraforaminal and lateral recess. Cadaver stabilised on a jig, bolts screwed into ilium to prevent pelvic movements. Fluoroscopic images taken at each hip position during SLR.

Method as above with ankle dorsiflexion and without ankle dorsiflexion. Same NRs as above.
<table>
<thead>
<tr>
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<th>Method of measurement</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Boyd et al. (2013)</td>
<td>10 embalmed cadavers aged 55-95 years</td>
<td>2 sequences of SLR: 1. HF (with knee extended) then DF 2. DF then HF (with knee extended) SN 5cms distal to ischial tuberosity (strain only), TN</td>
<td>Differential variable reluctance transducer inserted into each nerve with 2 barbed pins for strain. Digital caliper for excursion. Distance between a fixed metal markers in adjacent bones and distal barb of the transducer to determine excursion.</td>
<td>A maximum strain of around 8% was found in the SN during both sequences and for the TN with HF followed by DF. At the end of movement for either sequence, there was minimal difference (a maximum of 0.8% for TN ankle with HF/DF than DF/HF) in strain. Excursion TN ankle and knee move distal with DF and proximal with HF. Ranged from ~4mm TN knee with HF to 6mm TN ankle with DF.</td>
</tr>
</tbody>
</table>
### Appendix 12 Slider and Tensioner Studies

#### Results

**At wrist:** Sig > nerve excursion sliding position (mean 12.4mm) than all positions (*P*<0.0002) and lowest peak strain. Tensioner position and positions with EE and WE had sig> peak strain (~4%) than slider or mvts of wrist in elbow flexion (*p*<0.0005).

**At prox humerus:** Greatest exc and strain with tensioner (13.7mm and ~4.2% strain), and other mvts with EE. Greatest strain WE with EE (~4.6%).

#### Method of measurement and nerve regions studied

- **Strain with linear displacement transducers:** 1. Median nerve prox to wrist, 2. Median nerve 12cms prox to med epicondyle. Excursion with digital vernier caliper compared to fixed marker distal radius and distal humerus.
- **Strain at wrist and elbow as above for median nerve (but 10cms prox to med epicondyle), and ulnar nerve just prox to elbow. Excursion as above.**
- **Ultrasound imaging of median nerve in longitudinal section, 7-10 cms proximal to med epicondyle.**
- **Ultrasound imaging of sciatic nerve in posterior proximal thigh.**

#### Movements

- **6 different versions of ULNT1:** slider, tensioner and simple single joint mvts in SH ABD (see fig 4.1). No cervical mvts.
- **1. Median nerve same mvts as above. 2. Ulnar nerve tensioner (WE, EF, SH ABD) and slider (WE, EE, SH ABD and WE, EF, SH ADD).**
- **6 different versions of ULNT 1: slider and tensioner and ILLF or CLLF of neck with EF or EE and vice versa. Wrist in neutral**
- **4 movements in slump position: tensioner (slump with Cx F +KE), Slider (slump with Cx E + KE), slump and Cx E, slump and KE.**

#### Participants

- **6 intact embalmed cadavers (65-92 years at death).**
- **2 intact embalmed cadavers (78 and 85 years at death)**
- **15 healthy volunteers (mean age 30+/- 8 years).**
- **31 healthy volunteers (21-61 years)**

#### Author

- **Coppieters and Alshami, 2007**
- **Coppieters and Butler, 2008**
- **Coppieters et al., 2009**
- **Ellis et al., 2012**
### Appendix 13 Effectiveness of neurodynamic treatment

<table>
<thead>
<tr>
<th>Authors</th>
<th>Participants</th>
<th>Treatment groups</th>
<th>Detail of treatment</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kornberg and Lew, 1989</td>
<td>28 Professional Australian Rules footballers with hamstring injury and positive slump test.</td>
<td>Usual care (not standardised) plus slump stretching, and usual care.</td>
<td>No detail of sets or reps or if sustained or oscillatory, or how often slump was performed.</td>
<td>Number of games missed in the season post hamstring injury.</td>
<td>16 players treated with usual care alone, 12 with usual care and slump stretching. Only 1 player treated with slump and usual care missed one match. All usual care players missed at least one game, with 10 missing 2, and one missing 6 games. The difference between missing games was statistically significantly (p&lt;0.001).</td>
</tr>
<tr>
<td>Tal Akabi and Rushton, 2000</td>
<td>21 patients diagnosed with carpal tunnel syndrome (CTS)</td>
<td>3 groups: longitudinal neurodynamic treatment, carpal bone mobilisation or control group.</td>
<td>Not clear who did the Rx. Grade, reps and progression based on patient presentation. No detail of number of treatments and if comparable in each group. Appeared that neurodynamic technique was a tensioner but not clear.</td>
<td>Daily pain scores (VAS), functional box scale, Pain relief scale, ROM wrist ext and flex and the ULNT (+ve or –ve test), proceed to surgery.</td>
<td>Significant differences were found between control and treatment groups for ROM wrist ext, VAS, pain relief score; but no differences between longitudinal or carpal bone mobilisations. Continue to surgery - 2/7 nerve Rx, 1/7 carpal mobs, 6/7 control.</td>
</tr>
<tr>
<td>Scrimshaw and Maher, 2001</td>
<td>81 patients post spinal surgery (discectomy, laminectomy or spinal fusion)</td>
<td>2 treatment groups 1. standard care and 2. standard care plus neural mob</td>
<td>Vague description of exercises for standard care (isometric and dynamic) 2-3 daily for 6 weeks. Neural mobs group-day 1 and 2 active SLR both legs and passive neck flexion progress to SLR with cervical flexion day 3. Additional neural exs for home but not specified</td>
<td>Global perceived effect, pain with VAS, McGill pain questionnaire and Quebec disability scale.</td>
<td>No sig difference between groups in any of outcome measures. Looked at between group differences and on all measures the mean difference suggested a less favourable response for Rx than the control group.</td>
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</table>
### Results

No baseline diffs in FAB. Sig diff in all OM between groups 1 and 2; greater improvements in group 2. Clinically meaningful improvement both groups for ODI (>6, 6.9 group 1 and 18.2 group 2). Slight improvement in centralisation (1.2 and 1.88 for grps 1 and 2 respectively) and NPRS (1.2, 2.33 respectively; clinically meaningful) for neck pain is 2.1, De La Llave et al., 2012).

- By the 6th session hip ROM was sig greater (? P value not stated) for group 1 compared to group 2. Sig maintained post session 9. Improvements in VAS at session 6 and 9, sig greater for group 1.

### Drop outs

- 8 in group 1 and 7 in group 2 at 1 month follow up, and 16 at 6 month (so final comparison 15 subjects group 1 and 14 group 2). No sig diff in measures except for functional scale of BWCTS, greater improvement in standard care (but by only 0.7).

### Outcome measures

- NPRS, ODI, centralising or peripheralising of symptoms. FABQ to assess for baseline diffs.

### Treatment groups

- **Group 1:** Lumbar mobilisation and exercise, 2. Lumbar mobs, exercise and slump stretching.
- **Group 2:** Standard care plus 2. Standard care plus ULNT1 R1 pre, 1 month and 6 month follow up.

### Participants

- 30 patients with LBP and leg pain

### Authors

- Cleland et al., 2006
- Sarkari and Multani, 2007
- Heebner and Roddey, 2008
<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
<td>Beneciuk et al., 2009</td>
<td>62 under and postgraduate students</td>
<td>2 groups: 1. ULNT1 tensioner, 2. Sham Rx</td>
<td>9 sessions, 2-3 x weekly. ULNT1 2 Rxs- 1. Tensioner with passive EE/EF x10 then static hold 10 secs, 2. Tensioner with sustained EE and active Cx CLLF (x 10 then static hold 10 secs). Sham- No sh depression, or Cx CLLF, SH ABD 45°, 45°ER and EE, forearm pron, WF/WE 10x then sustained hold x 10 secs.</td>
<td>Thermal pain sensitivity—first pain (A delta fibres) and temporal summation (TS) (c fibres and wind up), EE ROM during ULNT1, sensory descriptors during ULNT1 after 1 and 9 sessions and 1/52 after 9th session no jig used to standardise). Baseline diffs in PCS and Tampa VAS, PPT, thermal threshold and TS, clinical rating of pain (CRP), DASH, grip strength with hand dynamometer, sensation with Sommes-Weinstein monofilaments, sensory and motor NCS</td>
<td>Immediate inhibition of TS for tensioner technique, not sham. Improvements in first pain for both groups (not sig diff to each other). No sig changes for other time frames. No diff for EE ROM during ULNT for sham, but sig diff increase for tensioner (mean diff 8.6 degrees) at Rx 9 and 1/52 post. VAS ratings during ULNT also sig improved in tensioner group only (mean diff VAS 0.6).</td>
</tr>
<tr>
<td>Bialosky et al., 2009</td>
<td>40 female patients with CTS</td>
<td>2 groups 1. ULNT 1 tensioner 2. Sham.</td>
<td>Night splint for all. Group 1 full ULNT 1 position with wrist and finger ext oscillated ?? P1/P2/R2 Group 2- Cx spine neutral, sh girdle neutral, sh abd/ER 45°, EE 45°, forearm pronation with wrist and finger ext AA. 5 sets of 10 cycles 1st 3 Rx, 7 sets 10 cycles 4-6 sessions.</td>
<td>VAS, PPT, thermal threshold and TS, clinical rating of pain (CRP), DASH, grip strength with hand dynamometer, sensation with Sommes-Weinstein monofilaments, sensory and motor NCS</td>
<td>37% of group 1 and 61% group2 believed they had the Rx intervention. VAS, PPT, DASH,CRP, grip strength both groups sig improved at 3/52, no sig diff between groups. Thermal threshold not sig diff between groups or within groups. TS sig decrease in reported pain in group 1 compared to group 2 (group 2 increased TS pain). No diff sensation or NCS for either group</td>
</tr>
<tr>
<td>Adel, 2011</td>
<td>60 patients with chronic LBP and leg pain, +ve SLR and _ve lumbar flex/ext</td>
<td>2 groups: 1. Lumbar mobs and exercise 2. AA plus SLR</td>
<td>Six Physiotherapy sessions, 2 per week. Group 1 Protocol as for Cleland et al. (2006) Group 2 AA plus SLR tensioner 5 x sustained for 30 seconds (? Ankle oscillated rather than sustained).</td>
<td>Numeric pain rating scale (NPRS), ODI, centralisation of symptoms (regions of back and leg given a number 1- local back to 6 lower leg). Nerve root compression grade on MRI scan.</td>
<td>Separate T tests performed. Sig differences between groups for all measures, mean diff between groups- ODI 4.6, NPRS 1.2, centralisation 0.4. Greater improvements in the SLR group. Whilst sig diff reported on NR compression on MRI scan- the results not well displayed, unable to see the relevance of the numbers given.</td>
</tr>
</tbody>
</table>
Results

Paired sample T-tests or non-parametric equivalent. ROM, strength, VAS stat improved in both groups (from baseline but not between groups). Sig improved light touch in medial calcaneal nerve (MCN) both groups, but greater diffs observed in group 2 (If a between group analysis was sig). 2 pt discrimin sig diff in group 2 for MCN, not for group 1 (although lateral planar nerve was sig in group 1 but not group 2).

Nos in each groups: 19 NS, 27 D, 9 PNS, 19 M

A greater proportion of responders in PNS group (56%) than other groups (NS 11%, D 15%, M 11%).

Significant improvements in all outcome measures in the PNS group than all other groups, although pain measures not stats diff between PNS and NS (P=0.052).

PPT sig diff at C5-C6 between baseline and 1 week follow up, but very small diffs, not clinical sig. No other sig changes to PPT other sites.

NPRS sig improvements in current and worst pain from baseline to 1 week post Rx (greater than SDD and MCID).

### Authors
Kavlak et al., 2011
Schäfer et al., 2011
De-La-Llave-Rincon et al., 2012

### Participants
28 patients with tarsal tunnel syndrome (TTS)
74 patients with unilateral back and leg pain and tarsal tunnel syndrome (52 duration)
18 women with CTS

### Treatment groups
2 groups: 1. Strengthening and stretching exercises, ice, bandaging. 2. AA plus orthotics.
4 sub groups: 1. Neuropathic sensitised (NS), 2. Denervation (D), 3. Peripheral nerve sensitised (PNS), 4. Musculoskeletal (M)

### Treatment 1
6 weeks home exercises. Patients monitored every 10 days over 6 weeks. ??

### Treatment 2
6 weeks home exercises. Patients monitored every 10 days over 6 weeks. ??

### Outcome measures
- Pain on VAS, ROM ankle and subtalar joint with universal goniometer, manual examination of strength of foot muscles, 2 point discrimination, light touch with Semmes-Weinstein monofilaments, Tinel test, tibial nerve stretch test (TNST-sustained maximal ankle and foot DF/eversion)
- Pain NRPS, Roland Morris disability questionnaire (RMDQ), global perceived change scale (GPC), hospital anxiety and depression scale (HADS), FABQ
- PPT bilaterally on median, radial and ulnar nerves, C5-C6 zygapophyseal joints, carpal tunnel and tibialis anterior

### Detail of treatment
1. Interface - side lying lumbar lateral flexion 60 secs
2. Slider - hip flex/knee flex to hip ext/knee ext x 30 secs. Both repeated 5 times, 2 sets 5 mins 1 minute rest between sets

1. Potential interfaces mobilised (inc scalenes, biceps and transverse carpal ligament) for 30 minutes.
2. Nerve slider intervention 2 sets 5 mins 1 minute rest between sets

### Authors
Kavlak et al., 2011
Schäfer et al., 2011
De-La-Llave-Rincon et al., 2012
### Authors | Participants | Treatment groups | Detail of treatment | Outcome measures | Results |
---|---|---|---|---|---|
Nagrale et al., 2012 | 60 patients with LBP and referred leg pain without neurological compromise | Group 1- Lx spine mobs and stabilisation exs | Group 1- Lx PA mobs painful level 3 x 40 secs and all hypomobile levels 2 x 40 secs. Exs as for Cleland et al. (2006)(sets of 10 reps). Group 2- AA plus long sitting slump, Cx spine flex to P1 5 X 30 sec hold. Both groups 2 x weekly for 3/52. Group 2 also home slump exs x 2 reps of 30 secs | NPRS current pain. ODQ, FABQ. All at baseline, 1,2,3 and 6 weeks. | Both groups sig improvements in all 3 outcome measures from baseline to all time points. Sig greater improvements in all measures between group 1 and group 2. Marked changes in NRPS and ODI above MCID. No values for MCID for FABQ but change to score by week 6 of around 23 for group 2 and 13 for group 1. |
Nee et al., 2012 | 60 patients with non-traumatic nerve related neck and arm pain. | Experimental group and control group | Control group (20)- advised to continue normal activities. Experimental group (40)- AA plus 4 Rx over 2/52 of education, Manual therapy-contralateral Cx glide, shoulder girdle oscillation and cranio-Cx flexion exs. Home programme of sliding and tensioning ULNT1 exs 10-15 reps 3 x daily. | 15 point global rating of change scale (GROC) (as a measure of improvement (>=+4 on scale of -7 to +7) and harm(GROC <=-2)), NPRS neck and arm pain (current, highest and lowest prev 24 hours), Neck disability index (NDI), patients specific functional scale(PFS). Recording of adverse event. | 2 lost from each group at follow up. 21/38 exp group improvement in GROC only 1/18 in control group (sig better in exp group- but no p value). Worse GROC at follow up 3/38 exp group and 4/18 control. Clinically important changes in NPRS neck and arm pain in 13% exp group, 1% control group, NDI 11% exp, 1% control and PSFS 15% exp 1% control. Adverse event in 16/38 exp, all improved in <24 hours, none needed extra Rx and no change in outcome compared to those without adverse effects. |
Schmid et al., 2012 | 20 patients with mild to moderate CTS | Night splint or tendon and nerve gliding exs | Tendon gliding exs and slider ULNT 1 10 reps 10 x per day. | MRI scan to identify oedema Boston CT questionnaire, PSFS | Sig reduction in signal (less oedema) in both groups (no diff between). Sig diff in Boston CT and PSFS from baseline both groups (not between), but v small diffs (not clin important for Boston). |
Appendix 14 research ethics and governance approval
ultrasound reliability

01273 564029

3rd September 2018

Colette Ridealgh
Senior Lecturer
Course Leader MSc NMS Physiotherapy
Physiotherapy Division
School of Health Professions
University of Brighton
49 Darley Rd
Eastbourne
BN23 7UR

Dear Colette,

Title of Proposal:  Effects of the slump test on the deformation of the sciatic nerve: an ultrasonography and electromyography study

FREGC Application Number:  2005-39

We are writing to confirm that the above-mentioned amendments to your proposal have been approved by the Research Ethics and Governance Committee of the Faculty of Health and Social Science (FREGC) after an independent scientific and ethics review.

Although approval has been given to start the research work, it is the ultimate responsibility of the researchers to ensure that the work is conducted within the Research Ethics and Governance Framework of the University of Brighton, and if applicable, those of the Department of Health and any funding body. Approval of project is given for the duration of the research indicated in the application form, although FREGC may review this decision at any time and has the right to suspend or terminate this approval.

You are required to notify the Committee in writing if there are any substantial changes in the research methodology or any serious adverse events or accidents during the conduct of the study. As a requirement of the Governance Framework, please submit annual progress and completion reports to the Committee. You may not be need to prepare a separate progress report for the Committee as we would be happy to receive a copy of annual report submitted to funding body, NHS or other relevant body to satisfy this requirement. Please see the Guidance Notes of the Application Pack (Section 7) for further information.

Yours sincerely

[Signature]

Professor Julie Scholes PhD
Chair of Faculty of Health Research Ethics & Governance Committee
Appendix 15 subject information sheet and consent form ultrasound repeatability study
University of Brighton
School of Health Professions

Subject Information Sheet

Intra rater reliability of B mode ultrasound on longitudinal and transverse movement of the sciatic nerve during the straight leg raise test.

2 Invitation paragraph

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

3 What is the purpose of the study?

The study aims to look at how consistent a specialised piece of equipment (ultrasound) is in measuring movement of the sciatic nerve (the major nerve which passes down the back of your thigh) during a standard physiotherapy test (the straight leg raise test (SLR)). The study will take approximately 30 minutes, and you will be required to attend two times in total, thus the overall time you will need to commit to this study will be one hour.

4 Why have I been chosen?

You have been chosen for the study as you are fit and well without low back pain. You will need to meet the requirements for eligibility into the study as described below.

The following conditions do not apply to you

- Previous spinal surgery
- Neck, mid or low back pain or hip, knee or ankle problems within the last year
- Systemic disorders (eg Rheumatoid arthritis, diabetes, thyroid disease, HIV/AIDS)
- Neurological disorders (eg stroke, multiple sclerosis)
• Restriction in your back, neck, hip, ankle or knee range of motion which prevents you from being able to be positioned into the SLR test (these will be tested prior to commencement of the study).
• Cancer
• Severe Osteoporosis
• Pregnancy
• Allergy to elastoplast tape
• Body mass index greater than 30kg/m² (this will be calculated from your height and weight measurements)

5 **Do I have to take part?**

Your participation is entirely voluntary, if you are unsure about taking part then feel free to say no. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect you in any way.

6 **What will happen to me if I take part?**

You will be asked to change into a pair of shorts and then a short series of tests will be applied to your leg to ensure that the range of motion of your legs will allow you to be positioned into the SLR position (this position is explained below). You will also have your reflexes, muscle strength and sensation in your legs tested. Your height and weight will be taken.

You will be positioned on your side on a plinth with your leg on a wooden table top and an ultrasound probe (small plastic device) will be applied to the back of your thigh, a layer of gel will be applied between the probe and your skin to improve the contact between you and the probe (this may feel cold). A small measuring device will be applied to your skin either side of your knee joint with double sided adhesive tape. Two plastic splints will be applied to your feet to keep your ankle joints in a set position. Your hip will be moved forwards by the researcher and then held into place with a board and strap, and you knee bent. The research assistant will then straighten your knee a set amount, before it is kept in a semi bent position. This will then be repeated until the knee is completely straight or until tightness in your leg prevents the knee from moving any further. Your hip will then be re-positioned a little further forward, and the same knee movements repeated. You will be asked to inform the researcher if you have any discomfort during these movements. Measurements will be taken during these movements. The same procedure will then be repeated with the ultrasound probe in a slightly different position on the back of your thigh.

You will then be asked to return once more, on the same day of the week, at the same time.
7 **What do I have to do?**

Please bring shorts with you and do not partake in any vigorous exercise 12 hours prior to the study.

8 **What are the possible disadvantages and risks of taking part?**

There have been no side effects recorded from using the ultrasound machine. In theory the temperature could rise inside your leg as a result of the ultrasound waves, however the type and dose of ultrasound used in this study is very safe, and thus this is very unlikely to happen.

The SLR test is a commonly used test that physiotherapists use on a regular basis, and in some individuals some discomfort (such as a stretch feeling) is produced. You will be asked to inform the researcher if you have any discomfort during the test procedure and if you do, movements will be stopped. If you are unhappy at any point during the study, you are free to withdraw.

9 **What are the possible benefits of taking part?**

The benefits to you are minimal, however you will have the opportunity to contribute to a study that will enhance our knowledge of nerve examination and treatment.

10 **What if something goes wrong?**

You can contact the researcher or supervisor if any problems arise as a result of this study (contact details are given below), or if you would prefer to get in touch with someone independent of the study you should contact:

*Professor Valerie Hall*
*Head of the Centre for Nursing and Midwifery Research*
*University of Brighton*
*Mayfield House, Falmer, Brighton BN1 9PH*
*Tel 01273 644015*
*Email v.hall@brighton.ac.uk*

11 **Will my taking part in this study be kept confidential?**

All personal details will be kept separately from the actual data collected. These details will be stored on a computer that has a password only known to the researcher. The only other people that have access to these details are the dissertation supervisors.
12 **What will happen to the results of the research study?**

The results of the study will form part of a PhD thesis. In addition the researcher hopes to publish the results of this study in a journal and present the findings at a national or international conference. In this case, no participants will be mentioned by name, hence your confidentiality will be upheld at all times.

13 **Who has reviewed the study?**

The study has been reviewed by the University of Brighton Faculty of Health research ethics and governance committee and the academic supervisors.

14 **Contacts for Further Information**

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Supervisors</th>
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<tr>
<td>Colette Ridehalgh</td>
<td>Professor Ann Moore</td>
</tr>
<tr>
<td>School of Health</td>
<td>Clinical Research Centre for Health</td>
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<td>Professions</td>
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<td>Aldro Building, Eastbourne, BN20 7UR</td>
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<tr>
<td>49 Darley Rd</td>
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<tr>
<td>Eastbourne</td>
<td>Dr. Alan Hough</td>
</tr>
<tr>
<td>BN20 7UR</td>
<td>Senior Lecturer</td>
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<tr>
<td>01273 643686</td>
<td>Faculty of Health</td>
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<td></td>
<td>University of Plymouth</td>
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<td></td>
<td>Derriford Road, Plymouth PL6 8BH</td>
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<td>01752 588837</td>
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</tbody>
</table>

Thank you for taking part in this study.
Intra rater reliability of B mode ultrasound on longitudinal and transverse measures of the sciatic nerve during the straight leg raise test.

- I agree to take part in this research which is to look at how consistent a specialised piece of equipment (ultrasound) is in measuring movement of the sciatic nerve (the major nerve which passes down the back of your thigh) during a standard physiotherapy test (the SLR test).

- The experimenter has explained to my satisfaction the purpose of the experiment and the possible risks involved.

- I have had the principles and the procedure explained to me and I have also read the information sheet. I understand the principles and procedures fully.

- I am aware that I will be required to change into a pair of shorts, have a number of tests performed on me to look at range of motion of my legs and reflex, strength and sensation tests. I am also aware that I will have to lie on my side and have a plastic probe attached to the back of my thigh, before the researcher will place a support on my ankle and move my leg forward and take some measurements.

- I understand that there may be a small amount of discomfort produced during the test and that I will inform the researcher if this does occur.

- I understand that I will need to attend the human movement laboratory for 2, 30 minute sessions.

- I understand that any confidential information will be seen only by the researcher and will not be revealed to anyone else.

- I understand that I am free to withdraw from the investigation at any time.

Name (please print)………………………………………………………………………………

Signed………………………………………………………………………………………

Date…………………………………………………………………………………………
Appendix 16 Information sheet and consent form repeatability of pressure pain thresholds and vibration thresholds

University of Brighton
School of Health Professions

Participant Information Sheet Study 1

Reliability of measurements of vibration and pressure pain in people with leg pain thought to be referred from the spine

2 Invitation paragraph

You are being invited to take part in a research study. Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this information.

3 What is the purpose of the study?

The study aims to look at if two commonly used measures of sensation and pain are reliable between sessions in people who suffer with leg pain thought to be coming from their spine.

4 Why have I been chosen?

You have been chosen for the study as you have had low back pain and/or leg pain for 3 months or longer and are not currently receiving any treatment for this
condition. You will need to meet the requirements for eligibility into the study as
described below.

The following conditions do not apply to you

- Previous spinal surgery
- Current or previous medical diagnoses that may affect your participation in the
  study e.g. Rheumatoid Arthritis, diabetes, thyroid disease, HIV/AIDS, stroke,
  cancer, osteoporosis)
- Currently Pregnant
- Hip, knee or ankle disorders within the last year
- New unexplained bladder and bowel problems, and/or pins and needles in your
  genital region)
- Currently receiving treatment for the LBP/leg pain
- On regular high levels of pain medication (over the counter pain medication is
  fine, but you will be asked to stop taking this for 24 hours prior to the study)

5 Do I have to take part?

Your participation is entirely voluntary. If you are unsure about taking part then feel
free to decline. If you do decide to take part you will be given this information sheet
to keep and be asked to sign a consent form and send it back to the researcher (by
email cr19@bton.ac.uk or in the stamped addressed envelope sent to you). If you do
not want to participate, you are still asked to send back the form, and sign in the
section indicated on the form. If you decide to take part you are still free to withdraw
at any time without giving a reason. A decision to withdraw at any time, or a
decision not to take part, will not affect you in any way.

6 What will happen to me if I take part?

The researcher will first contact you by phone and ask you some questions to ensure
that you are able to take part in the study (these will include questions about your
back pain and any relevant medical history). If you are eligible to take part in the study you will be given a convenient time for you to attend the Human movement laboratory at the University of Brighton, Darley Rd, Eastbourne. You will have 2 specific tests performed twice in this session with a break of 30 minutes between them. The 2 specific tests will each take approximately ½ an hour. All appropriate travel costs will be met by the researcher and will be discussed prior to participation in the study.

You will be asked a number of questions by the researcher who is an experienced Physiotherapist with 19 years experience about your back and/or leg problem. You will then be asked to change into a pair of shorts and bra top (for ladies) before a number of tests will be applied:

- Your height and weight will be measured.
- You will be asked to move your back and leg and let the researcher know if you have any of your pain during these movements. You will be asked to lie on your stomach and the researcher will press on your spine with her hand and you will again be asked if this brings on your pain. The strength in your legs will be tested and your reflexes will be checked (you may have had this done by the doctor before- where the tendon in your knee and ankle is tapped to see if your leg jumps). The researcher will then apply some cotton wool lightly to your leg (or tissue paper if you do not tolerate cotton wool), and you will be asked if you can feel it.
- You will be asked to lie on your stomach whilst a small probe is applied to your pain free leg which will vibrate. You will be asked to let the researcher know when you feel the probe vibrating and then when it stops. Once you and the researcher are happy with this test it will be repeated on your painful leg.
- Another probe will be applied to your pain free leg which will gradually increase the feeling of pressure and you will be asked to push a button when this pressure sensation changes to discomfort (this will stop any further pressure from being applied). Once you are familiar with this, then the same procedure will occur on your painful leg and also on your arm. The order in
which the vibration test and the pressure test are applied will vary from subject to subject.

You will have a break of 30 minutes and then the vibration tests and pressure tests will be repeated.

7 What do I have to do?

Please do not drink caffeine, alcohol or take any pain medication for 24 hours prior to the study. You will need to remain in the laboratory between the test procedures where refreshments will be provided. However no caffeine will be given as it may affect the results of the study. Please could you bring a pair of shorts with you (if you do not have shorts, these will be provided by the researcher).

8 What are the possible disadvantages and risks of taking part?

There are no reported risks attached to the use of the two pieces of equipment.

9 What are the possible benefits of taking part?

There are no benefits to you directly from participating in the study, however the information from this study will be used in a larger study analysing the effects of a specific Physiotherapy treatment for patients with referred leg pain.

10 What if something goes wrong?

You can contact the researcher or supervisor if any problems arise as a result of this study (contact details are given below), or if you would prefer to get in touch with someone independent of the study you should contact:
Professor Valerie Hall  
Head of the Centre for Nursing and Midwifery Research  
University of Brighton  
Mayfield House, Falmer,  
Brighton BN1 9PH  
Tel 01273 644015  
Email v.hall@brighton.ac.uk

11 Will my taking part in this study be kept confidential?

All your personal details will be kept separately from the actual data collected. These details will be stored on a computer that has a password only known to the researcher. The only other people that have access to these details are the dissertation supervisors.

12 What will happen to the results of the research study?

The results of the study will form part of a PhD thesis. In addition the researcher hopes to publish the results of this study in a journal and present the findings at a national or international conference. In this case, no participants will be mentioned by name, hence your confidentiality will be upheld at all times.

13 Who has reviewed the study?

The study has been reviewed by the two academic supervisors and the University of Brighton faculty of research and governance committee.
14 Contacts for Further Information

**Researcher**
Colette Ridehalgh
School of Health Professions
Robert Dodd Building
49 Darley Rd
Eastbourne
BN20 7UR
01273 643686

**Supervisors**
Professor Ann Moore
Clinical Research Centre for Health Professions
Aldro Building, Eastbourne, BN20 7UR
01273 643647
Dr. Alan Hough
Senior Lecturer
Faculty of Health
University of Plymouth
Derriford Road, Plymouth PL6 8BH
01752 588837

Thank you for reading this information.
UNIVERSITY OF BRIGHTON
SCHOOL OF HEALTH PROFESSIONS

Participant Consent Form

Reliability of measurements of vibration and pressure pain in people with leg pain thought to be referred from the spine

- I agree to take part in this research which is to assess if two commonly used measures of sensation and pain are reliable between sessions in people who suffer with leg pain thought to be coming from their spine.

- The experimenter has explained to my satisfaction the purpose of the experiment and the possible risks involved.

- I have had the principles and the procedure explained to me and I have also read the information sheet. I understand the principles and procedures fully.

- I am aware that I will be required to attend the Human Movement laboratory, University of Brighton, Eastbourne.

- I am aware that the cost of travel will be met by the researcher.

- I am aware that I will be asked a series of questions by the researcher and then be asked to undress to shorts and vest top and have a number of specific tests done to my back and leg, I also am aware that I will have a vibrating probe and probe that produces pressure applied to my leg and arm.

- I understand that I will have 30 minutes to wait in the human movement laboratory before the two tests are repeated.

- I also understand that I must not consume caffeine or alcohol for 24 hours prior to participating in the study, or in the 30 minutes between sessions.

- I understand that any confidential information will be seen only by the researcher and will not be revealed to anyone else.

- I understand that the results from the study will form part of a doctoral study and may be published in an academic journal, but my identity will not be revealed at any time.
• I understand that I am free to withdraw from the investigation at any time.

Name (please print)………………………………………………………………………………

I do wish to participate in the study

Signed…………………………………………………………………………………………

Date…………………………………………………………………………………………

I do not wish to participate in the study

Signed ………………………………………………………………………………………

Date ………………………………………………………………………………………

Please return this form by email to cr19@bton.ac.uk or place in the stamped addressed envelope provided and post by return.
Appendix 17 Research and governance approval for repeatability of pressure pain threshold and vibration threshold

From: onbehalfof+J.Scholes+brighton.ac.uk@manuscriptcentral.com on behalf of J.Scholes@bton.ac.uk  
Sent: 17 December 2010 10:34  
To: Ridehalgh Colette  
Subject: Faculty of Health and Social Science Research Ethics and Governance Committee - Decision on Manuscript ID FREGC-10-040.R1

17-Dec-2010

Dear Ms. Ridehalgh:

It is a pleasure to approve your application entitled "Is the response to neurodynamic treatment linked to specific group characteristics in people with referred posterior leg pain? : Part one repeatability and pilot studies".

Please advise the Committee of any adverse incidents that occur whilst undertaking the research and make known any changes to the design of the project.

We wish you well with the project

Sincerely,  
Prof. Julie Scholes  
Chair, Faculty of Health and Social Science Research Ethics and Governance Committee J.Scholes@brighton.ac.uk
Appendix 18 Information sheet and consent form for non-NHS participants

University of Brighton
School of Health Professions

Participant Information Sheet

Straight leg raise; responses in patients with referred leg pain

1 Invitation paragraph

You are being invited to take part in a research study. Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this information.

2 What is the purpose of the study?

The study aims to look at how different groups of people who suffer with leg pain thought to be coming from their spine respond to a particular treatment commonly given by Physiotherapists.

3 Why have I been chosen?

You have been chosen for the study as you have low back pain and/or leg pain for 3 months or longer and are not currently receiving any treatment for this condition. You will need to meet the requirements for eligibility into the study as described below.

Unfortunately you will be unable to take part in the study if you have any of the following conditions

- Previous spinal surgery
- Current or previous medical diagnoses that may affect your participation in the study e.g. Rheumatoid Arthritis, diabetes, thyroid disease, HIV/AIDS, stroke, cancer, osteoporosis)
- Currently Pregnant
• Hip, knee or ankle disorders within the last year
• New unexplained bladder and bowel problems, and/or pins and needles in your genital region)
• Currently receiving treatment for the LBP/leg pain
• On regular high levels of pain medication (over the counter pain medication such as paracetamol or ibuprofen is fine, but you will be asked to stop taking this for 3 hours prior to the study)

4 Do I have to take part?

Your participation is entirely voluntary. If you are unsure about taking part then feel free to decline. If you do decide to take part you will be given this information sheet to keep for reference purposes and be asked to sign a consent form and send it back to the researcher by email (cr19@brighton.ac.uk) or in the stamped addressed envelope sent to you. If you decide to take part you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect you in any way.

5 What will happen to me if I take part?

A qualified Physiotherapist will organise an appointment with you to attend the Human Movement Laboratory at Darley Rd, Eastbourne. An assessment will take place (as described below) which will take approximately 1 hour. This will be a standard Physiotherapy assessment, with some additional tests and questions, and will analyse what is most likely causing your pain as well as assessing if you are eligible to participate in the study. If you are eligible to participate in the study, you will be given a convenient time to return to the human movement laboratory. The session in the human movement laboratory will last approximately 1 ½ hours. All appropriate travel costs to the laboratory will be met by the researcher and will be discussed prior to participation in the study.

Part 1 Initial assessment (Physiotherapy assessment)
You will be asked a number of questions by the Physiotherapist about your back and/or leg problem. A number of questionnaires will be used to assess how your pain affects certain aspects of your life.
You will then be asked to change into a pair of shorts and bra top (for ladies) before a number of tests will be applied. You will firstly be asked to move your back and leg and let the Physiotherapist know if any of your pain occurs. An example of some tests that might occur to your leg can been seen in the figures below.
The strength in your legs will be tested and your reflexes will be checked (you may have had this done by the doctor before- where the tendon in your knee and ankle is tapped to see if your leg jumps). The Physiotherapist will apply some cotton wool lightly to your leg (or tissue paper if you do not tolerate cotton wool), and you will be asked if you can feel it. The Physiotherapist will palpate certain areas on your leg to assess if any tenderness of these points occurs.

You will be asked to lie on your stomach and the Physiotherapist will press on your spine with her hand and you will again be asked if this brings on your pain. Additional tests may be performed by the Physiotherapist depending on what your individual requirements are (e.g. looking at your stomach or back muscles).

For some subjects, a piece of equipment which applies pressure to different aspects of your body will be placed on various points. You will be asked to let the researcher know what happens to the sensation of pressure as it increases up to a predetermined level.

If you are eligible to participate in the study, either the Physiotherapist will contact the researcher to organise an appointment directly, or if you would prefer, your contact details will be given to the researcher and she will contact you directly to organise the appointment. The physiotherapist will give you some advice on managing your condition before you leave.

**Part 2 Subsequent attendance**

You will be asked to change in to shorts and a vest top and have your height and weight measured. You will then be asked to lie on a plinth on your stomach if this is comfortable for you and a small plastic probe will be placed on your ankle bone of the unaffected side which will vibrate. You will be asked to let the researcher know when you feel the vibration and then when it disappears again. Once you and the researcher are happy with this test it will be repeated on your affected ankle bone and underneath surface of your foot.

Once the vibration test is complete another probe will be applied to your unaffected calf (similar to the pressure probe in the Physiotherapy assessment if this was applied to you) which will gradually increase the feeling of pressure and you will be
asked to push a button when this pressure sensation changes to discomfort (the probe will then be removed). Once you are familiar with this, then the same procedure will occur on your affected leg (back of calf, behind your knee) and also on your opposite arm. The order of the vibration test and the pressure test will vary from subject to subject, so it may be that you have the pressure test applied first.

You will then be asked to lie on your side and an ultrasound probe (small plastic device) will be applied to the back of your thigh, a layer of gel will be applied between the probe and your skin to improve the contact between you and the probe (this may feel cold). Two plastic splints will be applied to your feet to keep your feet and ankles still during the procedure. With your knee straight, your leg will be moved forwards a little and then stopped. This will be repeated a few times until either you feel a worsening of any of your symptoms (if you have some symptoms all of the time) or start to feel any symptoms (if you do not have them all of the time) or until your leg does not move any more (you may let the researcher know that it doesn’t want to go any further, or the researcher may feel that the leg has reached its maximum movement). During these movements the ultrasound machine will build up pictures of your nerve moving.

You will then be asked to lie on your back with one splint remaining on your foot, and your affected leg will be lifted from the plinth with your knee straight until you feel a worsening or onset of your symptoms (pain or other sensations) or the leg has reached its limit of movement as described above. Your knee will then be bent and straightened a few times (a Straight Leg Raise (SLR) mobilisation technique) before all of the measures taken previously are repeated (see figures below).

Your referring Physiotherapist will then contact you for a follow up appointment, ensuring that this is within the time frame that you would have been seen if you had not participated in the study.
6 What do I have to do?

Please do not drink caffeine or alcohol for 24 hours prior to the study, and do not take your pain medication for 3 hours prior to the study. Please bring a pair of shorts and vest top with you (if you do not have shorts, these will be provided by the researcher).

7 What are the possible disadvantages and risks of taking part?

The SLR is a test used by physiotherapists on a regular basis, and in some individuals the test may bring on your symptoms. You will be asked to inform the researcher if this occurs during the test procedure and if this happens, no additional movements will be added. The risks of increasing your symptoms after the study has completed will be minimised by asking you specific questions about your pain and doing certain tests to assess your eligibility into the study. If the researcher has concerns that your condition could be aggravated by the procedure you will be withdrawn from the study.

8 What are the possible benefits of taking part?

It is possible that the mobilisation technique applied to your leg may help to alleviate some of your symptoms, however this is not the aim of the study and any positive effects should be considered “a bonus”, and as such should not be expected. This form of treatment is only one of a number of possible treatments that could be given to you, and may not be the most beneficial; therefore you may not notice any improvement in your symptoms. The results of this study will provide important information about the use of this technique in people with different causes of back related leg pain.

9 What if something goes wrong?

You can contact the researcher or supervisors if any problems arise as a result of this study (contact details are given below), or if you would prefer to get in touch with someone independent of the study you should contact:

Professor Valerie Hall  
Head of the Centre for Nursing and Midwifery Research  
University of Brighton  
Mayfield House, Falmer,  
Brighton BN1 9PH  
Tel 01273 644015  
Email v.hall@brighton.ac.uk
10 **Will my taking part in this study be kept confidential?**

All personal details will be kept separately from the actual data collected. These details will be stored on a computer that has a password only known to the researcher. The only other people that have access to these details are the dissertation supervisors.

11 **What will happen to the results of the research study?**

The results of the study will form part of a PhD thesis. In addition the researcher hopes to publish the results of this study in a journal and present the findings at a national or international conference. In this case, no participants will be mentioned by name, hence your confidentiality will be upheld at all times.

12 **Who has reviewed the study?**

The study has been reviewed by the two academic supervisors, the University of Brighton faculty of research and governance committee.

13 **Contacts for Further Information**

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<td>Senior Lecturer</td>
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<td>Faculty of Health</td>
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Thank you for reading this information.
Participant Consent Form

**Straight leg raise; responses in patients with referred leg pain**

- I agree to take part in this research which is to look at how different groups of people who suffer from leg pain thought to be coming from their spine respond to a particular treatment commonly given by Physiotherapists.

- The experimenter has explained to my satisfaction the purpose of the experiment and the possible risks involved.

- I have had the principles and the procedure explained to me and I have also read the information sheet. I understand the principles and procedures fully.

- I am aware that I will be required to attend two sessions at the Human Movement laboratory, University of Brighton, Eastbourne.

- I am aware that the cost of travel to the Human Movement Laboratory will be met by the researcher.

- I am aware that I will be asked a series of questions by the Physiotherapist and then be asked to undress to shorts and bra top (for females) and have a number of specific tests done to my back and leg. I also am aware that I may have a probe which applies pressure to various points on my body.

- At the second attendance, I am aware that I will be asked to undress to shorts and vest top and have a vibrating probe and probe that produces pressure applied to my leg and arm.

- I understand that I will have to lie on my side and have an ultrasound probe placed to the back of my thigh before the researcher will move my leg and take some measurements. I am aware that some of my pain or other symptoms may be produced or made worse during the SLR test, and to inform the researcher if this occurs. I am aware my leg will be repeatedly moved (mobilisation treatment) after which the above measurements will be repeated. I also understand that I must not consume caffeine or alcohol for 24 hours and take any pain medication for 3 hours prior to participating in the study.
• I understand that any confidential information will be seen only by the researcher and will not be revealed to anyone else.

• I understand that the results from the study will form part of a doctoral study, but my identity will not be revealed at any time.

• I understand that I am free to withdraw from the investigation at any time.

Name (please print)………………………………………………………………………………

I wish to participate in the study

Signed…………………………………………………………………………………………

Date…………………………………………………………………………………………

Please return this form by email to cr19@brighton.ac.uk or place in the stamped addressed envelope provided and post by return.
**Participant Information Sheet**

**Straight leg raise; responses in patients with referred leg pain**

1 **Invitation paragraph**

You are being invited to take part in a research study. Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this information.

2 **What is the purpose of the study?**

The study aims to look at how different groups of people who suffer with leg pain thought to be coming from their spine respond to a particular treatment commonly given by Physiotherapists.

3 **Why have I been chosen?**

You have been chosen for the study as you have low back pain and/or leg pain for 3 months or longer and are not currently receiving any treatment for this condition.
You will need to meet the requirements for eligibility into the study as described below.

Unfortunately you will be unable to take part in the study if you have any of the following conditions:

- Previous spinal surgery
- Current or previous medical diagnoses that may affect your participation in the study (e.g. Rheumatoid Arthritis, diabetes, thyroid disease, HIV/AIDS, stroke, cancer, osteoporosis)
- Currently Pregnant
- Hip, knee or ankle disorders within the last year
- New unexplained bladder and bowel problems, and/or pins and needles in your genital region
- Currently receiving treatment for the LBP/leg pain
- On regular high levels of pain medication (over the counter pain medication such as paracetamol or ibuprofen is fine, but you will be asked to stop taking this for 3 hours prior to the study)

4 **Do I have to take part?**

Your participation is entirely voluntary. If you are unsure about taking part then feel free to decline. If you do decide to take part please sign the enclosed consent form and send it back to the Researcher by email (cr19@brighton.ac.uk) or in the stamped addressed envelope sent to you. If you decide to take part you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect your treatment in any way.

6 **What will happen to me if I take part?**

The Researcher will contact your local hospital physiotherapy department and let them know you have consented to participate in this study. The hospital physiotherapy team will organise an appointment for you to attend the hospital Physiotherapy department. An assessment will take place (as described below) which will take approximately 1 hour. This will be a standard Physiotherapy assessment and will analyse what is most likely causing your pain as well as assessing if you are eligible to participate in the study. If you are eligible to participate in the study, the physiotherapist will inform the Researcher, who will then contact you with a convenient time to attend the human movement laboratory at
the University of Brighton, Darley Rd, Eastbourne. If you are not eligible to participate in the study, you will continue to see your Physiotherapist in the usual way. The session in the human movement laboratory will last approximately 1 ½ hours.

**Part 1 Initial assessment (Physiotherapy department)**

The Physiotherapist will give you a number of questionnaires to complete to assess how your pain affects certain aspects of your life. You need to attend the department about 20 minutes early to fill these in, or they could be completed after your appointment has finished.

You will be asked a number of questions by the hospital Physiotherapist about your back and/or leg problem. You will then be asked to change into a pair of shorts and bra top (for ladies) before a number of assessments will be carried out. You will firstly be asked to move your back and leg and let the Physiotherapist know if any of your pain occurs. An example of some assessments that might occur to your leg can be seen in the figures below.

![Physiotherapist assessing patient](image)

The strength in your legs will be tested and your reflexes will be checked (you may have had this done by the doctor before- where the tendon in your knee and ankle is tapped to see if your leg jumps). The Physiotherapist will apply some cotton wool lightly to your leg (or tissue paper if you do not tolerate cotton wool), and you will be asked if you can feel it. The Physiotherapist will palpate certain areas on your leg to assess if any tenderness of these points occurs.

You will be asked to lie on your stomach and the Physiotherapist will press on your spine with her hand and you will again be asked if this brings on your pain. Additional tests may be performed by the Physiotherapist depending on what your individual requirements are (e.g. looking at your stomach or back muscles).

For some participants, a piece of equipment which applies pressure to different aspects of your body will be placed on various points. You will be asked to let the
physiotherapist know what happens to the sensation of pressure as it increases up to a predetermined level.
If you are eligible to participate in the study, the Physiotherapist will inform the researcher, who will then contact you directly to organise the appointment at the Human Movement Laboratory. The physiotherapist will give you some advice on managing your condition before you leave the Physiotherapy department.

Part 2 Human Movement Laboratory (Eastbourne)
You will then be asked to change into shorts and a vest top and have your height and weight measured. You will then be asked to lie on a plinth on your stomach if this is comfortable for you and a small plastic probe will be placed on your ankle bone of the unaffected side which will vibrate. You will be asked to let the researcher know when you feel the vibration and then when it disappears again. Once you and the researcher are happy with this test it will be repeated on your affected ankle bone and underneath surface of your foot.
Once the vibration test is complete another probe will be applied to your unaffected calf (similar to the pressure probe in the Physiotherapy assessment if this was applied to you) which will gradually increase the feeling of pressure and you will be asked to push a button when this pressure sensation changes to discomfort (the probe will then be removed). Once you are familiar with this, then the same procedure will occur on your affected leg (back of calf, behind your knee) and also on your opposite arm. The order of the vibration test and the pressure test will vary from participant to participant, so it may be that you have the pressure test applied first.

You will then be asked to lie on your side and an ultrasound probe (small plastic device) will be applied to the back of your thigh, a layer of gel will be applied between the probe and your skin to improve the contact between you and the probe (this may feel cold). Two plastic splints will be applied to your feet to keep your feet and ankles still during the procedure. With your knee straight, your leg will be moved forwards a little and then stopped. This will be repeated a few times until either you feel a worsening of any of your symptoms (if you have some symptoms all of the time) or start to feel any symptoms (if you do not have them all of the time) or until your leg does not move any more (you may let the researcher know that it doesn’t want to go any further, or the researcher may feel that the leg has reached its maximum movement). During these movements the ultrasound machine will build up pictures of your nerve moving.

You will then be asked to lie on your back with one splint remaining on your foot, and your affected leg will be lifted from the plinth with your knee straight until you feel a worsening or onset of your symptoms (pain or other sensations) or the leg has reached its limit of movement as described above. Your knee will then be bent and straightened a few times (a Straight Leg Raise (SLR) mobilisation technique) before all of the measures taken previously are repeated (see figures below).
When the session is over, the Researcher will inform your hospital physiotherapist that your participation in the study is complete. Your hospital Physiotherapist will then contact you to arrange further hospital appointment/s as necessary to treat your pain.

6 Expenses and payments
All appropriate travel costs to the laboratory will be met by the researcher and will be discussed prior to participation in the study.

7 What do I have to do?
Please do not drink caffeine or alcohol for 24 hours prior to attending the Human Movement Laboratory, and do not take your pain medication for 3 hours prior to attending the laboratory. Please could you bring a pair of shorts and vest top with you (if you do not have shorts, these will be provided by the researcher).

8 What are the alternatives for diagnosis or treatment?
This form of treatment is an important treatment for patients with referred leg pain, but it is only of many possible options. Other available treatments include mobilisations to the joints in your spine or specific exercises. Your Physiotherapist may choose to offer these treatments to you when you attend for your second appointment at the Physiotherapy Department. There are no greater risks or benefits associated with the treatment that will be applied in the Human Movement Laboratory than the others that could be given. If you would like more information, please speak to your physiotherapist.

9 What are the possible disadvantages and risks of taking part?
The SLR is a test used by physiotherapists on a regular basis, and in some individuals the test may bring on your symptoms. You will be asked to inform the researcher if this occurs during the test procedure and if this happens, no additional movements will be added. The risks of increasing your symptoms after the study has completed will be minimised by asking you specific questions about your pain and
doing certain tests to assess your eligibility into the study. If the researcher has concerns that your condition could be aggravated by the procedure you will be withdrawn from the study.

10 What are the possible benefits of taking part?

It is possible that the mobilisation technique applied to your leg may help to alleviate some of your symptoms, however this is not the aim of the study and any positive effects should be considered “a bonus”, and as such should not be expected. This form of treatment is only one of a number of possible treatments that could be given to you, and may not be the most beneficial; therefore you may not notice any improvement in your symptoms. The results of this study will provide important information about the use of this technique in people with different causes of back related leg pain.

11 What happens when the research study stops?
Your Hospital Physiotherapist will continue to treat you in the usual way.

12 What will happen if I don’t want to carry on with the study?
If you withdraw from the study, we will destroy all your identifiable data. You hospital physiotherapist will be informed that your participation in the study is complete and you will be contacted by the hospital physiotherapy department to continue with standard NHS care.

13 What if something goes wrong?

You can contact the researcher or supervisors if any problems arise as a result of this study (contact details are given below), or if you would prefer to get in touch with someone independent of the study or wish to complain formally, you may do so by contacting:

Professor Valerie Hall  
Head of the Centre for Nursing and Midwifery Research  
University of Brighton  
Mayfield House, Falmer,  
Brighton BN1 9PH  
Tel 01273 644015  
Email v.hall@brighton.ac.uk

In the event that something goes wrong and you are harmed during the research and this is due to someone’s negligence, then you may have grounds for legal action for compensation against the University of Brighton, but you may have to pay legal costs.
14 **Involvement of the General Practitioner/Family Doctor (GP)**
   You will be asked for permission to contact your G.P. to inform her/him of your participation in the study.

15 **Will my taking part in this study be kept confidential?**
   All personal details will be kept separately from the actual data collected. These details will be stored on a computer that has a password only known to the researcher. The only other person who will have access to your personal details will be the Physiotherapist who assessed you.

16 **What will happen to the results of the research study?**
   The results of the study will form part of a PhD thesis. In addition the researcher hopes to publish the results of this study in a journal and present the findings at a national or international conference. In this case, no participants will be mentioned by name, hence your confidentiality will be upheld at all times.

17 **Who has reviewed the study?**
   The study has been reviewed by the two academic supervisors, the University of Brighton faculty of research and governance committee and the NHS ethics committee.

18 **Who is organising and funding the research?**
   The research is being sponsored and funded by the University of Brighton, and organised and conducted by the researcher who is a PhD student and lecturer at the University of Brighton.

19 **Contacts for Further Information**

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Supervisors</th>
</tr>
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<tbody>
<tr>
<td>Colette Ridehalgh</td>
<td>Professor Ann Moore</td>
</tr>
<tr>
<td>School of Health Professions</td>
<td>Clinical Research Centre for Health Professions</td>
</tr>
<tr>
<td>Robert Dodd Building</td>
<td>Aldro Building, Eastbourne, BN20 7UR</td>
</tr>
<tr>
<td>49 Darley Rd</td>
<td>Dr. Alan Hough</td>
</tr>
<tr>
<td>Eastbourne</td>
<td>Senior Lecturer</td>
</tr>
<tr>
<td>BN20 7UR</td>
<td>Faculty of Health</td>
</tr>
<tr>
<td>01273 643686</td>
<td>University of Plymouth</td>
</tr>
<tr>
<td></td>
<td>Derriford Road, Plymouth PL6 8BH</td>
</tr>
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<td></td>
<td>01752 588837</td>
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</table>

Thank you for reading this information.
Participant Consent Form

Straight leg raise; responses in patients with referred leg pain

- I confirm that I have read and understood the information sheet dated 21st June 2012 (version 3.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
- I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the University of Brighton, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to access to my records.
- I agree to my GP being informed of my participation in this study.
- 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.

Name (please print)…………………………………………………………………………………………………………………………
Signed………………………………………………………………………………………………………………………………………
Date…………………………………………………………………………………………………………………………………………

Please return this form by email to cr19@brighton.ac.uk or place in the stamped addressed envelope provided and post by return.
Appendix 20 Letter of invitation

Western Sussex Hospitals NHS Trust

Straight leg raise; responses in patients with referred leg pain

Dear Sir/Madam,

I am contacting you to see if you would like to participate in a study looking at how a standard Physiotherapy intervention affects different people with leg pain that is coming from their spine. This study forms the main part of a PhD which is being undertaken by a colleague at the University of Brighton. You are being sent this information as you are currently on the waiting list for physiotherapy treatment at Worthing hospital for referred leg pain.

Please find attached an information sheet and consent form. Please take your time to read this information as it is important that you fully understand what will happen to you in the study if you agree to participate. If you are happy to participate after reading this information please fill in the consent form enclosed and return it by post (in the stamped addressed envelope provided), or by email to the Researcher, Colette Ridehalgh, at cr19@brighton.ac.uk. If you would like to discuss any of the details of the study before consenting to participate, please email the Researcher on the above email address or phone 01273 643686.

If after reading the information sheet you decide that you would not like to participate, then no further action is required. You will be contacted by the hospital Physiotherapy department for an appointment in the usual way. Many thanks for taking the time to read this information.

Yours Sincerely,

Physiotherapy Department
Appendix 21 Faculty of Health research and governance committee ethical approval

From: Scholes Julie
Sent: 10 February 2012 10:00
To: Ridehalgh Colette
Cc: Moore Ann; Alanhough (alan.hough@plymouth.ac.uk); Flood Glynis
Subject: RE: Faculty of Health and Social Science Research Ethics and Governance Committee - Decision on Manuscript ID FREGC-11-065

Dear Colette,
Thank you for sending this set of revisions to me. I am happy to approve the amendments by Chair’s action.
We will need to have the revised documents uploaded to MC dashboard for our records. However, please do proceed with booking a slot with IRAS. I am happy to provide my electronic signature for the IRAS and the R&D forms.
You will need to remove the previous version to be able to upload this approved version. Please can you do this within a week — but as I have stated this should not delay you in the next stage of your IRAS submission.
Kind regards

Julie Scholes
Appendix 22 NRES Approval

NRES Committee London - Chelsea
Room 4W/12, 4th Floor West
Charing Cross Hospital
Fulham Palace Road
London W6 8RF
Telephone: 020 331 17282

27 March 2012

Ms Colette Ridehalgh
Senior Lecturer
University of Brighton
Robert Dodd Building
49 Darley Rd
Eastbourne
BN20 7UR

Dear Ms Ridehalgh

Study title: Is the response to neurodynamic treatment linked to specific group characteristics in people with referred leg pain?

REC reference: 12/LO/0397

Thank you for your letter of 26 March 2012, responding to the Committee’s request for further information on the above research and submitting revised documentation. The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

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

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

Non-NHS sites
The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

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

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

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation’s role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

*Document Version Date*

Covering Letter 16 February 2012

Covering Letter 26 March 2012

Evidence of insurance or indemnity 1 16 February 2012

GP/Consultant Information Sheets 1 16 February 2012

Investigator CV Ms Ridehalgh 16 February 2012

Letter from Sponsor FREGC-1-065 16 February 2012

Letter of invitation to participant 2 26 March 2012

Other: Prof Ann Moore Supervisor 1 cv 16 February 2012

Other: Dr Alan Hough Supervisor 2 cv 16 February 2012

Other: Rejection letter 1 26 March 2012

Participant Consent Form 2 26 March 2012

Participant Information Sheet 2 26 March 2012

Protocol 1 16 February 2012

Questionnaire: Fear Avoidance Beliefs FABQ for patients with Back Pain 1 16 February 2012

Questionnaire: Depression anxiety & stress score DASS21 1 16 February 2012

Questionnaire: Tampa Scale for Kinesiophobia validated 16 February 2012

Questionnaire: Oswestry Disability Questionnaire validated 16 February 2012

Questionnaire: Pain Catastrophizing Scale validated 16 February 2012

REC application 59355/294445/1/700 16 February 2012

Response to Request for Further Information 26 March 2012

Summary/Synopsis 1 16 February 2012

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

**After ethical review**

Reporting requirements
The attached document “After ethical review – guidance for researchers” gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback
You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

12/LO/0397 Please quote this number on all correspondence

With the Committee’s best wishes for the success of this project

Yours sincerely

Dr Shelley Dolan
Chair
Email: lara.callaghan@imperial.nhs.uk

Copy to: Professor Julie Scholes
Ms Helen Vaughan, Western Sussex Hospital NHS Trust

Appendix 23 R and D approval Brighton and Sussex University Hospitals Trust

R&D MANAGEMENT OFFICE
R&D Manager: Scott Harfield x7497
Research Governance Officer: Linda Henderson x3538
Please send all documents for approval to:
r&d.approvals@bsuh.nhs.uk
Ms Colette Ridehalgh
Robert Dodd Building
49 Darley Rd
Eastbourne
BN20 7UR

Dear Ms Colette Ridehalgh

Full Study Title: Is the response to neurodynamic treatment linked to specific group characteristics in people with referred leg pain?
R&D Ref No.: 12/070/RID
REC Ref: 12/LO/0397

I am writing to inform you that you have Trust approval to proceed with the above named project. This letter acknowledges that you have all the necessary internal and external regulatory approvals. Details of your research project and any associated supporting documentation will be stored on an electronic database administered by the R&D Department. The sites covered by this approval include:

- Royal Sussex County Hospital
- Princess Royal Hospital

Conditions of Approval
The approval covers the period stated in the Research Ethics Committee (REC) application and will be extended in line with any amendments agreed by the REC. Research must commence within 12 months of the issue date of this letter. Any delay beyond this may require a new review of the project resources.

Amendments
Project amendment details dated after the issue of this approval letter should be emailed to the R&D Office for formal approval.

ICH-GCP Monitoring
The Trust has a duty to ensure that all research is conducted in accordance with the Research Governance Framework and to ICH-GCP standards. In order to ensure compliance the Trust undertakes random audits. If your project is selected you will be given 4 weeks notice to prepare all documentation for inspection.

Pathology Services at BSUH
If you will be using the pathology services at Brighton & Sussex University Hospitals to analyse samples for
research purposes only (i.e. not taken to inform standard clinical care), these samples must be booked in for processing by the CIRU laboratory assistants. Please call 01273 696955 extension 7668 for advice.

**Imaging services at BSUH**

**R&D MANAGEMENT OFFICE**
R&D Manager: Scott Harfield x7497
Research Governance Officer: Linda Henderson x3538
Please send all documents for approval to:
r&d.approvals@bsuh.nhs.uk
E-mail: scott.harfield@bsuh.nhs.uk
linda.henderson@bsuh.nhs.uk

Page 2 of 2

If research participants will undergo imaging investigations that are additional to standard care you are reminded that referrals should be clearly identified with a research sticker. For further advice please contact 01273 696955 ext 7959.

I wish you luck with your project and would be grateful if you could inform me when the project is complete, or due to be closed on this site.

Yours sincerely
Scott Harfield
Research & Development Manager
Cc
Carbon Copy: (PI) Mr Andrew Laing
Appendix 24 R and D approval WSHT

Sussex NHS Research Consortium

Research Consortium Office
Worthing Hospital
Lyndhurst Road
Worthing
West Sussex
BN11 2DH

Tel: 01903 285027
Fax: 01903 209884
www.ssrc.nhs.uk

Ms. Colette Ridehalgh
Senior Lecturer
School of Health Professions
Robert Dodd Building
49 Darley Rd,
Eastbourne
BN20 7UR

04/09/2012

Dear Ms. Ridehalgh,

Our ID: 1505/WSHT/2012
TITLE: Is the response to neurodynamic treatment linked to specific group characteristics in people with referred leg pain?

Thank you for your application to the Sussex NHS Research Consortium for research governance approval of the above named study.

I am pleased to inform you that the study has been approved, and so may proceed. This approval is valid in the following Organisations:

- Western Sussex Hospitals NHS Trust – Mr. Chris Mercer, Consultant Physiotherapist, Worthing Hospital

The final list of documents reviewed and approved is as follows:

- IRAS NHS R&D Form (signed and dated 13/04/2012: submission code 59355/313789/14/592)
- IRAS NHS SSI Form (signed and dated 15/08/2012: submission code 59355/354427/6/195/66215/251486)
- Protocol (version 2, dated 16/06/2012)
- Depression Anxiety and Stress Score – DASS 21 (validated questionnaire)
- Fear Avoidance Beliefs Questionnaire (FABQ) (validated questionnaire 1993)
- GP Information Sheet (version 1, dated 16/04/2012)
- PIS/ICF (version 3.0, dated 21/08/2012)
- Invitation Letter (version 3.0, dated 21/06/2012)
- Oswestry Disability Questionnaire (validated)
- Tampa Scale for Kinesiophobia (validatated 1991)
- Rejection Letter (version 1, dated 16/04/2012)
- Pain Catastrophizing Scale (validated 1995)
- CV for Colette Ridehalgh (unsigned and dated 05/04/2012)
- CV for Mr. C. Mercer (unsigned and undated)
- Letter from the University of Brighton confirming sponsorship (signed and dated 21/06/2012)
- University of Brighton evidence of indemnity (unsigned and undated)
- NRES Committee London – Chelsea provisional opinion letter (signed and dated 16/03/2012)
• NRES Committee London – Chelsea approval letter (signed and dated 27/03/2012)
• IRAS NHS Notice of Amendment Form – amendment 1 (signed and dated 25/06/2012)
• NRES Committee London – Chelsea amendment 1 approval letter (signed and dated 13/07/2012)

Your research governance approval is valid providing you comply with the conditions set out below:
1. You commence your research within one year of the date of this letter. If you do not begin your work within this time, you will be required to resubmit your application.
2. You notify the Consortium Office should you deviate or make changes to the approved documents.
3. You alert the Consortium Office by contacting me, if significant developments occur as the study progresses, whether in relation to the safety of individuals or to scientific direction.
4. You complete and return the standard annual self-report study monitoring form when requested to do so at the end of each financial year. Failure to do this will result in the suspension of research governance approval.
5. You comply fully with the Department of Health Research Governance Framework, and in particular that you ensure that you are aware of and fully discharge your responsibilities in respect to Data Protection, Health and Safety, financial probity, ethics and scientific quality. You should refer in particular to Sections 3.5 and 3.6 of the Research Governance Framework.
6. You ensure that all information regarding patients or staff remains secure and strictly confidential at all times. You ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice, Data Protection Act and Human Rights Act. Unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

Good luck with your work.

Yours sincerely,

[Signature]

Mrs. Helen Vaughan
Senior Research Governance Officer

Email: helen.vaughan@wsht.nhs.uk
Tel: 01903 265222 x 4190
Fax: 01903 209584

cc: Mr. Chris Mercer, Consultant Physiotherapist, Worthing Hospital
Clare Meachin, Research Studies Manager, Western Sussex Hospitals NHS Trust
Dear Ms C Ridehalgh

2012

12th June

I am writing to inform you that you have R&D approval to proceed with the study as named below. This letter acknowledges that you have all the necessary internal and external regulatory approvals. The site covered by this approval is:

**Full Study : Neurodynamic – Straight leg raise; responses in patients with referred leg pain**

R&D Ref No. TN12-28

REC Ref: 12/LO/0397

CSP No

The final list of documents reviewed and approved are:

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<td>16th February 2012</td>
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<td>Letter from Sponsor</td>
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<td>Questionnaire: Depression anxiety &amp; stress score DASS21</td>
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<td>Ethics Letter</td>
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**Conditions of Approval**

The approval covers the period stated in the Research Ethics Committee (REC) application and will be extended in line with any amendments agreed by the REC. Research must commence within 12 months of the issue date of this letter. Any delay beyond this may require a new review of the study resources.

**Amendments**

Study amendment details dated after the issue of this approval letter should be emailed to the R&D Office for formal approval.

**ICH-GCP Monitoring**

The Trust has a duty to ensure that all research is conducted in accordance with the Research Governance Framework and to ICH-GCP standards. In order to ensure
compliance the Trust undertakes random monitoring. If your study is selected you will be given 4 weeks notice to prepare all documentation for inspection.

I wish you luck with your study and would grateful if you could inform me when the study is complete, or due to be closed on this site.

Yours sincerely

Teresa Baumber
Research Support Manager
Research and Development.
East Sussex Healthcare Trust.
Telephone  01323 417400 Ex 3042
Email: teresa.baumber@esht.nhs.uk
Patient with suspected spinally referred leg pain

Pain reproduced on spinal movements and spinal accessory movements?#

YES  NO

Positive SLR or slump test with structural differentiation

YES  NO

Positive neurological integrity (no more than 2 adjacent segments)

YES  NO

RADICULOPATHY

>2 levels or S+S Cauda equina

YES  NO

EXCLUDE URGENT REFERRAL

>2 S+S of central sensitisation?*

YES  NO

>8 tender points tested with algometer

YES  NO

Centrally sensitised

NO

Not centrally sensitised

REVIEW

# If pain not reproduced on planar movements, combined, repeated or sustained movements performed. PAIVMS performed in provocative position where indicated.

*Severity based on patient’s ability to be able to sustain their painful position. Irritability based on time to aggravate and time to ease symptoms on simple movements (Petty, 2011).

*S+S CS pain> 6 months, widespread areas of pain, hypersensitivity to warmth, cold or touch
Appendix 27 tender point assessment (taken from Jensen 2010)
Appendix 28 Physiotherapist assessment sheet

Neurodynamic research study patient participant findings

Length of time of current symptoms

SLR Test (DF/EV, DF/INV, PF/INV please detail)

Slump Test (DF/EV, DF/INV, PF/INV please detail)

Neurological Integrity findings

Subjective signs of Central Sensitisation  YES/NO (please circle)

Tender point assessment YES/NO (please circle)

If yes, number of painful points?

Final classification (please tick box)

<table>
<thead>
<tr>
<th>Somatic referred pain</th>
<th>Radicular pain</th>
<th>Radiculopathy</th>
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</thead>
</table>

Does patient meet the inclusion criteria for the study  YES/NO (please circle). If no please detail reason……………………………………………………………………………………………………………………………………………… code……………………………………
Appendix 29 Statistical analyses repeatability studies (examples are given. Further analyses can be found in the attached CD)

Analysis of Ultrasound Validity data

Reliability

Scale: ALL VARIABLES

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<thead>
<tr>
<th>Case Processing Summary</th>
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<tbody>
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\(^a\) Listwise deletion based on all variables in the procedure.

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ANOVA

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Grand Mean = 14.4766
Analysis of Ultrasound Reliability data

Normality results for ultrasonographic data

Tests of Normality

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<th>Hip</th>
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<td></td>
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<td>Test 2 Hip 30F</td>
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<td>.988</td>
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<td>Test 1 Hip 60F</td>
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Tests of Normality

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a. Lilliefors Significance Correction

*. This is a lower bound of the true significance.

Intracllass correlation analysis hip 30 degrees flexion

Case Processing Summary

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Two-way random effects model where both people effects and measures effects are random.

a. Type C intraclass correlation coefficients using a consistency definition-the between-measure variance is excluded from the denominator variance.

b. The estimator is the same, whether the interaction effect is present or not.
Reliability Statistics

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Intraclass Correlation Coefficient

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One-way random effects model where people effects are random.

Intraclass correlation analysis hip 30 degrees flexion

Case Processing Summary

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Intraclass Correlation Coefficient

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One-way random effects model where people effects are random.

Analysis of Vibration Threshold Reliability data

Normality results for vibration threshold data

Tests of Normality

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<thead>
<tr>
<th></th>
<th>Kolmogorov-Smirnov&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Shapiro-Wilk</th>
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<sup>a</sup> Lilliefors Significance Correction

Intraclass correlation analysis Vibration threshold data

Case Processing Summary

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Reliability Statistics

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Grand Mean = -.3956

### Case Processing Summary

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a. Listwise deletion based on all variables in the procedure.

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### ANOVA

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Grand Mean = -.1331
Calculation of SEM and SDD for VT data

SEM = √residual mean square
For lateral malleolus = √0.003 = 0.0548. Mean transformed data = 0.604 % SEM =9.1%
For 1st MT = √0.002 = 0.0447. Mean transformed data = 0.867 % SEM = 5.16%

SDD =1.96 x SEM x √2
For lateral malleolus = 0.1519 % SDD= 0.1519/0.604 x100 =25.1%
For 1st metatarsal =0.125 % SDD =0.125/0.867 x100 = 14.4

Analysis of Pressure Pain Threshold data

**Intraclass correlation analysis Pressure Pain Threshold data**

Deltoid mean of 1 and 2 readings

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\(^a\) Listwise deletion based on all variables in the procedure.

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Grand Mean = 4.5159

### Intraclass Correlation Coefficient

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One-way random effects model where people effects are random.

RELIABILITY deltoid mean of all 3 readings
/VARIABLES=PPTDELT1M3 PPTDELT2M3

### Case Processing Summary

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a. Listwise deletion based on all variables in the procedure.

### Reliability Statistics

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Grand Mean = 4.5242

### Intraclass Correlation Coefficient

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One-way random effects model where people effects are random.

RELIABILITY deltoid mean of 2nd and 3rd readings

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<td>Within People</td>
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Grand Mean = 4.5023

## Intraclass Correlation Coefficient

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One-way random effects model where people effects are random.
Appendix 30 Statistical analysis of chapter 8 (examples are given, further analyses can be found in the attached CD)

Normal Distributions of 3 outcome measures

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* This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Key SPPTDelt (somatic group PPT deltoid), SPPTTN (somatic group PPT tibial nerve), SPPTG (somatic group PPT gastrocnemius)
Key RR= radicular group

### Tests of Normality

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* This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Key RY= radiculopathy group

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* This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Key BCSVTLM = box-cox transformation somatic group vibration threshold lateral malleolus

BCSVT1MT= box-cox transformation somatic group vibration threshold 1\textsuperscript{st} metatarsal

### Tests of Normality

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* This is a lower bound of the true significance.
a. Lilliefors Significance Correction

Key RR= radicular groups

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* This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Key RY= radiculopathy group

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* This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Key SH30= somatic group sciatic nerve excursion with hip flexed to 30°

SH60= somatic group sciatic nerve excursion with hip flexed to 60°

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* This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Key RR=radicular group
Tests of Normality

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* This is a lower bound of the true significance.

<sup>a</sup> Lilliefors Significance Correction

Key RY = radiculopathy group

Examples of main analyses

*Mauchley's test of sphericity for PPT readings*

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

<sup>a</sup> Design: Intercept + Group

Within Subjects Design: Site + Time + Site * Time

<sup>b</sup> May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.
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*a: Computed using alpha = .05*
### Tests of Within-Subjects Contrasts

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a. Computed using alpha = .05

### Levene's Test of Equality of Error Variances

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Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Group
Within Subjects Design: Site + Time + Site * Time

### Tests of Between-Subjects Effects

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a. Computed using alpha = .05

### Test Results

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a. Computed using alpha = .05
Mauchley’s test of sphericity for PPT readings controlling for BMI

Mauchley’s Test of Sphericity

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Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + BMI + Group

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

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a. Computed using alpha = .05
Levene's Test of Equality of Error Variances

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Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + BMI + Group

Within Subjects Design: Site + Time + Site * Time

Tests of Between-Subjects Effects

<table>
<thead>
<tr>
<th>Source</th>
<th>Type III Sum of Squares</th>
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a. Computed using alpha = .05
### Test Results

**Measure: MEASURE_1**  
**Transformed Variable: AVERAGE**

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*a. Computed using alpha = .05*

### Pairwise Comparisons

**Measure: MEASURE_1**

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<th>(J) Group</th>
<th>Mean Difference (i - J)</th>
<th>Std. Error</th>
<th>Sig.</th>
<th>95% Confidence Interval for Difference</th>
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Based on estimated marginal means

* The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Sidak.

### Univariate Tests

**Measure: MEASURE_1**

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The F tests the effect of Group. This test is based on the linearly independent pairwise comparisons among the estimated marginal means.

*a. Computed using alpha = .05*
### VT analysis

#### Tests of Within-Subjects Effects

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^n: a. Computed using alpha = .05

### Tests of Between-Subjects Effects

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^n: a. Computed using alpha = .05
Pairwise Comparisons

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<th>Std. Error</th>
<th>Sig.</th>
<th>95% Confidence Interval for Difference ( ^b )</th>
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Based on estimated marginal means

* The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Sidak.

Age and VT between subject effects

Tests of Between-Subjects Effects

Measure: MEASURE_1
Transformed Variable: Average

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Assumption of homogeneity age:group (VT)

Tests of Between-Subjects Effects

Measure: MEASURE_1
Transformed Variable: Average

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### Sciatic Nerve excursion analysis

Tests of Within-Subjects Effects

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Key: site 1 = H30° position  
Site 2 = H60° position

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a. Computed using alpha = .05
Levene's Test of Equality of Error Variances

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Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Group
   Within Subjects Design: Site + Time + Site * Time

Tests of Between-Subjects Effects

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a. Computed using alpha = 0.05
Adjustment in sciatic nerve excursion for pain below the knee

Tests of Within-Subjects Effects

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a. Computed using alpha = .05
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*a. Computed using alpha = .05*

### Tests of Within-Subjects Effects

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*a. Computed using alpha = .05*

**Testing for assumption of homogeneity- see hip* time* below knee**
Appendix 32 List of Author’s research publications and conference presentations

Publications


Conference Presentations
Invited speaker MACP conference, London, October 2012 “Is the response to neurodynamic treatment linked to specific group characteristics in people with referred posterior leg pain?”

Ridehalgh, C., Moore, A., Hough, A. Repeatability and normative values of measuring sciatic nerve excursion during the straight leg raise with B mode ultrasound. Rendezvous of hands and minds. Proceedings IFOMPT Quebec, September 2012

Ridehalgh, C., Moore, A., Hough, A Repeatability of vibration thresholds and pressure pain thresholds in individuals with spinally referred leg pain Rendez-vous of hands and minds. Proceedings IFOMPT Quebec, September 2012


Other
Entered for REF University of Brighton 2014.
Awarded The Greg Grieve MACP Research award 2012
Awarded the MACP Small Project Grant 2012