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# FOOT, ANKLE AND LOWER LIMB SOMATOSENSORY DYSFUNCTION IN STROKE

by

# **TERENCE RAYMOND GORST**

A thesis submitted to Plymouth University

in partial fulfilment for the degree of

DOCTOR OF PHILOSOPHY

School of Health Professions

Faculty of Health and Human Sciences

December 2017

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Finally, to my beautiful girls, Kiara and Gracie. Without you, I am nothing. To you both, I dedicate this thesis.

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# **AUTHOR'S DECLARATION**

At no time during the registration for the Doctor of Philosophy has the author been registered for any other University award without prior agreement of the Graduate Committee.

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Poster Presentations related to the work within this thesis are listed below:

1. **Gorst T**, Marsden J, Paton, J. Morrison S, Lyddon, A, Cramp M & Freeman, J. Foot and ankle impairments affect mobility and balance in stroke (FAiMiS); the views of people with stroke. UK Stroke Forum, December 2013, Harrogate, UK

2. **Gorst T**, Marsden J, Paton, J. Morrison S, Lyddon, A, Cramp M & Freeman, J. Foot and ankle impairments affect mobility and balance in stroke (FAiMiS); the views of people with stroke. Plymouth Hospitals Trust Annual Research Conference, 2013, Plymouth UK.

3. **Gorst T**, Freeman J & Marsden J. The reliability and validity of three novel measures of lower limb somatosensory discrimination tests in chronic stroke. . Physiotherapy UK, Chartered Society of Physiotherapy Congress, November 2017, Liverpool, UK.

4. Cramp M, Lyddon A, **Gorst T**, Freeman J, Paton J, Morrison S, Marsden J Exploring the impact of foot and ankle impairments on mobility in people with stroke. ACPIN-INPA International Neurophysiotherapy Conference, 2016, London UK

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2. **Gorst T,** Marsden J, Paton, J. Morrison S, Lyddon A, Freeman J. & Cramp M. A cross sectional study investigating foot and ankle impairments in people with stroke. European Stroke Conference, April 2016. Venice, Italy.

3. **Gorst T**. Measurement and impact of somatosensory dysfunction in stroke. Neuro Expo, London EXCEL, London UK 2016

4. **Gorst T**. The development and evaluation of three novel measures of lower limb somatosensory discrimination in chronic stroke. Plymouth University Faculty of Health and Human Sciences Research Conference, June 2017, Plymouth, UK,

5. Cramp M, **Gorst T**, Paton, J. Morrison S, Lyddon A, Freeman J. & Marsden J. Foot and ankle impairments as predictors of mobility and balance after stroke (FAiMiS study). UK Stroke Forum, December 2017, Liverpool, UK

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# Foot, ankle and lower limb somatosensory dysfunction in stroke

### Abstract

The extent to which sensory impairments in the foot, ankle and lower limb persist into the chronic phase of stroke is unclear. Furthermore, the extent to which these impairments influence walking, balance and falls is not well understood. This thesis investigated the prevalence, functional importance and measurement of lower limb somatosensory impairments in ambulatory people with chronic stroke.

### Methods

This thesis comprised three studies: the first, a qualitative investigation, explored the views and experiences of people with chronic stroke (n=13). This led to the second study: a cross sectional observational study in which the prevalence, distribution and functional relevance of lower limb sensory impairments were investigated in chronic stroke participants (n=180) and healthy controls (n=46). The final study, informed by the findings from the first two studies, a "synthesis" review of current sensory measures and patient and carer involvement, developed and evaluated three novel, functionally oriented measures of lower limb somatosensory discrimination in chronic stroke (n=32) and healthy controls (n=32).

### Results

People with stroke felt problems with foot, ankle and lower limb sensation affected their walking, balance and contributed to falls. Furthermore, sensory impairments in the lower limb are prevalent with up to 59% of chronic stroke survivors having a deficit of one or more somatosensory modality. Despite this, weak associations between traditional measures of tactile and proprioceptive sensation and walking, balance and

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falls were demonstrated. Novel, functionally oriented measures of tactile and proprioceptive discrimination were developed and evaluated. These measures were reliable and valid, showing greater sensitivity to predicting the presence of sensory impairments and had stronger associations with functional measures than traditional sensory tests.

# Conclusions

This thesis has provided a comprehensive picture of lower limb somatosensory dysfunction in chronic stroke survivors. Sensory impairments persist into the chronic phase of stroke in the majority of stroke survivors. The extent to which such impairments influence functional ability warrants further investigation. The use of functionally oriented measures that assess higher-level somatosensation is encouraged.

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# 1. Introduction and background

### 1.1. Stroke

Every four minutes and forty-eight seconds, someone in the UK experiences a cerebrovascular event (CVE) or stroke (Townsend, 2012). Derived from the Greek word *apoplessein* meaning 'to strike down', the medical term apoplexy is most commonly known today as *stroke*. The term was recently defined as "central nervous system infarction (tissue death) involving brain, spinal cord, or retinal cell death attributable to lack of oxygen, and based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury" (Sacco et al, 2013). This sudden and often devastating illness is the largest cause of adult disability in the UK (Adamson et al, 2004) and represents a major health problem. Direct healthcare costs associated with stroke in the UK have been reported as £4billion per year, or 5% of National Health Service (NHS) expenditure (Saka et al, 2009). Informal care and lost productivity are further estimated to cost £4.9 billion per year.

Improved acute care and survival rates mean 1.1million people are today living with the effects of stroke with over half of these stroke survivors dependent on others for everyday activities of living (RCP, 2012). A greater proportion of people surviving the acute stroke episode mean stroke is shifting away from being a major killer, to becoming a long-term chronic condition (Feigin et al, 2010; Crichton et al, 2016). Multiple impacts on individuals, health care systems and society suggest a greater need to focus attention on the long-term consequences and management and needs of people with stroke to reduce the global stroke burden (Feigin et al, 2010; van Mierlo et al, 2014).

## 1.2. Clinical features and impact of Stroke

The clinical manifestations of stroke vary widely, depending on the site and extent of the lesion (Bamford et al, 1991). Stroke can result in significant impairments of movement, sensation, emotion, cognition, swallowing, communication and continence. These impairments are not mutually exclusive; whilst each can have debilitating effects independently, impairment in one area often affects performance in another. Such impairments inevitably have significant consequences on wellbeing, ability and participation in society.

The patients' desire to regain the ability to walk safely and independently, both at home and in the community, often drives the focus of stroke rehabilitation (Lord et al, 2004). It is reported that 60-80% of stroke survivors gain "independent walking" (Veerbeek et al, 2011), yet one third of those regaining this ability, are unable or lack the confidence to walk unsupervised in the community (Lord et al, 2004; van de Port, 2008). When other parameters are examined, the impact of stroke on walking and function may be much more extensive. Impaired balance (Tyson et al, 2006; Durcan et al, 2016), reduced walking speed (Salbach et al, 2014; Schmid et al, 2007), lower walking distance (Fulk et al, 2010), increased falls (Batchelor et al, 2012; Said et al, 2008), and feeling less integrated into their communities as a result of these mobility issues (Wood et al, 2010) have all been reported.

In an attempt to address these issues, clinical and research efforts have focused on gait, and the *gross* motor performance of the lower limb with changes in walking mobility well documented after stroke (van Swigchem et al, 2013; Patterson et al, 2010; Allen et al, 2011). The impact of stroke on the foot/ankle and the role of the

foot/ankle in functional decline in people with stroke has received relatively little attention (Bowen et al, 2016; Kunkel et al, 2017). The foot and ankle complex represent the only interface between the ground and the person. It is a highly specialised unit, vital for sensing and responding to relative ground/body motion and changes in support surface properties. It is key to effecting an appropriate motor response during functional weight bearing movements and when balancing. Although lower limb impairments are considered a greater indicator of participation restriction than upper limb impairments (Desrosiers, 2003), little research has focused on detailed analysis of the foot and ankle. Further, there has been little recognition of the need for rehabilitation to consider the impact on the foot and ankle and the resultant health needs (RCP, 2016) and further research is required to support the development of targeted and appropriate multidisciplinary rehabilitation care after stroke.

# 1.3. Thesis overview

My intention as a researcher and practicing clinician has been to ensure any research work has at its core the patient, reflecting and responding to their experience. This thesis has evolved since inception and during its development, with its focus changing as further enquiry was undertaken and data was interrogated. A qualitative approach in the first instance (study 1), as part of a wider programme of research, explored foot and ankle impairments from the perspective of the person with stroke. The findings from this qualitative study highlighted multiple foot and ankle impairments contributed to functional difficulties, including pain, sensory changes and weakness. Whilst all reported impairments appeared to affect day-to-day functional ability, descriptions of lower limb sensory impairments, were particularly compelling and impactful. Participants reported not knowing where the hemi-foot or leg was in space

and not feeling fully aware of the ground beneath the hemi-foot, which substantially affected their outdoor walking, balance and contributed to falls. These findings, and the limited evidence in the literature of lower limb sensory impairment (relative to motor impairment), identified the need for further research in this area. A more detailed examination of foot, ankle and lower limb sensory impairment was thus needed in this cohort of participants to further inform the impact of sensory changes on mobility, balance and falls. Study 2 thus focussed specifically on somatosensory dysfunction in chronic stroke participants, with the emphasis expanded to include foot, ankle and the whole lower limb. Reported falls was also included as an outcome measure in study 2 in response to the participant reports in study 1. Interrogation of the findings from study 2, suggested potential drawbacks of existing clinical tests of foot/ankle and lower limb somatosensation. In response, novel tests of lower limb tactile and proprioceptive somatosensory discrimination, informed by patient, carer and public involvement (PCPI) and a review of existing measures (chapter 5), were developed. The evaluation of these measures is the focus of study 3.

The following introductory sections therefore initially provide an overview of foot and ankle function, both generally and within the context of stroke. Subsequent sections review foot, ankle *and* lower limb somatosensation in more detail, with reference to the somatosensory system, its interaction with movement and the role of lower limb somatosensation in mobility and balance in stroke.

# 1.4. The importance of foot and ankle function

The foot and ankle represent a complex, multi-articular unit. Biomechanically, the foot has two important aims: to support the body weight (static foot) and to serve as a

lever to propel the body forward (dynamic foot) (Wright et al, 2012; Bramble and Lieberman 2004). The ankle forms the kinetic linkage between the lower limb and the foot, allowing the foot to interact with the ground. As the basis for human locomotion, the foot is involved in all phases of ground contact from shock absorption to support to propulsion and thus is equipped with a wide range of functional properties.

In supporting the body's weight, the foot and ankle represent the end of the kinetic chain that opposes external resistance so are required to distribute and dissipate compressive, tensile, shearing, and rotatory forces (Abboud, 2002). In addition to the body's "shock absorbers", bearing up to 13 times body weight during running (Burdett, 1981), the foot and ankle are important determinants of postural sway and control. Several authors have provided evidence that body sway in quiet standing is like the motion of an inverted pendulum pivoted at the ankle joint (Fitzpatrick et al. 1992; Winter et al. 1998; Gatev et al, 1999). This model proposes that the body's centre of mass (COM) is tracked and subsequently regulated by movement of the centre of pressure (COP) through the feet (Winter et al, 1998). A given movement of the body's COM forwards or backwards is counteracted by ankle plantarflexor/dorsiflexor muscle activation. Small movements/contractions at the ankle can therefore sustain large movements of the high COM.

The foot and ankle must also accommodate and adapt to a changing pattern of loading during locomotion and stance as the COM of the body moves. During initial contact, the foot's function involves shock absorption, deceleration of downward movement, weight-bearing stabilisation, and preservation of progression (Perry & Burnfield, 2010). After the initial contact, the foot rapidly moves through eccentrically controlled plantar

flexion (1<sup>st</sup> rocker) to gain full ground contact and mid-stance stabilisation. Ankle dorsiflexion allows the body to progress forwards over the foot (2<sup>nd</sup> rocker) where the foot becomes a firm support and a rigid lever. This is followed by rapid ankle plantarflexion to help propel the body forward during this final component of the stance phase (Perry & Burnfield, 2010).

The foot and ankle must be relatively compliant during stance, as structural deformations within the foot provide somatosensory information (Wright et al, 2012; Kavounoudias et al. 1998) store, and subsequently release, elastic energy to aid energy conservation during gait. Dorsiflexion at the ankle during mid swing contributes to adequate toe clearance by reducing the relative length of the leg. In doing so, less knee flexion and hip flexion is required, further contributing to energy efficiency. Individuals who have difficulty with ankle dorsiflexion may compensate by increasing knee flexion, hip external rotation and/or pelvic tilt to achieve toe clearance (Kim and Eng, 2004). Efficient foot and ankle function thus involves the precise coordination of multiple segments and joint mechanisms, which strongly influence the interaction between the whole lower limb and the ground (Forghany et al, 2014; Goble et al, 2011; Gravano et al, 2011).

Impairment to this functional unit inevitably may impede many functional tasks. For example, studies of older adults have demonstrated associations between ankle dorsi/plantarflexor strength and postural sway (Menz et al, 2005), walking speed (Tiedmann et al, 2005), sit-to-stand (Lord et al, 2002) and the functional movements of stooping, crouching, and kneeling (Hernandez et al, 2010). Reduced ankle range of motion in both the sagittal and frontal planes has been associated with impaired

balance ability (Mecagni et al, 2000), whilst reduced ankle dorsiflexion and plantar tactile sensation has been identified as a significant independent predictor of falls (Menz et al, 2006). Spink et al (2011) examined the feet of 305 men and women aged 63- 95 and found that foot, and ankle characteristics, particularly plantar flexor strength of the hallux and ankle inversion/eversion range of motion, are important determinants of balance and functional ability in older people. Deshpande et al (2010) further investigated foot and ankle somatosensation in 799 elderly and found tactile sensation in the sole of the foot and ankle proprioception, predicted standing balance performance (p=0.002), dynamic balance performance (p<0.001) and gait speed (p=0.003).

### 1.5. Foot and ankle function post stroke

Almost half of people with stroke report foot problems (Bowen et al, 2016). Whilst the findings from the evidence produced by studies of the elderly provide some insight, following stroke, multiple neurological impairments occur. A recent survey of 145 people with stroke (time since stroke (TSS) =45 months) identified 17 self-reported foot problems. Weakness and limited movement in the feet/ankles, reduced sensation, and pain were the three most common (Bowen et al, 2016). In addition, foot deformity (Forghany, 2011; Kunkel et al, 2017), altered plantar tactile sensation (Tyson et al, 2013; Kunkel et al, 2017), reduced ankle proprioception (Yalcin et al, 2012), altered motor control (van Swigchem et al, 2013), reduced hallux range of movement (Kunkel et al, 2017), toe clawing (Laurent et al, 2010), and hitch-hikers toe (Yelnik, 2003), have all been observed post stroke.

The interaction between foot and ankle impairments, often on a background of agerelated changes, mean impairment-function relationships in the foot, ankle and lower limb are not clear. For example, Forghany et al (2011) found 30% of people with stroke had hemi-foot postural abnormalities, which were predicted by age, rather than stroke related impairments such as weakness or spasticity. Older, weaker stroke participants with foot abnormalities were, however, more likely to be restricted to household walking (Forghany et al, 2011). Ng & Hui-Chan (2012) investigated the interaction between ankle plantarflexor spasticity, and dorsiflexor weakness on walking endurance in 62 chronic, stroke participants with spastic hemiplegia (time since stroke (TSS) =5.2 years, Standard Deviation (SD) =3.7 years). Ankle dorsiflexor strength was strongly and significantly correlated with walking endurance (r=0.79, p<0.001) whereas plantarflexor spasticity was not (r=0.06; p>0.05). The findings suggest ankle dorsiflexors are major determinants of gait efficiency, but the interaction between spasticity and weakness is unclear. Spastic ankle plantarflexors have difficulty in generating sufficient control and force as agonists during ankle plantarflexion at the end of stance phase to assist with propulsion (Ng & Shepherd, 2000). Conversely, they might also act as active restraints during ankle dorsiflexion in mid stance or swing phase meaning net ankle dorsiflexion weakness may in part be due to spastic plantarflexors. Stroke related impairments resulting in inadequate ankle dorsiflexion during gait include weakness of dorsiflexors, spasticity of plantarflexors, passive stiffness of the plantarflexors, and abnormal, increased muscle co-activation (Lamontagne et al, 2002).

The relative contributions of lower limb motor weakness, spasticity and sensory impairments were investigated in 26 people with mild-moderate, chronic stroke

(TSS=10 months, SD=12 months) (Hsu et al, 2003). Regression analyses revealed that hip flexor and knee extensor strength, were the most important independent determinants of comfortable and fast gait speed. Second was ankle plantarflexor spasticity and third, lower limb sensation. Spasticity of the affected plantarflexors however was the most important independent determinant of temporal and spatial gait asymmetry during comfortable and fast speed gait. A recent systematic review supported that lower limb weakness in stroke was most consistently associated with reduced gait velocity, with ankle dorsiflexor strength most strongly correlated (Mentiplay et al, 2015).

Sensory impairments have also been implicated in functional ability post stroke. Work by Lee et al (2004) investigated proprioceptive ability, in 11 chronic stroke participants (TSS=43 months, SD=32 months). They assessed movement sense at the ankle in both dorsiflexion and plantarflexion conditions, finding that movement sense overall was significantly and moderately- strongly correlated with walking endurance (r=0.44-0.63, p<0.05). Such findings, albeit in a relatively small sample, suggest that knowledge of foot position improves walking speed and efficiency over longer distances. In contrast, Lin et al, (2012) demonstrated in 35 people with chronic stroke (TSS=54 months, SD= 49 months) that spatio-temporal stride characteristics during gait were not significantly affected by impaired ankle proprioception. They suggested that in chronic stroke, visual sensory inputs dominate and may compensate for reduced foot position awareness.

The quantitative studies described above provide some objective evidence of the nature of foot and ankle impairments and their impact on function and mobility post

stroke. They highlight the multi-factorial nature of foot and ankle impairments post stroke but do little to enhance our understanding of *how* foot and ankle impairments interact with each other or indeed, affect function. To help address this issue, qualitative work was undertaken as part of this thesis (study 1, chapter2). It provided further insight into how impairment to somatosensation interacted with, and affected movement and foot-ground interactions during walking and balance in people with stroke.

# 1.6. The sensory systems, somatosensory system and movement

# 1.6.1. The sensory systems

The maintenance of body/postural orientation and equilibrium during standing (static postural control) and movement (dynamic postural control) is reliant on a complex interaction between sensory and motor systems (Horak, 2006; Macpherson & Horak, 2013). The sensory system that influences static and dynamic postural control comprises an integrated and highly adaptive subsystem, which involves visual, vestibular and somatosensory inputs (Shumway-Cook & Woolacott, 2012) (Fig 1.1)



Figure 1-1: The sensory systems involved in balance and postural control

The vestibular organ measures the angular and linear acceleration of the head with respect to the gravitational field (Goldberg, Walker & Hudspeth, 2013). The visual system provides visual information about the environment, initially encoded in retinocentric co-ordinates, along with ocular proprioceptive information about the position of the eyes relative to the head (Goldberg & Walker, 2013). The somatosensory system provides information from muscle spindles that provide proprioception, measuring muscle length and velocity (Gardner & Johnson 2013a). Further somatosensory information is provided by tactile sensors in the soles of the feet, ligamentous structures and the Golgi tendon organs, providing pressure, structural deformation and tendon force information, respectively (Wright et al, 2012; Gardner & Johnson 2013a).

Individual and task factors, along with environmental factors, such as changes in terrain and light, for example, further demand a constant change in the relative contribution of different sensations to postural control. Continual adjustment or "reweighting" between these systems occurs to sustain postural stability during many functional tasks (Bonan et al, 2013; Smania et al, 2008). It is suggested that in healthy adults, in a well-lit environment, with a firm base of support, the relative sensory reliance or "weighting" between these sensory systems are somatosensory (70%), vision (10%) and vestibular (20%) (Peterka, 2002). Through the systematic manipulation of sensory inputs intended to perturb the system, the ability of the Central Nervous System (CNS) to reorganise the relative weighting on the existing inputs can be quantified by postural sway or gait deviations (Smania et al, 2008; Chien et al, 2014). For example, in healthy people, when the reliability of lower limb somatosensation was disrupted through support surface oscillations, the relative

sensory contributions arise from vestibular (70%), vision (20%) and somatosensation (10%) to maintain postural stability (Peterka, 2002).

Based on the integration of this multisensory information, an estimation of the body or limb position is made, appropriate actions are determined and subsequently the CNS sends signals to the muscles, to initiate corrective joint torques and movement (Macpherson & Horak, 2013; Horak, 2006).

# 1.6.2. The somatosensory system

The primary sensory modality providing the sense of body position and movement is the somatosensory system. It comprises specialised receptors that provide individuals with a sense of limb position, movement and tension (proprioception) and the somatic sensations of touch, pain, temperature, and itch. Sense of touch provides perceptions of pressure, vibration and texture (McGlone & Spence, 2010) while proprioception alludes to the perception of tension/force, body/joint movement, and limb relative position (Han et al, 2016; Proske & Gandevia, 2012). Specialised mechanoreceptors in the glabrous skin of the sole of the foot (and hand) have slow and fast adaption speeds and are able to detect displacement, velocity and acceleration of the skin surface (Hennig, 2009). The specialised low-threshold mechanoreceptors, Merkel discs and Ruffini corpuscle end organs, are slow adapting (SA) cutaneous mechanoreceptors, which respond during continuous mechanical stimulation of the skin, such as during stance and postural sway. Meissner and Pacinian corpuscles conversely are rapidly adapting (RA) low threshold cutaneous mechanoreceptors, which respond to initial and final contact of a mechanical stimulus to the skin (McGlone & Spence, 2010), such as during heel strike and toe off. With regard to proprioception, afferent information

is generated from muscle spindles of the foot and lower limb, while other sources of proprioceptive information, including cutaneous and joint mechanoreceptors, are also important for determining the position of the foot and ankle and/or signalling limits of range of motion (Lowrey et al, 2010; Goble et al, 2011; Proske & Gandevia, 2012). Muscle mechanoreceptors, namely, Golgi tendon organs further provide critical information in relation to tension and force.

Information related to the different sensory modalities from these peripheral mechanoreceptors, travel via ascending and separate pathways up the spinal cord and brainstem into the thalamic nuclei terminating in the somatosensory cortex (Fig 1.2A &B). For example, fine discriminatory touch information, and joint position sense are transmitted via the dorsal column-medial lemniscus pathway (DCML). Crude touch, pain and temperature are conveyed by the anterolateral system, or spinothalamic pathway. Proprioceptive information is transmitted via several ascending pathways: these include the DCML, so pass via the medulla and thalamus and then to the somatosensory cortex to provide conscious proprioception; and via the dorsal and ventral spinocerebellar pathways, to the cerebellum to provide unconscious proprioception (Lisberger & Thach, 2013; Gardner & Johnson, 2013a).

Ascending pathways transmitting somatosensory modalities are organised so information is transmitted both hierarchically and in parallel. The ventroposterior nuclei complex of the thalamus, which itself sits within the diencephalon, represents the main termination site for ascending somatosensory pathways (Fig 1.3). It consists of two major nuclei, the ventral posterior lateral (VPL) and ventral posterior medial (VPM), and a smaller nucleus, the ventral posterior inferior (VPI) (Fig. 1.3). The DCML

forms the main input to the VPM and VPL nuclei, projecting fine touch, vibration and upper limb joint position sense. The VPI nucleus receives pain and temperature input from the spinothalamic tract. From the VPM and VPL, thalamocortical pathways project into Brodmann's Area 3a, 3b, 1 and 2, collectively referred to as the primary somatosensory cortex (S1). It is in S1 that sensory information is initially processed but

Fig 1-2. (With permission) Ascending somatosensory pathways. **A**, two main pathways conveying somatosensory information to the cerebral cortex; the dorsal column/medial lemniscal (DCML) and the spinothalamic pathways. **B**, Dorsal and ventral spinocerebellar pathways carrying tactile and proprioceptive information to the cerebellum from the upper and lower parts of the body.



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it also begins higher-order processing, such as feature extraction (Gardner & Johnson, 2013a). The secondary somatosensory cortex (S2) receives input primarily from S1 and is thought to play a role in filtering information for focus and discrimination (Amaral, 2013). S2 also projects directly into insular cortices, which are further suggested to have a diverse range of functions from pain perception through to the processing of social emotions (Nieuwenhuys, 2012). The Posterior Parietal Cortex (PPC), which has direct projections from S1 is considered a higher-order sensory cortex, similar to an association cortex, and integrates the different sensory modalities necessary for sensory perception (Rizzolatti & Kalaski, 2013).

Fig 1-3. (With permission) Diagram of connections from the somatosensory receiving nuclei of the thalamus to the somatosensory cortex of the parietal lobe. Collectively areas 3a, 3b, 1, and 2 are referred to as S1 (primary somatosensory cortex).



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Key: CS = central sulcus; VPI, ventral posterior Inferior; VPL, ventral posterior lateral; VPS, ventral posterior superior

Compared to motor output, the neural correlates of somatosensory function in humans are largely unexplored, although functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) studies are increasingly identifying the networks involved in somatosensory processing. Contralateral S1, bilateral S2 and the contralateral PPC are classically active during touch. Further imaging studies demonstrate that the perception of touch involves not only somatosensory cortices, but further brain regions: Brodmann Area's 5 & 7 in the posterior parietal cortex (Ackerley & Kavounndias, 2012; Hartman et al, 2008); precuneus (Borstad et al, 2012); insular cortex and putamen (Preusser et al, 2015). All have been implicated in sensory discrimination tasks and further highlight the widespread involvement of neural structures in somatosensory perceptual processing. Proprioceptive information is also processed at the spinal level, brain stem and higher cortical centres, as well as subcortical cerebral nuclei and cerebellum (Bosco and Poppele, 2001; Amaral, 2013; Lisberger and Thach, 2013; Pearson and Gordon, 2013) where it is directly involved in shaping and controlling motor outputs such as reflexes and movement.

With the growing insight into the neurophysiology underlying somatosensory processing, and lessons from Psychology, it is widely recognized that it is sensory *perception* that ultimately guides and informs contextual, goal oriented, decisionmaking and behaviour (Romo & Salinas, 2001). That is, sensation refers predominantly to the first stages in the functioning of the senses, from the effect of a physical stimulus on mechanoreceptors in skin and muscle, to their transduction and transmittal from the peripheral nervous system along pathways to the sensory areas of the brain. Sensory perception, however, involves the supraspinal and cortical structures where the "raw" sensation is processed, organized and interpreted so that it may be used to guide decision making and movement (Gardner & Johnson, 2013b; Gold and Ding, 2013). It is thus our perception of a stimulus that ultimately guides and informs movement and behaviour. However, impairment to central cognitive and emotional functions such as selective and divided attention, working memory, and fatigue are potentially key confounders to the somatosensory experience, particularly when higher-level sensory processes are involved. It is perhaps this that makes the sensory experience a very personal and subjective one, which can lead to erroneous interpretations (e.g. illusions). Inevitably, this makes it challenging to quantify.

# 1.6.3. Somatosensation and movement

Proprioception and touch perception are the most frequently studied of the somatic senses because of the key role they are suggested to play in voluntary human movement and motor control. Within this thesis, reference to somatosensory or sensory or afferent is in the context of cutaneous touch/tactile sensation and/or proprioceptive sensation. Exploration of the other somatic sensations such as pain, temperature and itch are beyond the scope of this thesis.

Somatosensory input influences motor responses because the CNS uses and integrates information from the periphery in order to plan and execute appropriate movement or motor responses (Wolpert, Pearson & Ghez, 2013; Chien et al, 2014; Floel, 2004). In this process, it is proposed that with the motor command, a replication of that command (efference copy) is sent to an internal forward model, used to predict the expected motor outcome (Von Holst & Mittelstaedt, 1950). The efference copy, combined with somatosensory information about the current body position, is entered in a feedforward prediction model (Wolpert et al, 2011). The feedforward model
predicts the somatosensory consequences of the movement (corollary discharge) which is compared with the actual somatosensory feedback. Discrepancies between predicted and actual somatosensory input are relayed back to the structures encoding the translation of motor planning into motor command, closing the sensory-motor loop (Perruchoud et al, 2014). Accurate somatosensory input is thus strongly implicated in the generation of smooth and coordinated movements (Wolpert, Pearson & Ghez, 2013), the maintenance of normal body posture and orientation, and the regulation of balance and postural control (Macpherson & Horak, 2013). Studies of patients with intact motor pathways and tactile and proprioceptive deficits because of polyneuropathy (Hohne et al, 2012; Bringoux et al, 2016; Sanes et al, 1984) or pure sensory stroke (Kato & Izumiyama, 2015) report substantially impaired motor function, balance and spatial orientation, particularly when vision was excluded.

The role of tactile input and proprioception are also strongly implicated in motor learning, particularly in the early learning stages of a movement (Bernardi et al, 2015). Sensory comparison of actual with intended movement, as discussed, is theorised to be important for motor learning because it updates an internal forward model of the motor command (Wolpert et al, 2011). Laboratory based experiments involving the upper limb have highlighted the importance of accurate somatosensory inputs to motor learning. Vidoni et al (2010) demonstrated that motor task practice with concomitant artificially reduced cutaneous somatosensation from repetitive Transcranial Magnetic Stimulation (rTMS) to the primary somatosensory cortex (s1), impaired motor learning of a simple joint position task. Similarly, Bernadi et al (2015) designed an upper limb-reaching task to a target of uncertain origin, and demonstrated that upper limb passive movement with performance reinforcement

produced similar rates and degrees of learning to active, self-generated active movement training. The authors suggest that in the early stages of motor learning, the somatosensory system rather than the motor system, dominates motor skill acquisition.

Proprioception is also strongly implicated in triggering the corrective responses that might occur following a balance disturbance, such as a trip, for example. When a muscle is rapidly stretched, 1A afferent (proprioceptive) muscle spindles detect the velocity and direction of muscle length change (Proske & Gandevia, 2012). This change triggers a stretch reflex, actioning an appropriate corrective motor response. The implication being that during a trip or balance disturbance for example, feedback from 1A proprioceptive afferents trigger appropriate and potentially fall-saving motor responses (Grey et al, 2004). Impairment to this neural pathway may result in subdued feedback and a slower response to a perturbation, and has been suggested to be an unrecognised falls determinant (Marks, 2015).

The functional role of specific groups of sensory receptors in regulating human locomotion and movement is however uncertain because they interact with each other and with central rhythm-generating centres in a complex manner (Gravano et al 2011). It is widely acknowledged that more complex spinal networks exist within the grey matter of the spinal cord (Pearson & Gordon, 2013; Guertin, 2009). One of these networks, the central pattern generator (CPG) for locomotion, has been identified as a group of interneurons that activate motor neurons in an appropriate sequence and intensity to generate motor patterns. They are localised, for the most part, in the lumbar part of the spinal cord in humans (Dimitrijevic et al, 1998). In a recent review

of CPG for locomotion, Guertin (2013) suggested the best evidence of its existence in humans is from Dimitrijevic et al (1998). In this study, epidural electrical stimulation of the spinal cord near L1-L2 induced rhythmic, alternating stance and swing phases of the lower limbs in lying SCI patients with complete injury. Although human studies are limited (for obvious reasons), the compelling evidence derived from decerebrate animals, shows that basic locomotor patterns, adaptions to changes in speed, and stepping can be produced by the CPG for locomotion (Guertin, 2009; Grillner et al, 2008; Graham-Brown, 1911). Such studies indicate that the whilst the control of less complex walking tasks may be largely driven without cortical input, sensory feedback is still occurring to facilitate, for example, adaptation to speed. One of the key influences on the CPG for locomotion are peripheral inputs. Experiments utilizing natural stimulation of muscle receptors demonstrate that afferent input to the CPG's arise mainly from Golgi tendon organ Ib afferents (Andersson & Grillner, 1983; Sillar et al, 1986). The outcome on the decerebrate cat limb is that an increased load of limb extensors during the stance phase enhances and prolongs extensor activity, while simultaneously delaying the transition to the swing phase of the step cycle (Conway et al, 1987; Duysens & Pearson, 1980).

However, although the basic motor pattern for stepping is generated in the spinal cord, fine control of walking involves various brain regions, including cerebral motor cortex, cerebellum, and brain stem (Dietz, 1996). For over-ground walking, a CPG does not appear to be sufficient. Supraspinal control is needed to provide both the drive for locomotion as well as the coordination to negotiate a complex environment. Recent electroencephalography (EEG) studies in human participants demonstrate increased activity levels in supra-spinal cortical areas during more challenging locomotor tasks.

For example, compared with regular treadmill walking, narrow beam walking shows greater EEG activity in, amongst other areas, sensorimotor cortices (Sipp et al, 2013). Similarly, greater cortical activity was recorded in somatosensory (and motor) cortices during active stepping, compared with passive stepping (Wagner et al, 2012). More recently, Bradford et al (2016) reported significant differences in cortical activity in brain regions related to sensory processing and integration during incline walking compared with flat walking. The net implication from these studies is that cortical activity is involved in the neural control of locomotion, with the suggestion that the cortex is in a "heightened state" to monitor somatosensory feedback during more complex locomotion (Bradford et al, 2016). The extent, however, to which increased muscle activity during more physically demanding tasks drives somatosensory activity, is unclear. Further, scalp EEG recordings are susceptible to mechanical disturbance, particularly during more vigorous physical movements (Castermans et al, 2014) so caution must be used when interpreting these findings. Nonetheless, functionally oriented monitoring of neural activity via EEG recordings provide support to the implication that accurate somatosensory information is important during more demanding functional tasks such as community walking and stepping. Such tasks require cognitive flexibility and higher attentional resources to address voluntary motor requirements while attending to a range of environmental stimuli or concurrent tasks (Patla, 2001; Lord et al, 2006; Park et al, 2011).

#### 1.7. Functional importance of foot, ankle and lower limb somatosensation

More evidence is being presented that demonstrates the importance of the foot as a sensory organ (Collings et al, 2015; Zehr et al, 2014; Zhang & Li, 2013; Wright et al, 2012; Deshpande et al, 2008; Hennig, 2009). To adapt to external cues or altered walking conditions, changes in plantar pressures, limb positions and loading must be detected, relayed and integrated by the CNS. Impairment in one or all of these afferent inputs has implications on gait, balance and falls. Foot-support interactions and appropriate sensory signals are thought to be an integral part of the CNS networks that underlie the adaptive control of walking (Guertin, 2013; Duysens et al, 1980) as a variety of sensory receptors are activated by limb loading and movement. These include Golgi tendon organs, muscle spindles, cutaneous receptors, and various load mechanoreceptors in the foot arch. The detection of mechanical stimuli by the foot has been shown to influence balance during static and dynamic postural activities, stepping control, and gait kinetics in healthy populations. For example, Perry et al (2001) found that anesthetising the sole of the foot (through plantar cooling), resulted in altered compensatory stepping reactions to perturbation and delays in gait termination. Kavounoudias et al (1998) demonstrated that site specific plantar transcutaneous vibration evoked directional postural responses in standing, whilst cutaneous stimulation of discrete regions of the feet produced a "sensory steering" effect during locomotion in healthy participants (Zehr et al, 2014). Collings et al (2015) further found that discrete stimulation of the lateral rear foot with textured in-shoe insoles, changed gait kinetics in the second half of the gait cycle.

Pathological sensory malfunction of the plantar aspect of the foot, as seen in peripheral neuropathy (PN), multiple sclerosis (MS) and elderly populations, for

example, has also shown to impact gait parameters and balance. Zhang & Li (2013) found that plantar pressure distribution in the foot were significantly different in those with sensory loss as a result of diabetic peripheral neuropathy (DPN) compared to those without, during standing. Plantar distribution during walking, however, was not affected by sensory status, suggesting that other factors such as foot deformity and muscle weakness may be important. Qui et al (2012) found that enhancing plantar input, through textured surfaces underfoot in elderly patients, significantly decreased postural sway, during challenging static balance conditions. Whilst in a cohort of MS patients, Kalron et al (2015) demonstrated that in-shoe textured insoles, worn over a four-week period, significantly improved postural sway, but did not significantly affect spatiotemporal parameters of gait, or plantar sensory ability.

It is suggested that in the absence of visual and vestibular inputs, an ankle proprioception perceptual error as small as 0.1° can lead to approximately a 1.8-mm lateral postural deviation of the whole body centre of mass (Gilsing, 1995). In healthy participants, stimulation of plantarflexor muscle spindle afferents via vibration of tendo-achilles, affects spatiotemporal parameters of gait (Mullie & Duclos, 2014) and leads to stereotyped postural response in standing in healthy persons. Reduced ankle, knee and hip proprioception has been associated with falls in the elderly (Lord et al, 1991; Wingert et al, 2014; Callaghan et al, 2015). Lower limb proprioceptive ability has also been strongly implicated in high level, successful sports performance. In a series of studies, Han et al (2014, 2016) demonstrated ankle proprioception to be significantly predictive of sport performance, extending up to Olympic level and strongly predictive of injury (Witchalls, et al, 2012). In the elderly, foot and ankle somatosensory performance predicts standing balance performance (p=0.002), dynamic balance

performance (p<0.001) and gait speed (p=0.003) (Deshpande et al, 2010). A recent systematic review investigating mobility-related consequences of reduced lower limb peripheral nerve function with age indicated that peripheral nerve function impairment at various levels of severity is related to poor mobility, independent of diabetes (Ward et al, 2016).

#### 1.7.1. Lower limb somatosensory dysfunction post stroke

Cutaneous and proprioceptive sensation in people post stroke have been investigated for more than 40 years (Anderson, 1971). The reported prevalence of sensory impairment following stroke varies widely with estimates reported as low as 7% (Schmid et al, 2013) and as high as 85% (Kim & Choi-Kwon, 1995). It is generally suggested that impairment of one or more aspect of the somatosensory system affects c.50-60% of people during the early phase of stroke recovery (Tyson et al, 2008; Connell et al, 2008; Carey, 1995). However, acute somatosensory impairments account for just 46% of the variance in lower limb tactile sensation and 51% of proprioception at six months with changes in somatosensory performance variable over time post stroke and unpredictable both within and between patients (Connell et al, 2008; Winward et al 2007). Few studies have investigated sensory impairments into the chronic phase of stroke (i.e. >6 months post stroke) although, as with acute/subacute populations, prevalence levels vary widely. A recent survey of self-reported foot problems in people with stroke (TSS=45 months) found that reduced sensation was the second most commonly reported impairment after weakness (Bowen et al, 2016). Schmid et al (2013) reported tactile deficit to pin prick in the feet of 7% (n= 12/160) of stroke patients (TSS=82 months, SD =101 months). Robinson et al (2011) in their cohort of 30 chronic stroke (TSS=39 months; SD=26 months), found 13% had impaired

proprioception in the great toe. Conversely, Yalcin et al (2012) found 70% of their cohort of chronic stroke (n=14/20; TSS=27 months; SD=44 months) had tactile and /or proprioceptive deficits in the hemi-paretic foot/ankle. The prevalence of lower limb somatosensory impairments into the chronic phase of stroke therefore remains unclear. Furthermore, the clinical recognition of the hand as a sensory organ has meant the literature on sensory impairment and treatment post stroke has focused predominantly on the upper limb. Relatively speaking, sensory changes in the lower limb have received little attention.

# **1.7.2.** Interaction between lower limb somatosensory dysfunction and function in chronic stroke

Some insight can be obtained from the studies highlighted earlier in which strong links exist between lower limb sensation and function in elderly and peripheral neuropathy populations (Deshpande et al, 2010; Ward et al, 2016). Case studies of patients with intact motor pathways and pure sensory stroke (Kato & Izumiyama, 2015) also illustrate the substantial movement and functional difficulties that stem from pure somatosensory deficits. Further insight may be gained from interventional studies in which the characteristic asymmetrical hemiplegic gait is diminished following amplified movements of the hemi limb through split belt and body weighted treadmill paradigms (Reisman et al, 2007, 2009; Lam et al, 2009; Kahn et al, 2009). Such interventions it is suggested provide exaggerated movement patterns are disrupted (Wutzke et al, 2013). In addition, some insight can be gleaned from the single qualitative study (Connell et al, 2014) in which the patient experience of sensory impairment was investigated. Although sensory impairments were of concern to participants, their

impact was difficult to articulate, tending to describe sensory impairments in terms of movement dysfunction.

Data from studies of people with acute/sub-acute stroke may also provide some insight. Recently, Tyson et al (2013) pooled the lower limb sensory-motor data of 459 acute/sub- acute stroke patients. They found that lower limb proprioception and tactile sensation, combined and independent, did not significantly predict mobility (p=0.12) or balance (p=0.07) but did significantly predict activities for daily living (ADL) (p=0.04). Several studies have also reported that those with acute sensory impairments *and* motor impairments achieve lower functional outcomes than those with motor impairments alone (Niam et al, 1999; Han & Law-Gibson, 2002; Patel et al, 2000). Stroke severity, independence in ADL, as well as weakness, have been reported as significant independent factors influencing sensory impairment (Tyson et al, 2008) and recovery (Connell et al, 2008).

To date existing studies have undertaken a broad-brush approach wherein multiple variables are examined utilising non-standardised measures. To provide a clear and compelling investigation of the role of somatosensation in functional ability, studies are needed that employ robust and standardised sensory measures. This will enable the identification of significant associations should they exist. For example, Robinson et al (2011) in their cross sectional study of 30 people with chronic stroke found tactile sensibility at the foot, measured with Q-tip, and manually assessed movement detection sense at the 1st metatarsal joint, was not significantly associated with community ambulation ability or falls. Schmid et al (2013) investigated the circumstances and consequences of falls among 160 people with chronic stroke. They

found lower limb sensory function, as measured solely by pinprick detection to the plantar foot as part of the National Institutes of Health Stroke Scale (NIHSS), was not significantly associated with falls incidence, in chronic ambulatory stroke.

In contrast, studies of chronic stroke, which have greater focus on sensory function and/or use, more comprehensive sensory assessments, tend to report stronger and more significant associations between lower limb sensation and function. For example, Lee et al (2015) in their cohort of 46 chronic stroke participants (TSS= 60 months; SD=36 months) assessed tactile and proprioceptive sensation of the entire lower limb. They found that whilst their measure of community ambulation and lower limb somatosensation were not significantly associated (r=0.21; p>0.05), Berg Balance Scale (r=0.34, p<0.01) and gait speed (10 meter walk speed) (r=0.29, p<0.01) were significantly, albeit weakly, correlated. Hsu et al (2003), using the FMA-S, found moderate and significant correlations between lower limb sensation scores (tactile and proprioception) and gait velocity (r=0.40; p<0.05) in their cohort of 26 chronic stroke (TSS =10 months; SD =12 months). The findings from correlational studies therefore provide contrasting evidence and highlight the need for well-structured, observational studies, which focus on sensory function and use more comprehensive, robust, standardised sensory measures.

The findings from interventional studies in which somatosensory ability is augmented do not necessarily enhance our understanding. Sensory interventions in people with stroke have for the large part focussed on the upper limb (Carey et al, 2011; Doyle, 2010) with a dearth of good quality, robust interventional studies in the lower limb (Walker et al, 2014; Morioka et al, 2003; Lynch et al, 2007; Hilier & Dunsford, 2006). In

the lower limb, broadly speaking, intervention studies have attempted to improve sensory deficits through passive or active sensory approaches. Passive sensory interventions, through Transcutaneous Electrical Nerve Stimulation (TENS) or textured insoles, for example, assert that enhanced or augmented sensory input increases cortical motor excitability after the period of stimulation (Meesen et al, 2011). No single intervention has demonstrated superiority and systematic reviews for textured insoles (Orth et al, 2013; Paton et al, 2016) and electrical stimulation (Laufer et al, 2011; Robbins et al, 2006) remain equivocal in their findings.

More recently however, a paired-sample randomized cross-over pilot trial in 29 chronic ambulatory stroke patients (TSS not reported) by Tyson et al (2013) investigated the feasibility and potential efficacy of wearing an 'activeTENS' sock during everyday activities. Their intervention involved a single session delivering 70– 130 Hz, five-second cycle, lasting approximately two hours in total. They found that measures of balance, gait speed, ankle plantarflexor strength and ankle proprioception significantly improved following the active TENS intervention with no adverse reactions reported.

Similarly, Walker et al (2014) in a cohort of 12 chronic stroke (TSS=102 months, SD =84 months), investigated the effect of 30Hz transcutaneous electrical stimulation to the medial plantar nerve of the paretic foot. By applying a cutaneous stimulation at 95% of the motor threshold to avoid producing muscular contraction, the stimulation reportedly produced a tactile sensation on the plantar surface of the foot. Participants completed 20 trials of a foot stepping test to a given target, in which targeting error was measured without stimulation, during stimulation and post stimulation. Significant

reductions in medial-lateral error were observed in the stimulation (p=0.008) and poststimulation conditions (p=0.03) compared to the pre-stimulation condition. However, the order of each condition was not randomised across participants, so a learning effect on the task cannot be discounted. The small sample of this study also means results must be interpreted with caution with regard to generalisability.

Passive interventions have yet to promote functional carry-over effects or learning, once the stimulation has stopped (Tyson et al, 2013; Shamay et al, 2007; Yan & Hui-Chan, 2009). It has been suggested that practice and exposure to sensory stimuli alone may not be sufficient to achieve changes characteristic of perceptual learning (Carey & Matyas, 2005; Morioka et al, 2003).

Utilising a more active, perceptual learning based approach has demonstrated some promising results in upper limb studies (Carey et al, 2011, Byl et al, 2003, 2009) although there have been few good quality studies specific to the lower limb in people with stroke. The most notable have been carried in acute/sub-acute populations. Morioka and Yagi (2003) completed a pilot randomised control trial (RCT) of 26 acute/sub-acute stroke participants (mean time since stroke =62 days, SD=21 days) which investigated the efficacy of sensory retraining of the plantar aspect of the hemiparetic foot. The experimental group, in additional to standard inpatient rehabilitation, completed 10 days of sensory retraining which involved discriminating between rubber surfaces of differing degrees of hardness during weight bearing. They found that the experimental group did not show significant differences in plantar sensitivity, measured by two-point discrimination, but did have significantly lower postural sway, as measured by stabilometry. The recruitment strategy to this RCT however meant

that 55% of eligible participants declined to participate so sample bias is a distinct possibility. Furthermore, sample selection was not based on sensory status and sensory retraining was carried out entirely in standing which has been shown to improve postural sway post-stroke in isolation (van Peppen et al, 2003).

Lynch et al (2007) conducted a small pilot RCT (n=21) comparing sensory retraining of the hemi-paretic foot in acute/subacute stroke patients (time since stroke = 13-122 days) v's relaxation (sham). They used principles of sensory retraining similar to those used in studies of the hand (Carey et al 2011; Byl et al, 2003); these included education regarding sensory loss, practice in touch localisation at several points in the sole of the foot, hardness, texture and temperature discrimination tasks, and proprioceptive retraining of the big toe and ankle. The authors found no significant differences between the experimental and relaxation groups in light touch sensation, proprioception, balance, gait speed, walking aid use, or walking independence. Service delivery issues mid-study meant recruitment targets were not met so the study was poorly powered to detect changes between groups, with only a 13% chance of detecting a group effect. Such studies do not support the link between lower limb somatosensation and functional measures.

Hilier & Dunsford (2006) utilised a single-case, repeated –measures design to determine the efficacy of sensory retraining of the hemi-paretic foot in three chronic (> 2 years) stroke patients on parameters of postural control. The intervention was similar to that described by Lynch et al (2007) and involved three, weekly 45-minute sessions, over a two-week period. Whilst they found statistically significant improvements between pre- and post- intervention in two of their three subjects in

terms of tactile sensation, the results only demonstrated a positive change in participants' postural shift from double leg stance to single leg stance (Hilier & Dunsford, 2006). It is difficult to generalise the findings from this study because of the very small sample size and lack of control.

#### 1.8. Summary

The extent and prevalence of lower limb somatosensory impairments amongst chronic ambulatory stroke participants is unclear. Variable and unpredictable recovery in the acute/sub-acute phase of stroke mean somatosensory dysfunction in the chronic phase of stroke needs further investigation.

The degree to which impairments, subtle or otherwise, contribute to functional ability in chronic stroke is also unclear. Limited evidence is available to clarify the relationship between walking, balance and falls and lower limb somatosensation in people with chronic stroke. Instead, lower limb somatosensory function, due to its intrinsic links with motor function, is suggested to be a co-factor, rather than an independent factor or predictor of functional ability. It is also apparent that there is insufficient robust evidence from interventional sensory retraining studies specific to the lower limb, to demonstrate evidence of effect.

However, insights from neurophysiological studies, and those involving non-stroke populations highlight the importance of lower limb somatosensation in gait, postural control and balance. Deficits in lower limb somatosensation may contribute to and perpetuate the uncoordinated and inefficient inter- and intra- limb movements characteristic of the hemiplegic gait. Finally, the extent to which foot and ankle

impairments affect function from the perspective of people with chronic stroke has not been investigated.

#### 1.9. Thesis Aim

This PhD investigated lower limb sensory dysfunction in chronic stroke participants. With the emphasis on having the patient at its core, the starting point of this thesis was a qualitative study. The initial purpose of this first study was to investigate, from the perspective of those with stroke, what foot and ankle impairments they experienced because of their stroke, and how they felt these impairments affected their functional ability. This qualitative work revealed that deficits in lower limb somatosensation were frequently reported by those experiencing stroke and were problematic for walking and balance, and were felt to contribute to falls. These findings suggested that a more detailed examination of foot, ankle and lower limb sensory impairment was needed in this cohort of participants to further inform the impact of sensory changes on factors such as mobility, balance and falls. This led to the second study, an observational, cross sectional study examining the impact of lower limb sensory loss, as determined by clinical tests post stroke. This study and a further review revealed potential drawbacks of existing clinical tests of foot/ankle and lower limb somatosensation which led to patient, carer and public involvement (PCPI) and the development and evaluation of novel tests of lower limb tactile and proprioceptive discrimination, which was the focus of the third study.

It is hoped this thesis will lead to an enhanced understanding of the impact of lower limb sensory impairments in chronic stroke and inform the assessment and potentially future development of sensory retraining approaches specific to the lower limb.

# 1.10. Thesis Objectives

The specific objectives of this thesis are to:

- Explore the nature and impact of foot and ankle impairments post stroke from the perspective of community dwelling, people with stroke.
- 2) Map the prevalence, type and distribution of lower limb sensory impairments and explore their association with walking, balance and falls, in communitydwelling chronic stroke survivors.
- To develop novel functionally oriented lower limb sensory discrimination measures, evaluate their psychometric properties and investigate their relationship with measures of walking, balance and falls.

2.0. Study 1: Foot and ankle impairments: a qualitative study exploring the views and experiences of people with stroke

#### 2.1. Chapter Overview

This chapter highlights the first study of this thesis: a qualitative study in which the views of people with stroke were explored with regard to the nature and impact of foot and ankle problems. This first study does not focus specifically on sensation, but provides a general description of the foot and ankle impairments experienced post stroke, and how these impairments affect people's lives and their mobility. It aims to provide greater insight into the issues faced by those who have experienced stroke first hand. It was from this study that the main (sensory) impetus of this thesis was derived.

## 2.2. Introduction

The quantitative studies highlighted in the introductory chapter provide some evidence concerning the extent of foot and ankle impairments and their relationship with quantitative measures of function and mobility post stroke. There remains, however, limited insight into 'how' or 'why' these impairments affect "function", or which impairments are most debilitating. The endorsement of the International Classification of Functioning (ICF) by the World Health Assembly (WHO, 2001) turned the spotlight toward understanding functioning and disability as multidimensional concepts that do not just relate to physical features such as walking speed/distance, joint range of movement etc. Understanding functioning and disability must also incorporate psychological features and recognise each person's life situation, activities, social role and participation. To gain a better insight into the complexities of

functioning and the impact of illness and disability on people's lives, we must therefore incorporate research methods that facilitate this deeper exploration as well as those that let us objectively measure function and performance.

There is a widely accepted view that the experiences of patients provide invaluable insight into the real issues, which can help develop complex interventions to facilitate recovery and health (Campbell, 2007; Burton, 2000). The utilisation of qualitative research approaches, which seek to explore people's experiences and understanding, is becoming increasingly popular in clinical and healthcare research (Bartesaghi, 2017; Malterud, 2001). Data collected from qualitative methods is naturally occurring (Silverman, 2011), contextual and rich in meaning, providing insight into the 'hows' and 'whys' of a particular experience or social phenomena (Castelloe, 2017).

Historically, qualitative studies have been used less frequently than quantitative studies, and regarded with scepticism by the medical and healthcare community (Petty et al, 2012; Malterud, 2001). Using both qualitative and quantitative approaches in a complementary manner to explore a topic has become more common in healthcare research, and is viewed as preferable to using one or the other, particularly in implementation research (Palinkas et al, 2011; Aarons, 2011; Dixon-Woods et al, 2004). This thesis incorporates both qualitative and quantitative approaches, utilising qualitative methods initially to help inform subsequent, quantitative phases.

#### 2.3. Study aim & objectives

The aim of this first study was to explore qualitatively, from the perspective of individuals with stroke, the impact of foot and ankle impairments on mobility and balance following stroke. It formed part of a multi-phased programme of research

entitled "Foot and Ankle impairment affecting Mobility in Stroke" (FAiMiS). This programme involved a multidisciplinary collaboration of physiotherapists and podiatrists from the Universities of Plymouth, East London, West of England and Brighton. Study 1 was therefore not undertaken to specifically investigate sensory impairments, but chronologically, it was the first study of this thesis, because it was during this time, I was employed as a research assistant with the opportunity to develop and undertake a body of work towards a PhD. The objectives of this qualitative study thus reflect those of the FAiMiS research programme.

Specifically, the objectives were to explore:

i) How do people with stroke perceive impairments of the foot and ankle to impact on life after stroke?

ii) How do people with stroke perceive impairments of the foot and ankle to contribute to difficulties they have with mobility and balance following stroke?

iii) What aspects (with specific reference to foot and ankle) do people with stroke feel contribute to these difficulties which may include, for instance, stiffness and pain?

iv) What advice/interventions have been made available to people with stroke to help manage these foot and ankle difficulties?

#### 2.4. Research approach and study design

A qualitative research approach was undertaken using face-to-face semi-structured interviews as the primary data collection method. The intention was to obtain a pragmatic worldview. This allows the use of whatever methodological approach works best in order to answer the research question (Robson et al 2002). The questions in

this study were concerned with exploring, from the perspective of individuals with stroke, how foot and ankle impairments affected mobility and balance following stroke; and in determining what foot and ankle factors were believed to affect mobility and balance. This research design was selected because it is considered particularly useful for applied research where the objectives are set in advance, the time scale is short and there is a need to relate the findings of the qualitative work to a quantitative study (Pope & Mays, 2006).

Using semi-structured interviews allowed respondents to answer questions in as much detail as they wanted whilst allowing the researcher to seek clarification or encourage elaboration of pertinent issues (Keats, 2000). They also promoted a relaxed and informal atmosphere, which encouraged respondents to be open and honest, which may further validate information about attitudes, values and opinions.

## 2.5. Methods

This study was approved by the National Research Ethics Service, North East Committee (2/NE/0416).

#### 2.5.1. Interview Schedule development

The interview schedule (section 2.5.7 and Appendix 1) was developed by the research team (TG & JF) based on the aims and objectives of the FAiMiS study and its objectives, which were set out in section 2.3. A review of the literature and discussion with experienced clinicians also helped inform the interview schedule. In accordance with Paterson and Scott-Findlay's (2002) guidelines, three pilot interviews were carried out with stroke survivors that confirmed the interview schedule and procedure were appropriate. These pilot interviews did not highlight any issues with the schedule that required revision and so a further ten face-to-face, semi-structured, audio recorded interviews were then conducted by a single interviewer (TG) using the same schedule.

#### 2.5.2. Sampling

A purposive, maximum variation sampling strategy was used (Patton, 2002) to recruit individuals who had lived with stroke for longer than three months and reported stroke-related foot and ankle problems. Purposive sampling is widely used in qualitative research to identify and select "information-rich" individuals who are especially knowledgeable or experienced with the phenomenon of interest (Cresswell & Plano Clark, 2011; Patton, 2002). This sampling strategy was employed to ensure that the sample a) had self-reported foot and ankle impairments and b) varied in terms of age, gender, time since stroke, side affected by stroke and general level of function. Adopting such a strategy aimed at ensuring the sample reflected the wide diversity of people affected by stroke.

#### 2.5.3. Participant identification and recruitment

Participants were identified and recruited through stroke groups local to the South West of England (as identified by the Stroke Association) and through the South West Stroke Research Network (SWSRN) database. In the case of local stroke groups, the respective group coordinator was contacted by the researcher to explain the study and the recruitment strategy. If amenable, a verbal presentation of the study was given to the local stroke groups (average group size n=12) by the researcher. Following the presentation, potential participants were given a letter of invitation (Appendix 2) and/or a Participant Information Sheet (PIS) (Appendix 2) and an opportunity to ask further questions, if interested in the study.

In the case of the SWSRN database, the database coordinator forwarded the PIS to potential participants who lived within a 30-mile radius of either Plymouth University or North Devon (the researcher's clinical base). All participants registered on the SWSRN database were stroke survivors who had expressed an interest in being contacted about future stroke research. The PIS given to both recruitment streams was identical and included the researcher's contact details so the emphasis was on potential participants to contact the researcher to discuss their inclusion in the study and/or ask any further questions about the study. A sampling matrix was used during this subsequent electronic/telephone communication to purposively select participants. Those who did not meet the below criteria were thanked for their time and interest and explained the reasons.

#### 2.5.4. Participant inclusion criteria

Criteria for participant selection were developed by the research team, which comprised five physiotherapists (the researcher and four academic physiotherapists) and two academic podiatrists. To be eligible for inclusion, participants needed to:

Be ≥18 years old;

Have a confirmed diagnosis of stroke (not necessarily their first);

Be  $\geq$ 3 months post stroke;

Report perceived foot and ankle problems as a result of stroke;

Report no pre-stroke foot and ankle impairments;

Be able to converse in English at a level considered appropriate to conduct an interview;

Be willing and able to give informed consent.

#### 2.5.5. Data Saturation

Collecting data until saturation point is an essential component of qualitative research (Fusch & Ness, 2015) and attracts much debate (Mason, 2010; Fusch & Ness, 2015). Data saturation is recognised when there is considered enough information to replicate the study (O'Reilly & Parker, 2012), when additional new information is no longer being obtained, and when further coding is no longer feasible (Guest et al., 2006). That is, the point at which no new information or themes arose from the subsequent interviews. Recruitment, sampling, data collection, and data analysis were therefore undertaken concurrently, rather than as separate stages in a chronological and linear process. As data was collected and transcribed, immediate and ongoing analysis of each transcript contributed to the formation and development of a themes list and an outline thematic framework. This list and thematic framework was updated following each interview and referred to during ongoing supervisory sessions with JF, both initially and as each interview was completed. Data analysis therefore ran concurrently with recruitment and data collection so data saturation could be established using the criteria set out above. Specifying sample size at the beginning of this study was therefore neither possible nor appropriate.

## 2.5.6. Data Collection

Individual, face-to-face, semi-structured, audio-recorded interviews were employed as the primary data collection method. Interviews were arranged at a time and place considered preferable to the participant. Demographic and diagnostic information was also collected at this time, by use of a standardised written form (Appendix 3).

Informal conversation occurred prior to starting the interview with the aim of placing the participant at ease and offering them the opportunity to ask further questions. Participants were reminded that their participation was voluntary, and that all interviews would be recorded, transcribed verbatim and anonymised. At this point written informed consent was gained. Twelve participants were interviewed at home and one at their local community hospital in a private room. The interviews were carried out between March and June 2013.

#### 2.5.7. The Interview Schedule

An interview schedule (Appendix 1) with examples of potential prompts was used to guide the conversation and encourage disclosure and elaboration of thoughts and feelings relevant to the study objectives. It was conducted with sufficient flexibility to enable participants to raise issues they considered important. Using an interview schedule reduces the (inevitable) influence of interviewer effect, ensures that all areas/topics have been explored and ensures the core set of questions remain consistent across interviews (Keats, 2000). An outline of the interview schedule is provided in table 2.1.

Interviews lasted on average fifty minutes (range 40 to 65 minutes) and on one occasion a third party was present during the interview although they did not contribute verbally. Thirteen interviews were carried out, by which time data saturation had been reached in that no further themes were arising from the data. This was confirmed through review and discussion by a second party (JF).

- 1. Could you tell me about how you have been affected by your stroke?
- 2. Could you tell me how your stroke has affected your foot and ankle?
- 3. Do you feel any of these foot and ankle problems affect how steady you feel on your feet?
- 4. Do you feel these problems affect your walking?
- 5. Could you tell me whether you feel your foot and ankle problems have affected any other aspects of your life?
- 6. Could you tell me about any advice or interventions you have been given to help manage the problems with your foot and ankle?

**Table 2.1**. Outline of the Interview Schedule. See Appendix 1 for full Schedule.

## 2.5.8. Data Analysis

#### 2.5.8.1. Framework analysis

The Framework approach sits within a broad family of analysis methods often termed thematic analysis or qualitative content analysis (Gale et al, 2013). It is a qualitative method of data analysis that is suited for health research (Gale et al, 2013); seeking to draw descriptive and/or explanatory conclusions clustered around themes (Ritchie & Spencer, 1993). It is especially adapted to research that has specific questions, a limited time frame, a sample in mind (i.e. stroke participants with foot/ankle impairments) and *a priori* issues (e.g. impact of impairments) (Srivastava & Thomson, 2009). Although framework analysis may generate theories, the prime concern is to describe and interpret what is happening in a particular setting (Ritchie & Spencer, 1993). The framework method is not aligned with a particular epistemological, philosophical or theoretical approach. It is a flexible tool that can be adapted for use with many qualitative approaches that aim to generate theomes (Gale et al, 2013).

There are several key features of the framework analysis approach as outlined by several authors (Smith & Firth, 2011; Srivastava & Thomson, 2009; Ritchie & Spencer, 1994; Gale et al, 2013). Firstly, it is heavily based in and driven by the original accounts and observations of the people it is about. For example, verbatim quotes are used to guide and inform theme generation. Secondly, it is dynamic and open to change, evolving as more data is collected and analysed. The use of a "qualitative spreadsheet" or coding matrix, allows ongoing review and revisiting of themes as data emerges. Thirdly, it is comprehensive in that it allows a full rather than partial or selective, review of the material collected. Large data sets can be managed in order to provide a holistic, descriptive overview. Finally, it is transparent in that raw data is retrievable and accessible to others so the analytical process and interpretations derived from it can be viewed and judged by people other than the primary analyst. This enabled the researcher to explore data in depth while simultaneously maintaining an effective and transparent audit trail, which enhances the rigour of the analytical processes and the credibility of the findings (Ritchie & Lewis, 2003).

The researcher transcribed all but one of the interviews verbatim and field notes were taken during each interview. In one case, expressive dysphasia made transcription difficult and hence, in line with recommendations set out by Lloyd et al, (2006) the audio recording and field notes were used for analysis. The transcribed interviews were coded, grouped into sub-themes, summarised into main themes, and charted and interpreted using a framework approach utilising software package QSR NVivo 9.2. Analysis of the data followed several systematic stages to ensure transparency as described by Ritchie and Lewis (2003) and outlined below:

- Familiarisation: familiarisation of the researcher with the transcripts collected (reading and re-reading);
- 2) Identifying a thematic framework: recognising emerging themes;
- Indexing: identifying portions or sections of the data that correspond to particular themes;
- Charting: arranging specific pieces of data that were indexed in the previous stage in charts of the themes;
- 5) Mapping and interpretation: analysing the key characteristics as laid out in the charts. Reflecting on the original data and analytical stages to ensure participant accounts are accurately presented and to reduce the possibility of misinterpretation; interpreting/finding meaning and explaining the concepts and themes; seeking wider application of concepts and themes

## 2.5.8.2. Ensuring Rigor

Trustworthiness and credibility of the interpretation of the data were optimized through several strategies. Each of the pilot interviews were transcribed in turn, after which analysis and discussion was held between the PhD researcher at supervisory sessions with JF. A coding reliability check was also completed on the three pilot interviews in these sessions and was deemed acceptable (Miles & Huberman, 1994). As further interviews were undertaken, regular meetings were held which allowed peer de-briefing and review, which ensured decisions could be evaluated and defended (Cresswell, 2009). It was felt that using participant validation (i.e. returning to study participants) by asking them to validate analyses was not appropriate. This approach can be time consuming, may result in participants' wanting to modify their initial responses, and can pose problems when presenting large volumes of detailed data to likely non-academics (Burnard et al, 2008).

## 2.5.8.3. Reflexivity

The researcher's own personal experience and situation is recognised as having the potential to influence the research process and the manner in which the data were interpreted (Carpenter and Suto, 2008). Cresswell (2009) highlights the researcher as situated within the research itself, not separate from it. In this study, the researcher engaged in an ongoing process of reflexivity. This was particularly important given their professional role as a neurological physiotherapist. Decisions were therefore recorded and reflected upon in a research diary, from where they were challenged and justified within supervisor de-briefing sessions. Supervision sessions were used to reflect on potential interviewer influence, to ensure questions/prompts were not too leading through checking prompts used, and seeing where prompts could have been extended.

#### 2.5.8.4. Study Quality

The COnsolidated criteria for REporting Qualitative research (COREQ) (Tong et al, 2007), was retrospectively used to evaluate the reporting of important aspects of the study such as: research team, study methods, context of the study, findings, analysis and interpretations. Each item in the 32-item checklist was met by this study.

#### 2.6. Results

#### **2.6.1.** Participant characteristics

Participant names were replaced with pseudonyms to ensure confidentiality but also to maintain an element of personality to each participant. Thirteen participants were interviewed. As intended, these covered a wide range of demographic and clinical characteristics. Six were female with a mean age of 66 years 6 months (SD=12 years 2 months; range 38-78 years). The mean time since stroke was 4 years 4 months (SD=6 years 2 months, range 4 months to 20 years). Seven participants had experienced a right stroke and six a left stroke. Levels of mobility ranged from being independently mobile without walking aid through to requiring maximum assistance of one person with all transfers. Ten participants reported falling since their stroke (table 2.2).

Participant	Gender	Age	Time Since Stroke	Hemi Side	Level of walking ability/use of walking aids	History of falls
			Years (y) and months (m)			
Larry	Male	78	10 y 8 m	R	Independent with walking stick	Y
Margaret	Female	70	1 y 1 m	L	Transfers only, quad stick	Y
Neil	Male	72	1 y 6 m	L	Independently mobile indoors; supervision outdoors; walking stick	Y
Barry	Male	70	20 y 1 m	R	Independent with walking stick	Y
Mark	Male	56	5 y	L	Independent no aid	Y
Paul	Male	62	1 y4 m	R	Independent no aid	Y
Jane	Female	76	1 y 5 m	L	Transfers only, quad stick	Y
Marion	Female	69	6 m	L	Independent with walking stick	Y
Jim	Male	78	4 m	R	Independent no aid	Ν
Rebecca	Female	38	6 y	L	Independent no aid	Y
Nigel	Male	42	11m	R	Independent no aid	Ν
Rose	Female	78	1y7m	R	Independent with walking stick	Ν
Sandra	Female	76	9m	R	Independently mobile indoors; supervision outdoors; walking stick	Y

Table 2.2. Participant Demographics (names pseudonymised); R=right, L=left

# 2.6.2. Themes

Three main themes were derived from the data, reflecting the underlying objectives of the study (Fig 2.1). These themes were termed 1) *Impact* which described the nature of impairments and how they contributed to mobility and balance; 2) *Standing Out* 

which described feelings of standing out, perceptions of disability and a desire to be "normal", and 3) *Help* which described the nature and extent of help and advice received.



Fig. 2.1 Schematic of themes and key sub themes

# 2.6.2.1. Theme 1: Impact; the nature of impairments and contribution to alterations in mobility and balance

Eleven of the 13 participants provided in-depth descriptions of the nature of the foot and ankle impairments they experienced as a direct result of their stroke. Impairments affected the toes, foot and ankle and included weakness, lack of control, altered sensation, altered tone/spasticity, pain, stiffness, and swelling.

All participants believed foot and ankle impairments contributed substantially to difficulties with mobility, balance and falls. Pain (n=4), tone/spasticity (n=4), weakness (n=11), lack of control (n= 10), and impaired sensory inputs (n= 11) were the impairments most commonly associated with mobility difficulties. Participants highlighted the marked impact these had on community mobility:

"Cos I've got this lack of feeling there, I'm a bit wary. Especially, if it's rough ground because I have to look down continually to see where I'm walking. Crossing the road is a lottery. I can't look at the traffic and look down at the road at the same time. That is a bit of a problem. I've got to be very, very careful". Barry

Difficulties with lack of volitional motor control and the unpredictable nature of this

control at the ankle and foot meant foot placement could also be a lottery, which was

likely to increase falls risk:

"...I struggle because I don't know which way my foot is going to drop. If it drops flat then I can walk Ok but if it drops sideways, then my ankle rolls over on itself and I'm liable to fall over..." Mark

The vital role of the toes in maintaining equilibrium was also reported:

"...normally you press down with your toes don't you? I don't think my toes will go down. Cos like your toes grip to stop yourself from falling forward..." Margaret Some, however, perceived the lack of control in the toes was not due to weakness, but

more to do with the toes "having a mind of their own":

"...I didn't even know they [the toes] could do that. So they bunch up, they cramp, so they have moments of calm but they've got a mind of their own. I don't know what causes that. That glamorous spasticity word isn't it? Rebecca

Tone and spasticity, its presence being predominantly in the toes and foot, impacted

on the role the foot and toes play in maintaining balance:

"...All the time I've got tension in the foot, it never feels relaxed. There's so much more tension in whatever that foot has to do. It can't do anything naturally. If that foot is in its clamped up position then it's this balance thing again because I think I'm not using my foot as a base that sort of balances..." Paul

Altered sensory inputs were described by all but two participants, with wide variations

in both the type and extent of sensory impairments. For example, people described

altered feelings of temperature (n =2), reduced feeling/feedback from the foot/ankle (n

= 8), the foot and ankle "just not feeling right" (n=4), through to "the foot doesn't feel

it belongs to me" (n = 3). Most (n= 10) highlighted the difficulty associated with being

unable to accurately discriminate or confidently detect the floor surface and foot

position with an increased risk of falls especially on rough or uneven ground:

"...it is lack of feeling in the foot and that it doesn't tell me if I am on a flat surface or an inclined surface or tipping my ankle over, I haven't got so much feeling coming back to my brain..." Larry

Some people clearly attributed altered sensation with impairments in balance

highlighting the inextricable link between sensory and motor function:

"...I've got no feeling in the foot so I can't feel, I can't get my balance properly, if that makes sense. You know, when your foot is working properly, you can feel the ball of your foot and your toes, and by using your toes and that, you go push yourself to keep your balance..." Mark For others sensory impairment affected walking pattern, community ambulation and the increased need for concentration:

"...When I put my foot down and I don't get any response, that no feeling comes back that I've got it down and therefore I hesitate to move the other foot forward. When I think about it, it's ok, I can walk in a fairly straight line, but when I get distracted by something else, that's when I stagger... so much so that a policeman stopped me once and smelt my breath..." Larry

All participants felt some restriction on where they could go or were cautious and

thoughtful about where they could go, directly as a result of their foot and ankle

problems. The biggest restriction on mobility, which was mentioned by all but one

participant (who was not mobile outdoors), was being able to manage rough/uneven

and unfamiliar terrain:

"...I have to be careful where I'm walking... because if it's uneven or you know rough or anything like that. I'm conscious that I'm likely to sort of trip on things because this wretched foot doesn't lift up, very often it doesn't lift. It flops and it drags..." Jim

Conversely, the same participant had a very different perspective when it came to

walking in a different environment:

"I do know that I'm very happy where I know that the surface is flat, say walking through the hospital on Wednesday going to the gym, it's alright" Jim

The presence of pain in the foot and ankle was also highlighted as a problem in a third

of respondents (n=4). For all respondents with pain, it was sometimes sufficient to stop

them from walking at all:

"...I get pain in my foot more than anywhere. It feels like walking on glass or it's burning. It's the oddest thing. I avoid walking." Rebecca

Increased stiffness through the foot and ankle was associated with increased effort

with one participant describing his ankle joint as if it was "rusted up":

"...it's very stiff and very slow. It's hard work basically to do it [move the foot]. I suppose the joints have rusted up with the stroke..." Barry

Whilst swelling was reported in four participants, they did it not relate it to any

functional impact, and did not appear to be concerned by its presence:

"...My ankle actually swells up quite easily after I've done any exercise. It doesn't seem to affect me. But that's something none of the doctors have ever said that's going to be a problem, they've always sort of said that's to be expected so I've never taken any notice of it and I don't' think that impairs my movement..." Barry

# 2.6.2.2. Theme 2: *Standing Out*; "I felt like I had three heads"

All but two participants described how they felt their foot and ankle impairments

made them "stand out" from others. They reported feeling very conscious of "being

disabled", expressing a desire to "be normal". A number of participants described how

acutely aware they had become of their physical appearance to others. This was often

manifested by their embarrassment about the type of footwear they had to wear, or

the abnormal way they walked because of their foot and ankle impairments:

"... when I was walking towards someone and my foot would be turning inwards and it looks, well it doesn't look very nice... It's having the confidence in people looking at me and not seeing that I am disabled..." Mark

For one participant, it was about wanting to make any orthotic as inconspicuous as

possible so she did not appear disabled:

".... so hence the orthotic. But I didn't want anything more obvious than this. I've been offered something that will keep it so rigid which is fine if you don't mind looking disabled. Which I do.." Rebecca Whereas for others, wearing footwear out of context created feelings of social unacceptability resulting in both embarrassment (Paul) and resentment/frustration in Rebecca's case:

"Having to wear trainers with everything makes me feel as if, like a duck out of water you know. I don't feel naturally acceptable in different situations. I went into the hairdressers the other day and they knew that I had had a stroke but I went in with these [trainers] on and he said 'cor crikey, you're alright now you're going out for a run aren't you?'" Paul

"...I can only wear flat shoes for ever more, so that is the Devil's work! It is the Devils work!! It's huge. Flat shoes...?!! They're all boring. Completely boring. I mean it's hideous. It was up there with one of the worst things that can happen. It was in my top five, never wearing heels again. Absolutely vile. Who wears flat shoes when they dress up? Nobody!..." Rebecca

Others however found ways of adapting to the "forced use" of particular

footwear as a result of their foot and ankle impairments:

".... I can't wear high heels when I go out. No matter what clothes I wear, I've got to wear trainers. I would like sometimes to put a different pair of shoes on. I'm going to a wedding soon so I don't really want to wear trainers to that. But I'll put silk ribbons on them if I do..." Margaret.

Concerns around feeling conspicuous and a loss of normality were often related to

the type of footwear they had to wear as a consequence of their stroke:

"...I don't want shoes that look like they've been made for a purpose. You know I want to wear what everybody else is wearing. I want to fit in. I've never ever wanted to fit in but I suppose with this you do want to fit in. You want to be in the realms of normal because you know that there is an element of abnormality." Rebecca

This was also reflected with respect to comparing oneself against peers in relation to

walking and functioning:

"...one of my friends was walking in front of me and I was looking at her thinking now why can't I walk like that. She was striding, she's older than me, and she was there striding along and I'm thinking oh it
must be lovely to be able to walk like that. There's me struggling along behind." Jane

However, there was a tension between the disadvantages felt about the appearance of

orthotics and the functional gains that could be made by wearing them, which often

promoted reassurance and confidence:

"...with the orthotic I've got now, it stops the foot from turning in and stops it from dropping. So every time I lift my foot, I know it's going to go down flat. So it makes my walking a lot stronger and makes me a lot more confident in my walking. I hardly fall over at all these days...." Mark

# 2.6.2.3. Theme 3: Help; Specific advice & interventions received

The overriding sentiment by the majority of participants was that advice and/or

interventions had been made available to address their gait and mobility problems,

although few participants referred to a specific focus of this intervention on the foot

and/or ankle. Separating "generic" advice/intervention that addressed stroke

impairments per se from specific foot and ankle-focussed advice/intervention

appeared particularly difficult for those participants whose stroke caused widespread

impairments. All but three participants received input from physiotherapy. The

predominant focus appeared to be on gait re-education and gross motor performance

of the lower limb although there was occasionally some specific foot/ankle advice:

"...the thing that I remember most about everything was the heel and toe thing that the physio talked about...and the keeping of a regular stride... rather than dragging this foot along after me..." Jim

Some recalled that specific concerns about their foot and ankle function were not addressed:

"....Nobody's particularly picked up on the toes scuffing I don't think. They were more concerned about stopping my knee flicking back..." Marion Whereas others chose not to report their concerns to their attending clinician:

"...I've never really pointed it out. I haven't really said to anyone "oh look, my toes are curling up, why?" Paul

Five participants had either trialled or were regular users of ankle-foot orthoses (AFO)

with the physiotherapist being the main referrer into a specialist orthotic service:

"She took me to [the orthotist] and showed him what was happening with the foot and he made me the boot" (AFO) Margaret

Only one participant reported being seen by a Podiatrist who:

"....showed me my options basically. Do you want this or this? This will do x-y-z. What do you want it to do? He said you can have something that keeps your foot very static...a rod up the back of your leg basically which I just couldn't bear....but I wanted something that's subtle..." Rebecca

Those that had been issued with off the shelf AFO's by the physiotherapist were less

successful:

"It's supposed to keep my leg square to the shoe. But it doesn't seem to make any difference". Neil

Provision of an AFO made a significant difference to some participants with one

participant purchasing the AFO via the internet as the "off the shelf" versions were

uncomfortable:

"...with the orthotic I've got now, which I bought off the internet, erm it stops the foot from turning in and stops it from dropping. So every time I lift my foot, I know it's going to go down flat. So it makes my walking a lot stronger and makes me a lot more confident in my walking. I hardly fall over at all these days..." Mark

Although there were some perceived repercussions of frequent use of the AFO:

"The only thing I've found is that my foot is weaker than it was. I think that's because I wear the orthotic now, it means my muscles don't move so much so they are a lot weaker than they were..." Mark

Interestingly, despite all participants reporting altered sensory input, some very

significantly so, none specifically reported any sensory re-education based

intervention.

Functional electrical stimulation (FES) was only used with one participant specifically at

the foot and ankle although it was reported that this was with limited success:

"I was given a FES to wear for my foot. Which when I went to lift my foot it fired a pulse which made my foot straighten out instead of inverting. So it was going down more flat which was good for me, but I just didn't like the FES. I didn't like the feeling of the pulse going through my leg..." Mark.

# 2.7. Discussion

The results of this study provide a unique insight into the nature and impact of foot and ankle impairments on mobility and balance from the perspective of the stroke survivor. They highlight the wide ranging and significant impact of these impairments on stroke survivor's everyday lives and highlight areas for service development and future research. Impairments such as pain, reduced sensation, weakness, and lack of volitional control in the foot and toes were most notably reported to impact on functional mobility. The results of this study were broadly in line with a recent survey of people with stroke. Bowen et al (2016) surveyed 145 people with stroke and found 43% of respondents reported foot problems. Weakness was reported most frequently, followed by reduced sensation, and pain. Almost a third of all respondents also reported that foot and ankle problems influenced balance with a higher incidence of foot problems in those who reported falling (Bowen et al, 2016). In this study, pain in the foot appeared to have a profound effect on mobility for some, who chose to entirely avoid walking when pain was present or drastically shorten the time spent on their feet. Descriptors of pain suggested symptoms of central or neuropathic origin rather than mechanical, as pain was not necessarily reported in response to movement, but appeared to reflect disordered sensory processing. The average time since stroke (of those four people who reported pain) was two years three months, suggestive of chronic rather than acute pain. Neuropathic pain syndrome, which is a direct consequence of ischaemic damage, is especially challenging to study because it usually observes an unpredictable latent period, which may be up to 18 months between stroke onset and development of pain or discomfort (Anderson, 1995). Our study suggests that pain can still have a significant impact on mobility many months or even years after formal discharge from stroke services, and because of the apparent central nature, the pain may not follow predictable patterns or periods. Whilst pain syndromes may be poorly understood, this study further adds to existing qualitative work which highlights the significant effect of pain per se on quality of life after stroke (Jönsson, 2006) and functional independence (O'Donnell, 2013). The need for clinicians, especially those involved with community-dwelling stroke survivors to be aware of the potential latency and impact of foot pain following stroke, is therefore crucial.

Apparent tactile sensory impairment of the foot and proprioceptive deficits at the ankle were reported equally by participants, with some experiencing a combination of these two sensory impairments supporting observational studies of sensory loss (Tyson et al, 2008; Connell et al 2008). Loss of sensory feedback from the foot was reported frequently. Particular concerns included not knowing the position of the foot in space,

having a lack of awareness of what it was doing or difficulty discriminating the type and orientation of the supporting surface under foot. These impairments were reported to lead to difficulties with walking patterns, stepping up curbs, maintaining balance, adapting to different walking surfaces and gradients, co-managing the attentional demands of the environment and fear of falling. This study suggests that mobility and balance are affected by foot and ankle sensory impairments in stroke as has been established in MS (Cattaneo, 2009), peripheral neuropathies (Ward et al, 2016; Courtemanche et al, 1996) and to an extent, stroke (Hsu et al, 2003; Tyson et al, 2013a). It further adds to recent qualitative work, which highlighted that somatosensory impairments are of concern to stroke survivors because of the impact on function, particularly when they return home (Connell et al, 2014). It also highlights the potential contribution of lower limb somatosensory impairment to reduced functional community ambulation which is suggested as a key component of community integration and "getting back to normal" (Lord et al, 2004; Chau, 2009). The need to investigate the extent and nature of lower limb somatosensory impairments in people with chronic stroke is clear, as evidence after stroke is largely limited to acute/sub-acute phases (Connell et al, 2008; Tyson et al, 2008, 2013), the upper extremities (Doyle, 2010). The effect of foot, ankle and lower limb sensory impairment is not fully understood (Kunkel et al, 2017; Wutzke et al, 2013).

Whilst sensory impairment is suggested as a co-factor in disability and recovery, some authors have demonstrated that it is not an independent factor when strength or motor performance are included (Feys et al, 2000; Tyson et al, 2008). Lack of automatic and volitional motor control of both toes and ankle due to weakness and spasticity, highlighted issues with catching toes during swing phase, lateral ankle instability during stance phase of gait, static standing balance, and multi-directional responses to perturbation and distraction. Worries about tripping, negotiating uneven or rough terrain, walking slowly, and an increased fear of falling were common. Such worries affected community ambulation and integration, quality of life and return to independence. Foot and ankle impairments appear to contribute to these factors, which are commonly reported by patients after stroke (Moeller & Carpenter, 2013; Wood et al, 2010).

Participants conveyed the feeling that their deficits in motor control and sensory awareness could be relatively well managed in predictable, flat, and quiet environments with most difficulties arising when the environment became unfamiliar, uneven or busy. Rough ground, busy streets and traffic caused challenges that did not necessarily occur indoors or during clinic-based therapy. These findings support previous research highlighting the role and impact of environmental factors (Lord et al, 2006; Shumway-Cook et al, 2002) and cognitive motor- interference (Plummer et al, 2013) on mobility and disability and add credence to a shift in therapeutic focus from clinic-based gait retraining to goal-directed and task specific training within variable environments (Park et al, 2011). They may also part explain why large proportions of independently mobile stroke survivors either cannot or are reluctant to mobilise without supervision in the community (van de Port, 2008).

Foot and ankle impairments following stroke were associated with perceptions of standing out, feeling disabled, and a loss of "normality". The impact of stroke on survivors is repeatedly described as "loss" in the qualitative literature, with the significance of reduced functional ability being explained in terms of loss of activities,

abilities, personal characteristics and independence and a desire to be normal again (McKevitt et al, 2003). This has also found to be the case in other long-term neurological conditions (Grose et al, 2012). Within the context of this study, these feelings were predominantly driven by footwear choices (or lack of), the nature of participants' walking pattern because of their foot/ankle impairment and the need to wear an AFO. Feelings regarding footwear and the use of an AFO tended to be stronger in the female participants who reported feeling self-conscious because of both the appearance of the AFO and the resultant loss of footwear choice because of the need to accommodate an AFO. The impact of footwear or lack of footwear choice has been established in other non-stroke populations (Naidoo et al, 2011) yet despite its importance, footwear advice following stroke is minimal (Ng et al, 2010). All of these factors contributed to people feeling self-conscious about their physical appearance, which has shown to be a strong predictor of general self-esteem (Howes et al, 2005). Low self-esteem following stroke is not uncommon and can influence participation restriction (Ahuja et al, 2013; Chau et al, 2009).

Conversely, whilst some participants reported that the presence of an AFO may reinforce "abnormality" or evoke feelings of disability, the *effect* of wearing one was to "normalise" gait patterns and thereby improve perceived physical appearance. This suggests that the aesthetics of orthotics and adaptive footwear, as well as their therapeutic objective, need to be taken into account when prescribed by health professionals. It emphasises the need for health-care professionals to be aware of how distressing negative perceptions of others can be for people with stroke.

Our study asked participants to highlight what advice and interventions they had received with respect to their foot and ankle problems. Whilst most had received input from a physiotherapist, the participants reported the focus of that input tended to be on generic gait re-education, motor retraining and strengthening, in the context of the gross performance of the lower limb. All but two participants reported somatosensory impairments, yet none specifically recalled receiving sensory retraining. Current stroke guidelines (RCP, 2016) pay relatively little attention to (lower limb) sensory loss after stroke compared to motor loss, reflecting the limited evidence base regarding its impact as an independent impairment. Recent qualitative work has identified somatosensory impairments as a concern for people in the chronic phase of stroke, although articulating the impact of sensory loss in a non-motor context was difficult (Connell et al 2014). Somewhat inevitably, stroke rehabilitation remains focussed on addressing foot drop and motor recovery (RCP, 2016; Galvin et al, 2009). Clinical convention and therapist report (Pumpa et al, 2015) suggest sensory retraining is more fastidiously administered to sensory impairment of the hand. Furthermore, sensory impairments are not necessarily thought of by people with stroke as under the physiotherapist's remit (Connell et al, 2014). There is a dearth of evidence applying the learnings from the hand to the foot (Lynch et al, 2007; Morioka et al, 2003; Hilier & Dunsford, 2006; Wutzke et al, 2013).

Only one participant reported being seen by a podiatrist, regarding the prescription and provision of orthotics. Podiatry services or podiatrists are not referred to in the current stroke guidelines (RCP, 2016). This may offer some explanation as why, despite its potential importance to people with stroke, few receive advice about foot care or footwear (Ng et al, 2010). Only one participant had trialled FES for foot drop

suggesting its use may be underutilised, despite recommendations (RCP, 2016) and stroke survivors reporting an overall preference for FES over AFO's (Bulley et al, 2011).

## 2.7.1. Study Strengths

The research aim was to explore patients' perceptions regarding how foot and ankle impairments affect their walking, their balance and their functioning. The study's utilisation of semi-structured interviews allowed the use of conversation, discussion, as well as questioning, to provide insight into the real issues people with stroke face because of foot and ankle impairments. The interview format was intentionally designed to enable a natural exploratory conversation, which, as a result, provided both depth and quantity of rich data. It allowed participants to elaborate and explain how their impairments contributed to the real issues they faced because of their stroke. Themes were generated from verbatim transcriptions recognising the importance and significance of the language used by participants; essential in gaining insight into their perceptions and opinions around how foot and ankle impairments affect their functioning, their lives. In the author's opinion, the use of "patient voice" through semi-structured interviews provided rich and original data to construct a research narrative. It hopefully gives this study, and the subsequent quantitative studies, an invaluable, real quality.

# 2.7.2. Study limitations

This study has several limitations. Firstly, the participants' enthusiasm to provide information that would satisfy the researcher, who was a physiotherapist, may have led to potential exaggerated and/or inaccurate descriptions. Whilst most participants were informed of the clinical background of the interviewer, it was emphasised at the beginning of the interview that responses would be anonymous and would not affect any current or future clinical care. Potential interviewer influence was recognised, as described in the reflexivity section, with a research diary, case notes and supervision sessions used to check phrasing of questions and prompts used, for example. Secondly, the majority of interviews were conducted with stroke survivors who were, on average just under four years post-stroke and were no longer receiving rehabilitation, so recall of treatments received may have been inaccurate. Stroke is known to affect memory processes, which may confound recall of treatment and rehabilitation. Thirdly, this study purposively recruited community-dwelling adults with self-reported and stroke-related foot and ankle impairments and therefore reflects the experiences of those with these specific impairments rather than the wider stroke population.

This study formed part of an existing programme of research so the extent to which its design and approach, and in particular the interview schedule, could be tailored specifically to reflect the sensory narrative of this thesis was limited. Whilst the study's breadth of focus provided insight into the impact of foot and ankle impairments, within the context of this thesis, retrospective changes might have been advantageous. For example, a greater understanding of the meaning of experiences because of somatosensory impairments may have been gained through utilising an alternative qualitative analysis; an Interpretative Phenomological approach to analysis for example, may have provided this. Further, the inclusion of objective sensori-motor measures might have provided greater descriptive detail of the study participants and given their subjective reports further context with regard to motor and somatosensory ability.

# 2.8. Conclusion

In conclusion, this qualitative study highlighted that, from the perspective of people with chronic stroke, foot and ankle impairments such as pain, altered somatosensory input, and weakness may substantially contribute to problems with community ambulation, balance and fear of falling. It suggested that specific foot and ankle impairments might also negatively contribute to perceptions of physical appearance and self- esteem. Therapeutic management approaches within clinical practice appear to focus mostly on the gross performance of the lower limb with little emphasis on the specific assessment or treatment of the foot or ankle.

This study has provided some insight into the experience of people with stroke with regard to the impact and nature of foot and ankle impairments, thereby helping to inform assessment and management within the clinical setting. Particularly insightful was the extent to which somatosensory impairments a) were present in the chronic phase post stroke b) significantly affected several aspects of function and c) were not seemingly targeted by rehabilitation approaches. This qualitative work supports recent work (Bowen et al, 2016; Wutzke, et al, 2013; Connell et al, 2014; Tyson et al, 2013) highlighting the need for further investigation into the nature, prevalence and severity of lower limb somatosensory impairment post stroke.

3.0. Study 2: The prevalence, distribution and functional importance of lower limb somatosensory impairments in chronic, ambulatory stroke participants: a cross sectional observational study

#### 3.1. Chapter Overview

The qualitative work in Chapter 2 explored the nature and impact of foot and ankle impairments on balance and mobility from the perspective of people living with stroke. Several impairments were identified, with one of the key concerns focussing around sensory deficits. Participants reported difficulties with knowing the position of the foot in space, having a lack of awareness of what the foot was doing and difficulty discriminating the type and orientation of the supporting surface under foot. These impairments, it was felt, contributed to difficulties with walking, stepping up curbs, maintaining balance, adapting to different walking surfaces and gradients and generally getting out-and-about. It highlighted that sensory impairments to the foot, and the whole of the lower limb, impacted on functional mobility, incidence of trips, balance and falls efficacy in an ambulatory stroke population living at home. Whilst study 1 demonstrated that the sensory experience of pain was also perceived by participants to contribute to walking and mobility difficulties, the required volume of work to incorporate post-stroke pain as an aspect of somatosensation was beyond the scope of this thesis. The potential severity, and complexity of post stroke pain, merits a focussed investigation and future consideration. This chapter presents the second study of this thesis; a cross sectional observational study in which lower limb somatosensory performance is quantitatively investigated in a cohort of 180 chronic, ambulatory stroke participants. The relationship between somatosensation and its relevance to aspects of functions such as balance, gait speed and falls is also explored.

### 3.2. Introduction

The disabling impact of stroke on factors such as walking ability, balance and falls have for the large part been most closely associated with deficits in lower limb motor output and motor control (van Swigchem et al, 2013; Kluding & Cajewski, 2009; Winward et al, 1999a). However, to successfully adapt to external cues or altered walking conditions, changes in plantar pressures, lower limb positions and loading must be detected, relayed and integrated by the Central Nervous System (CNS) (Ackerley & Kavounoudias, 2015; Zehr et al, 2014; Chisholm et al, 2016; Bradford et al, 2016). Lower limb somatosensory impairment has implications on walking ability, balance and falls, yet the prevalence and distribution of sensory impairments in community dwelling stroke has not been established. Further, the relationship between post-stroke lower limb sensory impairments and factors such as gait, balance and falls is poorly understood, particularly once patients return home.

Most studies have investigated the prevalence, distribution and functional impact of sensory impairment in hospitalised stroke patients in the acute/sub-acute phase (i.e. within two to four weeks post stroke) and/or the upper limb (Tyson et al, 2013; Tyson et al, 2008; Connell et al, 2008; Meyer et al, 2016). Prevalence figures indicate that sensory impairments, in the acute phase, range from 11% (Moskowitz et al, 1972) to 85% (Kim & Choi-Kwon, 1995), although it is generally suggested that c.50-67% of stroke patients in the acute phase of stroke have impairment to one or more somatosensory modality (Carey & Matyas, 2011; Tyson et al, 2008; Connell et al, 2008). However, acute somatosensory impairments account for just 46% of the variance in lower limb tactile sensation and 51% of proprioception at six months with changes in somatosensory performance variable and unpredictable both within and

between patients (Connell et al, 2008; Winward et al 2007). Few studies have investigated sensory impairments into the chronic phase of stroke (i.e. >6 months post stroke) although, as with acute/sub-acute populations, prevalence levels vary widely. Schmid et al (2013) reported tactile deficit to pin prick in the feet of 7% (n= 12/160) of stroke patients (time since stroke [TSS] =82 months, SD =101 months). Robinson et al (2011) in their cohort of 30 chronic stroke (time since stroke=39 months; SD=26 months) found 13% had impaired proprioception in the great toe. Conversely, Yalcin et al (2012) found 70% of their cohort of chronic stroke (n=14/20; TSS=27 months; SD=44 months) had tactile and /or proprioceptive deficits in the hemi-paretic foot/ankle. The prevalence of lower limb somatosensory impairments into the chronic phase of stroke is therefore unclear.

Consequently, clear and compelling evidence linking lower limb measures of somatosensation with measures of patient function in chronic stroke is yet to be established and so the contribution of somatosensory input to ongoing functional (dis)ability remains equivocal. Robinson et al's (2011) study also investigated the physical factors related to community ambulation and falls in their cohort of 30 chronic stroke. Tactile sensibility and movement detection sense at the 1st metatarsal joint was not significantly associated with community ambulation ability or falls. Similarly, Lee et al (2015) in their cohort of 46 chronic stroke participants (TSS = 60 months; SD=36 months) found no significant associations between community ambulation levels and lower limb somatosensation. Schmid et al (2013) found lower limb sensory loss as measured by the National Institutes for Health Stroke Scale (NIHSS), was not associated with falls risk in chronic ambulatory stroke. Recently, Tyson et al (2013) pooled the lower limb sensory-motor data of 459 acute/sub- acute

stroke patients. They found lower limb proprioception and tactile sensation, combined and independent, did not significantly predict mobility (p=0.12) or balance (p=0.07) but did significantly predict ADL's (p=0.04). Conversely, Hsu et al (2003) found moderate and significant correlations between lower limb sensation scores (tactile and proprioception) and gait velocity (r=0.40; p<0.05) in their cohort of 26 chronic stroke (TSS=10 months; SD =12 months).

With more people surviving stroke and experiencing its long term consequences (Crichton et al, 2016), a greater understanding of the factors that influence walking ability, balance and falls in the chronic stroke population is needed. Doing so would help inform targeted and appropriate rehabilitation service provision with the aim of minimising disability for this relatively understudied population. The prevalence and distribution of lower limb sensory impairment in chronic, ambulatory, community dwelling stroke survivors is not clear. More importantly, the impact and predictive value of foot, ankle and lower limb sensory impairment on walking ability, falls, and balance has yet to be established in this population.

# 3.3. Aims and objectives

The aim of this study was to investigate lower limb sensory impairment in chronic, community dwelling, ambulatory stroke survivors. The objectives were to:

- 1) Establish the prevalence, type and distribution of different lower limb somatosensory impairments in ambulatory chronic stroke survivors
- Compare chronic stroke patients with age- matched controls in their lower limb somatosensory performance

- Establish the association between lower limb somatosensory impairment and function in chronic stroke. Specifically:
  - a. the strength of correlation between lower limb somatosensation and functional measures of walking speed, balance ability, falls incidence or fear of falling and to establish
  - b. the extent to which somatosensation predicts functional ability when other potentially confounding variables are accounted for

The primary hypothesis is that, in line with the acute/sub-acute literature, (Meyer et al, 2016; Tyson et al, 2013; Connell et al, 2008; Tyson et al, 2008), lower limb sensory deficits will be common in chronic stroke. Secondly, based on the findings from the qualitative study (Study 1, chapter 2), lower limb somatosensory impairment will be moderately-strongly associated with functional ability, particularly dynamic balance, falls and fear of falling and perceived walking ability. Further, in line with previous findings (Mullie & Duclos, 2014; Qaiser et al, 2016; Kavounoudias et al, 2001; Qui et al, 2012) it is hypothesized that proprioception will be a stronger predictor of dynamic activities such as walking, falls and dynamic balance whereas tactile sensation will be more predictive of static balance and postural sway.

# 3.4. Methods

## 3.4.1 Research approach

This quantitative, cross-sectional observational study involved a one-off assessment of multiple foot and ankle impairments and function. The sensory data that is informing this study was collected in tandem with several other clinical measures of foot and ankle impairments and function, as part of a multi-centre, cross sectional

observational study. This large study represents the "Foot and Ankle impairment affecting Mobility in Stroke" (FAiMiS) study which involved a multidisciplinary collaboration of physiotherapists and podiatrists from the Universities of Plymouth, East London, West of England and Brighton. The clinical measures of foot and ankle impairment assessed included muscle strength, pain, range of movement, spasticity, static foot posture, dynamic foot loading and sensation. The use of additional sensory measures and/or alternative mobility measures was thus limited due to pragmatic considerations. Assessment time was suggested by the FAiMiS steering committee to not exceed 1 ½ hours to take into account factors such as participant fatigue and attentional levels.

## 3.4.2. Participants

#### 3.4.2.1. Identification and recruitment

A broad-reaching identification and recruitment strategy was employed to achieve the target recruitment of 180 stroke participants. Potential stroke participants were identified through: i) local stroke support groups; ii) local NHS community stroke services; ii) Stroke Association Support Services.

Control participants were identified and recruited through local social and leisure groups for older adults that have members who are functionally independent and of the appropriate age range (University of the 3<sup>rd</sup> Age, Age Concern) and family members of stroke participants.

Potential stroke and control participants interested in the study were given a Participant Information Sheet (PIS) (Appendix 4) which provided written information about the study and the contact details of the researcher should they have further questions and/or wish to be contacted about the study. Having given permission to be contacted, potential participants were screened via telephone and if selection criteria were met, an appointment was arranged at their local community hospital or university for assessment.

Recruitment of stroke patients was not performed consecutively and was conducted across two separate recruitment centres on predefined assessment days. Both control and stroke participants were recruited through convenience sampling. A recruitment flowchart cannot be provided because there are no data available on patients who refused, were unavailable or were ineligible for participation in the study.

# 3.4.2.2. Stroke participant inclusion/exclusion criteria

Individuals were eligible to participate if they were: aged 18 and above, had a stroke diagnosis confirmed via CT scan and clinical presentation, were a minimum of three months post-stroke diagnosis, community dwelling (including nursing/residential homes), able to independently transfer from bed to chair, able to walk independently at least 10m indoors (with or without walking aid) and were willing and able to give informed consent for participation in the study.

Individuals were excluded if they were: unable to read and understand the information sheet or explanation of the research and provide informed consent, diagnosed with other neurological diseases such as Parkinson's disease, multiple sclerosis, or had comorbidities/injuries that would significantly affect mobility and/or foot function e.g. rheumatological disease, surgery (vascular/orthopaedic), peripheral neuropathy.

# 3.4.2.3. Control participant inclusion/exclusion criteria

Individuals were included if they were aged 18 and above, able to walk independently at least 10m indoors (with or without walking aid), and willing and able to give informed consent for participation in the study. Exclusion criteria for control participants was the same as that for stroke participants.

## 3.4.3. Sample size

Sample size was determined in accordance with the FAiMiS study objectives in which up to 16 potential foot and ankle predictors and four balance and mobility predictors were investigated. Formal statistical sample size calculations indicated that a sample size of 180 stroke participants would allow for these multiple predictors. This represents at least one predictor variable for every 11.25 participants and is in keeping with statistical guidance for this type of study design (Tabachnick & Fidell, 2013). One objective of this thesis chapter is to explore the relationship between sensation and functional ability. Given the multi-modal and multi-body parts assessed in the Erasmus MC Nottingham Sensory assessment (EmNSA), this sample size would be sufficiently powered to allow for up to 16 sensory predictor variables to be used in multiple regression analysis. In light of the limited evidence of the predictive value of lower limb somatosensation on function ability, the precise number of predictor variables in this study was determined through exploratory analysis and therefore limited to 16.

This study also compared the severity of lower limb sensory impairment with that of age-matched, ambulatory healthy controls. Previous comparisons of the difference in impairments of ROM and ankle strength between paretic/non-paretic side and matched controls have found effect sizes ranging from 0.62 to 1.8 (Lin et al, 2005;

Keating et al, 2000). A conservative approach was therefore taken using the smaller effect size. To detect an effect size of 0.62 with a power =0.9 and alpha = 0.05/20=0.0025 (to account for multiple comparisons including sensory impairment, balance and walking measures) a minimum of 45 matched control participants were required to compare to the 180 stroke participants.

## 3.4.4. Plan of investigation

# 3.4.4.1 Assessment procedures

Participants attended a single assessment session. Discussion with the steering group, formed as part of the FAiMiS study, considered that testing sessions should last no longer than 1 ½ hours to take into account factors such as time commitment and fatigue. Completing the battery of clinical outcome measures, which included the EmNSA, was achievable in this period, allowing for up to 20 minutes of rest in each session. The assessments were conducted at sites local to the participant; Either University premises or local community hospital. In total, three assessment venues were used: University of East London human movement laboratory, North Devon District Hospital physiotherapy department, and Bideford Community Hospital, physiotherapy department. Assistance was provided to participants with regard to travel expenses. Two experienced neurological physiotherapists, one based in East London and one in North Devon, conducted the assessments.

### 3.4.4.2 Assessment measures

Demographic data including age, gender, medical history, and current mobility level was recorded along with details of stroke (location, hemisphere, time since stroke) at

the start of the assessment session (Case Report Form – Appendix 5) to describe the study population.

The battery of clinical assessments below were carried out according to a written protocol, which included standardised ordering, and tester/participant instructions. Variance from the protocol, were noted for each participant, and accounted for during data analysis. The following assessment measures were chosen based on their published validity and reliability, clinical feasibility and appropriateness in a stroke population. Further, the FAiMiS research team, based on results from study 1, agreed these measures collaboratively.

### Somatosensory assessment

The Erasmus MC modified Nottingham Sensory Assessment (EmNSA) (Stolk-Hornsveld, 2006) (Appendix 6) was administered to all participants as the measure of somatosensory performance. Whilst there is no single gold-standard measure of somatosensation, the EmNSA is considered one of the most psychometrically robust and clinically feasible measures available (Connell & Tyson, 2012). It includes tests of light touch (applied using cotton wool), pressure touch (applied using the assessor's finger), pinprick (using a neurotip), sharp blunt (using a neurotip) and proprioception (movement detection and discrimination). It was used to assess cutaneous sensation and proprioceptive sensation (detection and discrimination) in the toes, the foot, the ankle and the hip. Scoring is at an ordinal level with a score of 0=absent, 1 = impaired and 2=normal assigned to each of the four anatomical areas of the lower limb. Scoring classification is included in appendix 6.

Scores for each modality thus range from 0 (total loss of somatosensory function) to 8 (wholly intact somatosensory function). This scoring is replicated for each of five sensory modalities resulting in a range of 0 (total loss of all modalities) through to 40 (wholly intact in all modalities). As per the protocol, if light touch is scored 2 (normal), pinprick and pressure are not tested and automatically assigned a score of 2 (normal). Whilst a cut-off score has not been established by the authors (Stolk-Hornsveld, et al, 2006) a recent study of upper limb function suggested a cut-off score of ≤6/8 in a modality indicates the presence of somatosensory impairment (Meyer et al, 2016). A total score allowing the dichotomous classification of impaired/not impaired has not been established.

The intra-rater reliability of the tactile sensations, sharp-blunt discrimination and the proprioception items of the EmNSA are moderate to excellent with a range of weighted kappa coefficients between 0.58 and 1.00 (Stolk-Hornsveld et al, 2006). Likewise, the inter-rater reliabilities of these items are moderate to excellent with a range of weighted kappa coefficients between 0.46 and 1.00. It takes 10 to 15 minutes to complete. Further detail of testing protocol is included in Appendix 6.

#### Walking ability

10 metre (m) timed walk (Bohannon, 1997) (Appendix 7) is a performance measure used to assess walking speed in metres per second over a short distance. Three trials were completed with the average used as the final score. Use of walking aids and/or orthotics were permitted during this test. Both self-selected walking speed (normal pace) and fastest walking speed can be assessed and have been shown to strongly correlate (Flansbjer et al, 2005). In chronic stroke populations, the 10m walk has

demonstrated excellent test-retest reliability (ICC = 0.95 to 0.99) (Flansbjer et al, 2005), excellent inter-rater reliability (ICC = 0.99) (Tyson & Connell, 2009). It has been demonstrated to strongly correlate with dependence in instrumental activities of daily living (r = 0.76)(Tyson & Connell, 2009) and community ambulation (r=0.68) (Lee et al, 2015). This study used the fastest walking speed protocol from a flying start.

The Walking Impact Scale (WIS) (Holland et al, 2006) (Appendix 7) was used to assess the patient's perceived walking ability in the context of their stroke. The use of patient reported outcome measures of walking ability alongside objective measures of gait is recognised as a valuable combination in neurological populations (DoH, 2008; Bladh et al, 2012). The WIS is a standardised and validated patient based self- report scale of mobility, which was initially developed for people with multiple sclerosis (MS) (Hobart et al, 2003). It is a 12-item scale in which respondents are asked to score the perceived impact their stroke has had on various aspects of their walking ability. Preceding each statement, respondents are given the written prompt of 'In the past two weeks, how much has your stroke...' The 12 items cover abilities ranging from walking speed/distance/ smoothness, effort/concentration required during walking, through to stair climbing, standing and balancing. It is scored on a 5-point Likert scale (1=not at all, 2= a little, 3= moderately, 4=quite a bit, 5=extremely), with scores ranging from 12-60. A score of 1 on an item equates to no limitation, whilst a score of 5 equates to extreme limitation; hence, higher scores indicate greater perceived impact of stroke on functional walking ability. Items are summed to generate a total score, which is transformed to a 0-100 scale. The WIS has demonstrated excellent test-retest reliability in an MS population (Hobart et al, 2003) and has shown good responsiveness, validity and clinical feasibility in people with a range of neurological

conditions (Holland et al, 2006). The control participants completed the same scale, wording adjusted to reflect the perceived impact of overall health on walking ability.

# **Dynamic Balance**

*The Standing Forward Functional Reach* Test (Weiner et al, 1992) (Appendix 8) is a standardised, validated measure of dynamic balance that mirrors the everyday activity of reaching for objects beyond arm's length. It measures the maximum distance the participant can reach forward beyond arm's length (to the limits of stability) without moving their feet, using a ruler fixed at shoulder height. Age related norms are available, and values have been determined to predict the relative risk for falls in an elderly population (Duncan et al, 1992) with a score <15 cm indicative of falls risk in stroke (Acar & Karantas, 2010). It has demonstrated excellent test-retest reliability (ICC= 0.95), and inter-rater reliability (ICC=0.99). Evidence supports its validity, demonstrating moderate to strong correlations with the Rivermead Mobility Index (r=0.56) and the Berg Balance Scale (r=0.70) (Tyson & DeSouza, 2004). In line with the established protocol, three trials of reaching forwards with the non-hemiplegic arm were performed and the mean reach (cm) calculated.

#### Static balance

Postural control requires the ability to both orient to the environment and to maintain the centre of gravity within the weight-bearing base of support. Whilst this is referred to as "static" standing balance, it is a dynamic sensorimotor function that incorporates aspects of both anticipatory and reactive control (Shumway-Cook & Woolacott, 2012). Postural sway during quiet standing, also known as static posturography, is commonly and reliably used to assess static balance abilities in laboratory and clinical

environments (Ruhe et al, 2010; Masani et al, 2014). The centre of pressure (COP) is one of the most popular measurements when quantifying postural sway, with COP velocity reportedly most sensitive for detecting changes in balance abilities due to aging and/or neurological diseases (Lemay et al, 2013; Era et al, 2006; Masani et al, 2014). In this study, it was measured by recording quiet standing using a Tekscan pressure mat (Matscan, Biosense Medical, Essex UK), a low-profile pressure sensing mat that captures static and dynamic pressure measurement data for foot function, balance and sway. Using the FootMat software for researcher's package, centre of pressure (velocity) in an eyes open (EO) and eyes closed (EC) condition was collected. COP<sub>velocity</sub> was calculated by dividing the COP excursion (mm) by time standing (maximum of 30 seconds) for both EO and EC conditions. Postural sway (mm/s) was then calculated by subtracting EC COP<sub>velocity</sub> (mm/s) from EO COP<sub>velocity</sub> (mm/s). Whilst the Romberg's ratio (i.e. EC/EO) takes into account baseline sway and thus proportionate change from EO to EC conditions, this ratio calculation has demonstrated poor test-retest reliability in healthy subjects, despite fair to excellent reliability of EO and EC parameters (Tjernström et al, 2015). This is a portable, feasible, valid and reliable objective measure of static standing balance (Ruhe et al, 2010).

# **Falls Incidence**

Falls incidence was quantified through participant retrospective recall. Participants were asked if they had within the previous three months, experienced a fall, and if so, how many. The definition of a fall was given to each participant to minimise ambiguity about what constitutes a fall using Lamb's (2005) definition as a "slip or trip in which you lost your balance and landed on the floor or ground or lower level" (p. 1619). Furthermore, to minimise recall error and allow clarification, where a fall incident was reported, participants were also asked to recall the nature of the fall (trip, stumble, black out), where it happened (indoors, outdoors, supermarket, kitchen) and what they were doing at the time (changing direction, chatting, just walking, stepping up kerb).

It is recognised that retrospective reporting of falls is susceptible to a degree of recall error in the reporting of falls in the elderly (Ganz et al, 2005; Mackenzie et al, 2006). This may be even greater following stroke where the cognitive impairments can occur although in stroke, retrospective recall of falls has shown to agree in 83% of cases with prospective methods, with k=0.64, indicating good agreement (Kunkel et al, 2011). So whilst ideally falls data should be collected longitudinally and prospectively through diaries (Lamb et al, 2005) the cross sectional design of this study meant the practicalities of using diaries was not feasible. Further, the use of diaries may be more appropriate whenever accuracy of falls data is critical, such as in intervention or observational studies in which falls is the primary outcome.

Falls classification was based on previous literature with stroke participants grouped as non-fallers, single fallers (1 fall reported) and repeat fallers ( $\geq$ 2 falls reported). Research into falls and older people suggests single fallers tend to have different characteristics than repeat fallers (Lord et al, 2003) although this has yet to be established in the stroke literature (Batchelor et al, 2012; Schmid et al, 2013).

### Fear of falling

*Fear of falling* was measured using the *Falls Efficacy Scale - International* (FES - I) (Yardley et al, 2005)(Appendix 9) a 16-item self-report tool. It was developed from the

original 10-item Falls Efficacy Scale (FES) (Tinetti et al, 1990) and expanded to include six more challenging social activities (items 11-16) that may cause more concerns about falling than the basic FES activities. It measures an individual's level of concern about falling during social and physical activities inside and outside the home, whether or not the person actually does the activity. Fear of falling in stroke has important clinical considerations as it has shown to lead to activity restriction, psychological and physical deterioration (Batchelor et al, 2012; Belgen et al, 2006). As with measures of gait, subjective measures can complement objective measures to provide a fuller picture. The level of concern is measured on a four point Likert scale (1=not at all concerned, 2= somewhat concerned, 3= fairly concerned and 4=very concerned). It has demonstrated excellent internal validity (Cronbach's alpha=0.96) and excellent testretest reliability (ICC=0.96) amongst elderly populations (Yardley et al, 2005) whilst the original FES demonstrated excellent test-retest reliability (ICC= 0.97) in a stroke population (Hellstrom & Lindmark, 1999). Validity is supported by its ability to discriminate between previous falls and no falls in the elderly and between multiple and single fallers (p<0.001)(Delbaere et al, 2010).

## Ankle strength

Isometric ankle muscle strength was measured using a hand held Lafayette© manual muscle testing system (Model 01165, Lafayette Instrument Company, USA). The handheld dynamometer (HHD) measures the peak force in kilogrammes (kg) produced by a muscle as it contracts while pushing against resistance. A recent systematic review of HHD measures for assessment of isometric muscle strength in the clinical setting found the instrument to be a reliable and valid tool (Stark et al, 2011) and this approach has

been used widely in studies of stroke and other pathologies (Kluding & Gajewski, 2009; Spink et al, 2011; Carroll et al, 2013).

Isometric muscle strength of ankle dorsiflexors, plantarflexors, invertors and evertors was assessed using the 'make test', whereby the HHD was held stationary while participants actively exerted a maximal force against stationary resistance (Carroll et al, 2013). For all muscle strength testing each participant was positioned in long sitting on a therapy plinth, hips flexed and flexed knees placed over a standardised foam roll. The shank (lower limb) was subsequently aligned parallel to the floor using lateral malleolus and head of fibula as reference points. The shank was then supported in this position using foam cushion during testing so that the tested foot/ankle was suspended away from any surface. The tested limb was further stabilized through Velcro<sup>®</sup> straps fastened across the pelvis, mid-thigh and mid shin to discourage compensatory movements that may occur due to patient effort. The HHD was positioned in accordance with previous studies (Spink et al, 2011; Carroll et al, 2013). These being against the:

- lateral border of the foot distal to the base of the 5th metatarsal head to measure eversion;
- medial border of the foot, near the base of the 1<sup>st</sup> metatarsal head to measure inversion;
- metatarsal heads on the plantar surface of the foot to measure plantarflexion;
- the dorsal aspect of the foot proximal to the metatarsal heads to measure dorsiflexion.

Each participant performed submaximal test movements for familiarisation prior to testing. Testing of each muscle group required a contraction of five seconds, indicated by an audible beep from the HHD. Participants were all offered verbal encouragement during testing to sustain maximal contraction. Three repetitions were obtained for each movement direction, with a minimum rest period of 15-seconds between each contraction. The mean force output of the three trials was calculated for data analysis. Testing order was standardised with dorsiflexion tested first, followed by plantarflexion, inversion and finally eversion. Pilot study work completed by the FAiMiS study group indicated this to be a reliable and clinically feasible testing method.

# 3.4.5. Ethical considerations

# **Ethical review**

Ethical review was undertaken by the NHS Health Research Authority NRES Committee (13/SW/0302).

### Study funding

This study was funded by a research grant from the Dr William M. Scholl Podiatric Research and Development Fund (ref: FAiMiS). Funders had no influence on any aspect of this study.

# Informed consent

Written informed consent was obtained from all participants using procedures detailed by the Council of Research Ethics Committees (UK) and in accordance with the International Declaration of Helsinki (Goodyear et al, 2007). Due to the effects of stroke, it was anticipated that some participants would be unable to write with their dominant hand so were asked to make a written indication of consent using their nondominant hand. Where participants had difficulty reading the form, it was read to them. Consent forms were completed before any study- specific procedures were performed.

Judgement on the potential participant's capacity to give informed consent was made by the assessors. Both were neurological physiotherapists with several years' clinical experience of working with people with neurological conditions, including stroke, and both completed General Good Practice (GCP) training prior to commencement of the study.

# **Potential Harm**

Participants were fully informed of the nature of the research, risks and burdens, possible benefits, amount of involvement, the voluntary nature of participating, and the right to withdraw at any time, as set out in the study Participant Information Sheet (PIS). As impairments in balance and mobility are common in both stroke and elderly populations (Tyson et al, 2006), during any activities that could constitute a risk, precautions were taken. Stand by assistance, use of walking aids, chairs and/or wall bars were available during assessments of walking and balance.

# 3.4.6. Data analyses

Participants' clinical and demographic characteristics were summarised using frequencies and percentages, mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Somatosensory performance across each sensory modality were calculated using frequencies and percentages. All data was screened for outliers using mean and two standard deviation (2SD) calculations, along with box and stem-and-leaf plots. Normality of raw data was assessed using Shapiro-Wilks tests of

normality. Normality was assumed when p>0.05. There is currently no universally agreed scoring cut-off point with the EmNSA to enable a dichotomous classification of somatosensory performance into impaired or not impaired. Frequencies and percentages of participants scoring *sub-maximally* in each modality were presented. EmNSA total score data from control participants provides a normative reference and informed impairment classification of stroke participants. In addition, to allow direct comparisons with a recent study of upper limb sensory impairment (Meyer et al, 2016) the different somatosensory modalities were also dichotomized as impaired or not impaired based on a cut-off score of ≤6/8 for each modality. Thus, frequencies and percentages of participants scoring sub-maximally (i.e. ≤7/8) and "impaired" (i.e. ≤6/8) for a single modality, are presented.

Performance differences between stroke and control participants were analysed using chi-squared tests for independence, unpaired t-tests or Mann-Whitney U tests as appropriate, with the magnitude of the difference in the means/medians expressed as effect size. Effect size for normally distributed and parametric tests was calculated using Cohens *d* using the formula: *Cohen's*  $d = \frac{mean\ group\ 2-mean\ group\ 1}{pooled\ standard\ deviation}}$  where pooled standard deviation (SD) is calculated using the formula: *SD Pooled* =  $\sqrt{((SD1^2 + SD2^2) \div 2)}$ . The effect size for non-normally distributed data and Mann Whitney U tests was calculated using the formula where effect size =  $\frac{z\ score}{\sqrt{N}}$  as suggested by Grissom & Kim (2012). Cohen's (1988) evaluation criteria was used to interpret all effect sizes with <0.49 = small, 0.5-0.8 =medium and >0.8 = large.

Limited evidence linking lower limb somatosensory performance with measures of function meant exploratory analysis was conducted to investigate the direction,

magnitude and statistical significance of any associations. Associations between stroke participants' lower limb sensation, ankle strength and functional measures of mobility, balance and falls were assessed using Spearman's rank order correlation (rho) or Pearson product moment correlation coefficient (r) as appropriate. Strength of correlations were interpreted using Cohen's (1988) classification where  $\leq 0.29 =$  weak, 0.30- 0.49 = moderate and,  $\geq 0.50 =$  strong and significance is reported at 0.01 and 0.05 levels.

The factor most strongly linked with somatosensory deficits through correlational analyses was reported falls. Falls were also linked to lower limb sensory impairments by people with stroke, as reported in study 1 (qualitative study). Further analyses relating to falls and lower limb somatosesantion were thus completed. Where test performance of non-fallers, single fallers and repeat fallers was compared, several statistical analyses were used. A one way between groups ANOVA was used to assess differences between the groups in terms of age, gait speed and functional reach test. Post-hoc comparisons using the Tukey HSD test were used to indicate between which groups the significant differences existed. A chi-squared test for independence was used where falls groupings were compared in relation to indoor/outdoor walking category. Comparing falls groupings in time since stroke, Walking Impact Scale score, Timed Up and Go, falls confidence and postural sway, a Kruskal-Wallis test was used. Post-hoc analysis used Mann Whitney U tests. Statistical significance was set at 0.05 although where appropriate, Bonferroni adjustments were made to account for multiple comparisons and statistical significance amended and highlighted.

Direct logistic regression with forced entry was performed to assess the impact of a number of factors on the likelihood that participants reported one or more falls. These factors were derived from the exploratory analysis and the findings from other studies. Assumptions of logistic regression, as described by Pallant (2013), were observed with data assessed for multicollinearity, normality, and outliers. Assumptions of multicollinearity were deemed to be met if there were no inter-correlations  $\geq 0.7$ between independent variables. Independent variables were screened for normality using Shapiro-Wilks tests with normally distributed data indicated when p>0.05. Normal probability plot (p-p) of the regression standardised residual was inspected to identify outliers and determined using scatterplots and standardised residual values, with individual cases scoring more than 3.3 or less than -3.3 indicating outliers (Tabachnick & Fidell, 2013). Influence of outliers on the regression model as a whole were further analysed using Cook's distance with a value less than 1.0 considered not problematic (Tabachnick & Fidell, 2013). All data were analysed with SPSS version 22.0 for Windows statistical program.

#### Incomplete/missing data

One hundred and eighty stroke participants were recruited to this study. A full data set including all sensory, motor *and* mobility measures was obtained for 85% of recruited participants (n= 153). Sensory data for both tactile and proprioceptive components of the EmNSA was obtained for 163 participants, with missing or incomplete data for 17 participants. For all tactile modalities, there was complete data on 167 participants with incomplete/missing data reported for 13 participants. Reasons for non-completion of the tactile component included: Poor comprehension/unable to follow instructions (n=4); language difficulties (n=2);

hypersensitivity/pain (n=2); anxiety (n=1); and clothing restriction (n=4). For the proprioceptive part of the assessment, 173 participants had all body parts assessed with incomplete/missing data for seven participants. Reasons for non-completion were poor comprehension/unable to follow instructions (n=4); language difficulties (n=2); joint pain/restriction (n=1). No sensory data was missing for the control group.

For the strength data, complete data sets for ankle dorsiflexion, plantarflexion, inversion, and eversion were collected for 168 stroke participants and 46 control participants. Reasons for missing data in stroke participants were Equipment malfunction (n=3); foot/ankle joint pain (n=3); clonus/tremor (n=2) and poor comprehension/understanding of movement task (n=4).

For the mobility data, six stroke participants did not complete the Functional Reach Test (FRT), as they were unable to stand unsupported. Two participants did not complete the Falls Efficacy Scale (FES) and two did not complete the Walking Impact Scale (WIS) citing choice/personal reasons. One participant could not complete the Timed Up and Go (TUG) as they were unable to rise from the standardised chair unaided. These data suggest that the measures used in this study are highly clinically feasible tools to administer to a chronic stroke population.

For the purpose of data analyses, cases were excluded pairwise in that participants' data was excluded from the analysis to which that data refers but was included in relevant data analyses where complete data existed. This complete available data set represented 85% of the recruited sample size and given the size of the sample, excluding this data in the overall analysis did not affect statistical power.

## 3.4.7. Study quality

The 'STrengthening the Reporting of Observational studies in Epidemiology (STROBE)' (von Elm al, 2007) was used as a framework for this study. In line with STROBE recommendations, this study provided a clear presentation of what was planned, done and reported.

# 3.5. Results

# 3.5.1. Study population characteristics

Characteristics of both stroke and control participants are detailed in table 3-1. Data for age was normally distributed with no statistically significant differences in age or gender between stroke and control groups. The age profile of the stroke group was similar to that of other studies in which community-dwelling, chronic stroke survivors have been investigated (Durcan et al, 2016; Robinson et al, 2011; Lee et al, 2015).

Statistically significant differences were found between stroke and control groups with respect to self-reported indoor and outdoor walking ability, and reported falls using a chi-squared test for independence. Thirty-four percent (n=61/180) of the stroke group reported using a walking aid indoors, whereas no control participants reported using a walking aid when walking indoors. Eleven percent (n=5/46) of the control group reporting using a walking aid when outdoors compared with 55% (n=99/180) of the stroke group. Six percent of the stroke group (n=11/180) reported being unable to walk outdoors. With respect to falls reporting, 60% (n=108/180) of the stroke group reported no falls over the previous three month period, with 22% (n=39/180) reporting a single fall and 18% (n=33/180) reporting two or more falls (repeat fallers). By comparison, the majority of the control group (93%, n=43/46) reported no falls within

the last three month period with 7% (n=3/46) reporting at least one fall. No control participants reported two or more falls in the previous three months.

	Stroke	Control	<i>p</i> value
Characteristics	(n=180)	(n=46)	
Age, years, mean (SD)	67 (11)	66 (12)	0.65ª
Gender n (%)			
Male	107 (59)	22 (48)	0 156b
Female	73 (41)	24 (52)	0.150
Indoor walking ability n (%)			
Uses aid	61 (34)	0 (0)	0.000h
No aid used	119 (66)	46 (100)	0.0000
Outdoor walking ability n (%)			
Not able	11 (6)	0 (0)	
Uses aid	99 (55)	5 (11)	0.000b
No aid used	70 (39)	41 (89)	
No. of Falls Reported n (%)			
0	108 (60)	43 (93)	
1	39 (22)	3 (7)	
2	13 (7)	0	0.008b
3	10 (5.5)	0	
≥4	10 (5.5)	0	

Table 3-1. Stroke & control participant demographics, walking aid use and falls

a: *p* value from Mann-Whitney test; b: *p* value from Chi Squared test for independence

# 3.5.2. Mobility, balance and falls: stroke and control participants

Stroke participants' performances were significantly lower on each objective functional measure of walking and balance (Table 3-2). In addition, stroke participants' scores in the self-reported measures were significantly higher than controls. These objective and subjective differences indicate lower levels of observed and self-reported ability.
*Objective Measures (gait speed, functional reach test (FRT), Timed up and go (TUG), postural sway)* 

Gait speed and FRT data was normally distributed and was analysed using independent t-tests. The stroke group walked significantly slower than controls (t(222,)=-7.9 p<0.001, r=1.3) and also had a significantly smaller FRT scores than the controls (t(215)=-6.0 p<0.001, r=1.1), with effect size statistics indicating a very large difference. TUG and postural sway (COP<sub>velocity</sub>) data were not normally distributed so were analysed using Mann Whitney U tests. Stroke participants were significantly slower on the TUG (p<0.001) and had a significantly higher COP<sub>velocity</sub> EO-EC than controls (p<0.001). Effect sizes for both were medium.

#### Self-reported measures

All data for the self-reported measures were not normally distributed so were analysed using Mann Whitney U tests. The stroke group had significantly higher scores on the Falls Efficacy Scale (FES) than the control group (p<0.001) indicating a greater fear of falling (table 3-10) with the effect size statistic (r=0.48), indicating a medium difference. The stroke group scored significantly higher on the Walking Impact scale (WIS) (p<0.001; effect size r=0.52) indicating lower perceived walking ability with the magnitude of the difference medium. **Table 3-2** Comparison between stroke and control performance in objective and self-report measures of mobility, balance and falls.

Measure	Stroke	Control	p value	Effect
	(n=169)	(n=46)		Size
Objective measures				
Walking speed m/s, mean (SD)	1.1(0.6)	1.8(0.4)	P<0.001 <sup>a</sup>	1.3
FRT cm, mean (SD)	24.6(10.0)	34.2(6.9)	P<0.001 <sup>a</sup>	1.1
TUG mean seconds	19.3(15.0)	8.1(1.8)	P<0.001 <sup>b</sup>	0.52
COP <sub>velocity</sub> mm/s mean (SD)	9.7 (18.4)	1.0 (13.9)	P<0.001 <sup>b</sup>	0.22
Self-Report measures				
FES score median, (IQR, range)	34 (13)	20 (4)	P<0.001 <sup>b</sup>	0.48
WIS, median (IQR, range)	37 (14)	18 (8)	P<0.001 <sup>b</sup>	0.52
Falls Incidence in 3 months,				
median, (IQR, range)	0 (1, 7)	0 (0,1)	P<0.001 <sup>b</sup>	0.29

a: Independent sample t test; b Mann Whitney U test

**Abbreviations**: m/s, metres per second; SD, Standard Deviation; FRT, Functional Reach Test; cm, centimetres; TUG, Timed up and Go; COP, centre of pressure; mm/s, millimetres per second; FES Falls Efficacy Scale; IQR, Inner quartile range

Falls incidence. Stroke participants reported a mean 0.8 falls in the three months preceding the assessment (median =0, range =0 – 7). Conversely, in control participants the median number of falls was 0 (range=0-1) with 43/46 control participants reporting no falls and three reporting just one fall in the preceding three months. This difference was statistically significant (p<0.001) although the effect size calculation of this difference was small (r=0.29)

The clinical characteristics of stroke participants are described in table 3.2. The majority (68% n=122/180) had an ischaemic stroke within a cortical location (78% (n=141/180). Mean time since stroke was 33 months (SD=48 months) with 49% of participants (n=89/180) between 3-12 months post stroke.

Table 3-3. Stroke participant clinical characteristics (n=180)

Type of stroke	n (%)	Side most affected n (%)	n (%)
Ischaemic	122 (68)	Right	81 (45)
Haemorrhagic	40 (22)	Left	84 (47)
Unknown/Missing	18 (10)	Bilateral	11 (6)
		Unknown/missing	4 (2)

Stroke Location n (%)	n (%)	Time since stroke (months)	
Cortical	141 (78)	Mean (SD)	33(48)
Subcortical:			
Brainstem	9 (5)	Frequency	n (%)
Basal Ganglia	3 (2)	3-12 months	89 (49)
Cerebellum	16 (9)	13-24 months	33 (18)
Thalamus	1 (1)	25-48 months	21 (12)
Unknown/Missing	10 (5)	>49 months	37 (21)

#### 3.5.3. Prevalence and distribution of sensory impairments: stroke and control

#### participants

Overall, 25% (n=41) of the 163 stroke participants who completed the full EmNSA scored the maximum (40/40) and therefore 8/8 in each of the five modalities of light touch, pinprick, pressure, sharp-blunt and proprioception. Conversely, 75% (n= 122/163) of stroke participants completing the EmNSA scored sub-maximally ( $\leq$ 7/8) in at least one of the five sensory modalities when assessed on their most affected lower limb. The range was 7- 40/40 (see Fig 3-1).





Within the tactile modality, 74% of stroke patients (n=123/167) scored sub-maximally ( $\leq$ 31/32) in at least one tactile modality (i.e. light touch, pinprick, pressure, sharpblunt) with 26% (n=44/167) scoring maximally (32/32); range 0-32/32 (Fig 3.2). With reference to proprioception, 28% (n=48/173) of stroke participants scored sub-maximally ( $\leq$ 7/8) in at least one of the four lower limb joints (i.e. toe, ankle, knee, hip) with 72% (n=125/173) of stroke participants scoring the maximum 8/8 suggesting no proprioceptive deficit in all joints tested (range 4-8/8).

By comparison, 50% (n=23/46) of age matched controls scored sub-maximally (i.e. ≤39/40) with 50% scoring maximally (40/40). Range 34-40/40 (fig 3-1). Those scoring sub-maximally were due to sub-maximal scores in the tactile component of the EmNSA (range 26-32/32; fig 3-2). All control participants scored the maximum (8/8) on the proprioception component of the EmNSA.



**Fig 3-2.** Frequency distribution of stroke and control participants total tactile scores on the EmNSA

### 3.5.4. Sensory impairment by modality in stroke and control participants

By far, the tactile modality in which most stroke participants scored sub-maximally was that of sharp-blunt discrimination with impairment more common distally than proximally. Other tactile and proprioceptive modalities showed a similar trend in that distal areas were more frequently impaired than proximal (Table 3.4).

The total percentage of sensory abnormalities was highest for sharp-blunt discrimination with 32%, 41%, 56%, 71% of stroke participants scoring absent or impaired at the thigh, shin, foot and toes respectively. Next highest was impairment in light touch with 11%, 14%, 21%, 25% of stroke participants absent or impaired at the thigh, shin, foot and toes respectively.

Responses to pin prick and pressure tended to be evenly matched with 10%, 12%, 16%, and 17% showing an absence or impairment to pressure sensation in the thigh, shin,

foot and toes respectively and 10%, 10%, 14%, 15%, scoring absent or impaired in pin

prick throughout the thigh, shin, foot and toes respectively.

Lower									
Limb Area	Classification	Light <sup>-</sup>	Touch	Pres	sure	Pin Pr	ick	Sharp	/Blunt
		n	%	n	%	n	%	n	%
Thigh	Absent	6	3	3	2	3	2	11	7
	Impaired	14	8	14	8	14	8	42	25
	Normal	154	89	157	90	156	90	114	68
Shin	Absent	7	4	3	2	3	2	13	8
	Impaired	17	10	18	10	14	8	56	33
	Normal	154	86	157	88	160	90	101	59
Foot	Absent	8	4	5	4	5	4	17	10
	Impaired	30	17	22	12	18	10	79	46
	Normal	141	79	152	84	155	86	75	44
Toes	Absent	15	9	10	5	8	4	21	12
	Impaired	29	16	19	12	18	11	101	59
	Normal	135	75	150	83	152	85	49	29

Table 3.4. Prevalence and distribution of impairment to tactile modalities by body region in stroke participants

Overall, the percentage of tactile sensory abnormalities was remarkably similar across the differing modalities (excluding sharp blunt) and across the different lower limb areas. It should be noted that as per the EmNSA protocol (Stolk-Hornsveld et al, 2006) a normal score in light touch, automatically scores normal in both pressure and pinprick.

Impairment of proprioceptive sense showed the biggest difference between distal and proximal joints with 30% absent/impaired at the toes (1st MTPJ), 21% absent/impaired at the ankle, 5% absent/impaired at the knee and 3% impaired at the hip joint (table 3-

5).

**Table 3-5.** Prevalence and distribution of proprioception impairment by limb region in strokeparticipants

Lower Limb Area	Classification	Proprioception	
		n	%
Нір	Absent	0	0
	Impaired	6	3
	Normal	168	97
Knee	Absent	0	0
	Impaired	8	5
	Normal	165	95
Ankle	Absent	2	1
	Impaired	34	20
	Normal	140	79
Hallux (1st MTPJ)	Absent	5	3
	Impaired	48	27
	Normal	124	70

Overall, absent/impaired scores were more frequent distally in the toes and feet of stroke participants than proximally across all modalities with the biggest differences being across the sensory modalities of proprioception and sharp/blunt discrimination.

By comparison, the tactile modality in which most controls scored sub-maximally was also sharp-blunt with 23/46 (50%) scoring  $\leq$ 7/8 across the four lower limb areas. The distribution of sharp-blunt sub-maximal scoring occurred because of absent/impaired scoring predominantly in the toes (n=21) and the foot (n=10), with six and two participants scoring sub-maximally in sharp-blunt discrimination in the shin and thigh respectively. Three controls scored  $\leq 7/8$  on light touch, and one control scored  $\leq 7/8$  on pinprick. Conversely, all controls scored 8/8 for pressure sensation and 8/8 for proprioceptive sensation across the four lower limb areas.

There is currently no established or standardised cut off score to determine modality or overall sensory impairment using the EmNSA. Prevalence data with respect to submaximal scores in which at least one body part, in at least one modality was impaired, was presented above. Whether a sub-maximal score is sufficient to merit a classification as "impaired" is debatable. A recent study of the upper limb (Meyer et al, 2016) suggested a cut of score of  $\leq 6/8$  implies "impaired" in any one modality, although this appears to be an arbitrary score. Using this "impairment" cut off score to allow for comparison, 59% (n=96/163) stroke participants were impaired in at least one aspect of sensation. Twenty-one percent (n=35/167) had impaired light touch (LT), 14 % (n=23/167) pressure sensation (Pr) and 13% (n=22/167) pinprick (PP) (Fig 3-3). Twenty percent (n=34/173) of stroke participants scored  $\leq 6/8$  on the proprioception component of the EmNSA suggestive of a proprioceptive impairment whilst 55% (n=92/167) of stroke participants scored  $\leq 6/8$  on sharp-blunt discrimination.



**Fig 3-3.** Percentage of stroke sample scoring  $\leq 6/8$  for each sensory modality

Abbreviations: LT: light touch; Pr: pressure; PP: pin prick

By comparison, 10/46 (21%) of control participants scored  $\leq 6/8$  across the modality of sharp-blunt discrimination suggesting impairment, whilst one control scored  $\leq 6/8$  on pinprick sensation. No control participants scored  $\leq 6/8$  on light touch, pressure or proprioception.

#### 3.5.5. Cross modal sensory impairments; stroke participants

To investigate the distribution and presence of sensory impairment across different modalities, cross tabulation analysis was carried out. The somatosensory profile of 163 stroke participants was mapped showing the extent to which sensory deficits were experienced uniquely in isolation, or combined (Fig 3-4). Light touch, pressure and pin prick were grouped according to their classification as exteroceptive sensation. Sharpblunt testing was reported separately due to the implication it is a test of higher cortical processing, as was proprioception. Forty-one percent (n=67/163) of the chronic stroke participants scored >6/8 on each modality and were considered as having no somatosensory impairment. Just one participant (0.5%) had pure deficit in exteroceptive sensation (light touch, pinprick or pressure). Given the relationship between detection and discrimination, any deficit in exteroceptive sensation should also be accompanied by a deficit in sharp-blunt discrimination so this is potentially an error. One percent of participants (n=2/163) had pure deficit in proprioception. By far the greatest proportion of participants experiencing a single modality deficit was that of sharp blunt with 29.5% (n=48/163) scoring  $\leq 6/8$ .

**Fig 3-4**. Somatosensory profile of stroke participants (n=163) showing distributions of unique and combined somatosensory deficits



Forty-seven participants (28%) had a mixed picture exhibiting a combination of two or more sensory impairments. Within those 47 participants, 20 (i.e. 12% overall) were impaired in all three modalities (exteroception, proprioception and sharp blunt), scoring  $\leq 6/8$  in each modality suggestive of profound somatosensory impairment.

# 3.5.6. Sensory performance: stroke and controls

Despite similar frequency distributions of total EmNSA scores between stroke and control participants (fig 3-1 and 3-2), total tactile and proprioceptive scores were significantly different between the affected side and the "matched" control side. Mann- Whitney U tests confirmed highly statistically significant differences between the total tactile and proprioception scores between groups (Table 3-6)

EmNSA Scores Median (IQR, Range)	Stroke (n=163)	Control (n=46)	<i>p</i> value	Effect Size
Affected tactile total (/32)	30 (4,32)	31(2,6)	<0.001ª	0.51
Affected Proprioception total (/8)	8(1,4)	8(0,0)	<0.001ª	0.63
Non Affected tactile total (/32)	32(2,8)	31(2,7)	>0.05ª	0.06
Non affected proprioception total (/8)	8(0,4)	8(0,0)	>0.05ª	0.27

Table 3-6. Comparison of stroke and control participant total EmNSA scores

a; p values from Mann Whitney test;

The relative magnitude of these differences, as indicated by effect size statistics of 0.51 and 0.63, were medium. In contrast, there was no significant differences between the "non –affected" side and the "matched" control with effects sizes ranging from 0.06-0.27 (table 3-6).

The differences in the individual tactile modalities and proprioceptive components of the EmNSA by body part between the most affected side and the matched control side are further broken down in table 3-7. Bonferroni adjustments are made to account for the multiple comparisons i.e. four body parts and five different modalities (0.05/20=0.0025). This highlights that the differences between the control and stroke group were predominantly in sharp-blunt discrimination at each body location. In contrast, there were no statistically significant differences between stroke and controls other than proprioception scores at the 1<sup>st</sup> MTPJ. Table 3-7. Comparison of individual EmNSA scores by body part and sensory modality between stroke and control participants

Median EmNSA Score(IQR, Range)	Stroke (n=163)	Control (n-46)	X <sup>2</sup>
Toe			
Light Touch	2 (0,2)	2 (0,1)	0.021NS
Pressure	2 (0,2)	2 (0,0)	0.014NS
Pin Prick	2 (0,2)	2 (0,1)	0.066 NS
Sharp Blunt	1 (1,2)	2 (1,1)	0.001
Proprioception	2 (1,2)	2 (0,0)	0.000
Foot (ankle)			
Light Touch	2 (0,2)	2 (0,1)	0.003NS
Pressure	2 (0,2)	2 (0,0)	0.019NS
Pin Prick	2 (0,2)	2 (0,0)	0.036NS
Sharp Blunt	1 (1,2)	2 (0,1)	0.000
Proprioception	2 (0,2)	2 (0,0)	0.004NS
<u>Leg (knee)</u>			
Light Touch	2 (0,2)	2 (0,0)	0.031NS
Pressure	2 (0,2)	2 (0,0)	0.050 NS
Pin Prick	2 (0,2)	2 (0,1)	0.248 NS
Sharp Blunt	2 (1,2)	2 (0,1)	0.002
Proprioception	2 (0,1)	2 (0,0)	0.137 NS
<u>Thigh (hip)</u>			
Light Touch	2 (0,2)	2 (0,0)	0.055 NS
Pressure	2 (0,2)	2 (0,0)	0.088 NS
Pin Prick	2 (0,2)	2 (0,1)	0.236 NS
Sharp Blunt	2 (1,2)	2 (0,1)	0.001
Proprioception	2 (0,1)	2 (0,0)	0.202 NS

NS – Not significant at 0.0025 - adjusted for Bonferroni correction to account for multiple comparisons (0.05/20=0.0025)

# 3.5.7. Relationship between lower limb sensory-motor performance and measures of mobility, falls and balance in stroke participants

Table 3-8 shows the correlational matrix between lower limb sensory-motor performance and measures of mobility, falls and balance. Ankle strength in both frontal (inversion/eversion) and sagittal (dorsiflexion/plantarflexion) planes of movement showed moderate to strong correlations (r=0.46-0.69) and statistically significant (p<0.01) relationships with all measures of mobility (gait speed, WIS, and TUG). Increased ankle strength was associated with increased gait speed, reduced TUG and reduced WIS. Dorsiflexion (DF) and plantarflexion (PF) force output scores were most strongly and positively correlated with gait speed with correlations (r=0.69 and r=0.67) respectively. DF and PF were also moderately and negatively correlated with FES and FRT (r=0.41-0.44 and r=0.39-0.40) respectively, as was inversion and eversion (r=0.37 and r=0.34-0.35) respectively. Increased ankle strength was therefore associated with lower scores on the FES (i.e. lower fear of falling) and higher scores on the FRT (i.e. greater balance).

	Mobility			Fal	ls	Balance	
Parameter	Gait Spee	d WIS	TUG	Incidence	FES	FRT	СОР
Age <sup>a</sup>	-0.17*	-0.04	0.009	0.06	-0.04	-0.38**	0.25**
TSS <sup>a</sup>	-0.20**	-0.20**	-0.18*	0.11	0.29**	-0.14	-0.13
Tactile sensation <sup>b</sup>							
Тое	0.04	-0.18*	-0.13	-0.16*	-0.20**	0.02	-0.05
Foot	0.06	-0.17*	-0.13	-0.16*	-0.19*	0.08	0.09
Shin	0.06	-0.12*	-0.11	-0 .12	-0.07	0.12	0.03
Thigh	0.08	-0.15*	-0.16*	-0.10	-0.13	0.14	-0.10
<b>Proprioception</b> <sup>b</sup>							
Тое	0.10	-0.20**	-0.13	-0.24**	-0.09	0.07	-0.21**
Ankle	0.03	-0.15*	-0.09	-0.18*	-0.12	0.08	-0.21**
Knee	0.06	-0.19*	-0.07	-0.17*	-0.17	0.04	-0.09
Hip	0.10	-0.12	-0.04	-0.20**	-0.07	0.02	-0.03
Ankle strength <sup>a</sup>							
Dorsiflexion	0.69**	-0.53**	-0.57**	-0.08	-0.44**	-0.40**	0.16*
Plantarflexion	0.67**	-0.52**	-0.52**	-0.12	-0.41**	-0.39**	0.21**
Inversion	0.59**	-0.41**	-0.47**	-0.09	-0.37**	-0.35**	0.15*
Eversion	0.56**	-0.44**	-0.46**	-0.1	-0.37**	-0.34**	0.17*

**Table 3-8.** Correlations between age, time since stroke, tactile sensation, proprioception, strength and measures of mobility, falls and balance in stroke participants

\*p<0.05; \*\*p<0.01; a: Pearson's product moment correlation; b: Spearman's rank order correlation. Abbreviations: TSS, Time since stroke; WIS, Walking Impact Scale; TUG, Timed up and Go; FES, Falls Efficacy Scale; FRT, Functional Reach Test; COP, Centre of pressure velocity

Weak yet significant and positive correlations were demonstrated between ankle strength and COPvelocity (r=0.15-0.21; p<0.05/p<0.01). Conversely, no significant correlations were found between ankle strength and falls incidence. By comparison, lower limb proprioception (all joints) and distal tactile sensation (toes/feet) were significantly and positively correlated, albeit weakly, with falls incidence (r=0.16 – 0.24; p<0.05/p<0.01). Reduced sensation in these modalities were associated with a higher number of falls. There were also weak and significant negative correlations between distal tactile sensation and the FES (r=0.19-.0.20; p<0.05/p<0.01) in that reduced sensation was associated with a higher FES (i.e. increased fear of falling). No significant correlations were found between proprioception and FES. Weak yet significant correlations were also found between lower limb tactile sensation and proprioception (excluding hip) and the WIS, suggesting an association between sensation and perceived impact of stroke on walking ability.

In light of the association between sensation and falls, and supported by the findings from study 1 (qualitative study), further exploratory analyses were carried out to investigate the relationship between sensation and falls in the stroke group.

#### 3.5.8. Exploratory analysis of factors associated with falls

Factors such as demographics (age, gender), stroke factors (type of stroke, time since stroke, side of stroke), walking aid use, and performance in outcome measures relating to walking, balance and fear of falling were investigated (table 3-9). In addition, differences between the groupings with respect to sensory and motor performance were also analysed (table 3-9). To account for the multiple comparisons, Bonferroni corrections were made with statistical significance adjusted as indicated.

#### Classification of non-fallers, single fallers and repeat fallers

Falls data was collected through retrospective self-report as outlined in the methods section (section 3.4.4.2). Of the 180 participants recruited, falls data was obtained on all 180. When other measures were included in the analysis, these numbers differed slightly and are recorded as appropriate. Of the 180 stroke participants, 108 (60%) reported not experiencing a fall within the preceding three month period. Thirty-nine

participants (22%) reported just one fall (single fallers) and 33 (18%) reported falling at least twice (repeat fallers).

# Analysis of demographics, stroke characteristics and functional scores between stroke non-fallers, single fallers and repeat fallers (table 3-9)

#### **Demographics and falls**

One way groups ANOVA indicated no statistically significant differences between falls grouping and age (p=0.25) although repeat fallers were older than both non- and single fallers. There were also no statistically significant differences between gender and falls grouping (p=0.68) with the proportion of male/females within each grouping reflecting the overall profile of the sample.

#### Stroke related factors and falls

With regard to stroke factors, repeat fallers had lived with their stroke on average six months longer than non-fallers had and 14 months longer than single fallers had. Despite these differences, they were not statistically significant (p=0.32). Stroke type did not differ significantly across the falls groups (p=0.71) with the proportions of haemorrhagic/ischaemic stroke in each falls grouping being similar to that of the overall sample. Further, the side most affected by stroke was not significantly different across the falls groupings as indicated by a chi squared test for independence (p=0.09) with lateralisation similar to that of the overall sample. All stroke participants recorded as having bilateral symptoms (n=11) were in the no falls group.

#### Use of mobility aids and falls

Higher proportions of repeat fallers used walking aids to facilitate indoor and outdoor mobility compared to non/single fallers. Overall 33% (n=11/33) of repeat fallers used a

walking aid indoors compared with 23% (n=9/39) and 25% (n=27/108) of single and non-fallers respectively although these differences were not statistically significant (p=0.56). Similar proportions of each falls grouping report being unable to walk outside at all, with between 4-5% reliant on either a mobility scooter or wheelchair for outdoor mobility. Proportions of repeat fallers using a walking aid during outdoor mobility was marginally higher (48%, n=16/33) than in no fallers (46%, n=48/104) and single fallers (41%, n=16/38) although again, not statistically significant (p=0.95).

#### **Functional outcomes**

Walking speed did not differ significantly across the three fall groupings although repeat fallers were on average 0.2m/s slower than non/single fallers were. Whilst not statistically significant, a change +/- 0.14 m/s represents a clinically important difference (Tilson et al, 2010). Scoring on the WIS was significantly different between the three groups with repeat fallers scoring a mean of 43/60 and single fallers 41/60 and non-fallers 33/60. Follow up Mann Whitney U tests revealed significant difference in WIS score between no falls (Md=33, n=108) and single fallers (Md=41, n=39, U = 1361, z=-3.149, p=0.002, r=0.26). Comparing non fallers with repeat fallers a Mann Whitney U test revealed significant differences in WIS scores (U =1031, z=-3.556, p=<0.0001, r=0.29) indicating repeat fallers perceived their stroke had a greater impact on their walking ability than non-fallers.

Repeat fallers were on average 6 seconds slower than non-fallers on the Timed Up and Go test, but when adjusted with a Bonferroni correction, (0.05/6=0.0083), this difference was not statistically significant (p=0.02).

 Table 3-9 Differences between no-falls, single fallers and repeat fallers in age, stroke factors, walking ability and functional outcomes

Characteristic	No falls (n=108)	Single faller (n=39)	Repeat fallers (n=33)	p value
Age, years, mean (SD)	66.5 (12)	65.5 (11.5)	70 (12)	0.25ª
Gender				
Male	67 (62)	22 (56)	18 (54)	0.68 <sup>b</sup>
Female	41 (38)	17 (43)	15 (45)	
Time since stroke months	33 (46)	25 (44)	39 (58)	0.32 <sup>c</sup>
Type of stroke n (%)				
Haemorrhagic	23 (21)	12 (30)	6 (18)	
Ischaemic	72 (62)	26 (67)	25 (75)	0.71 <sup>b</sup>
Unknown	13 (11)	1 (3)	2 (6)	
Lateralisation n (%)				
Left	47 (43)	19 (49)	17 (51)	
Right	50 (47)	20 (51)	16 (49)	0.09 <sup>b</sup>
Bilateral	11 (10)	0 (0)	0 (0)	
Indoor walking ability n (%)				
Uses aid	27 (25)	9 (23)	11 (33)	OFC
No aid used	81 (75)	30 (77)	22 (67)	0.50
Outdoor walking ability n (%)				
Not able	6 (4)	2 (5)	1 (4)	
Uses aid	48 (46)	16 (41)	16 (48)	0.95 <sup>b</sup>
No aid used	54 (50)	21 (54)	16 (48)	
Functional Outcomes		11(00)		0.053
Gait Speed mys mean (SD)	1.1 (0.5)	1.1 (U.6)	0.9 (0.5)	0.05
wis, median (/60)	33 (14)	41 (12)	43 (12) 22 (46)	<0.0001°*
IUG, seconds mean (SD)	16 (10)	20 (15)	22 (16)	0.02°
FES, median (764)	32 (13)	35 (11)	37 (11)	
Postural sway COP velocity, median mm/s	8.4 (17.5)	8.9 (21)	16.4 (19)	0.07
FRT cm mean (SD)	26 (9)	23 (11)	21 (11)	0.008ª*

\*Statistically significant with Bonferroni adjustments and significance set at 0.05/6=0.0083

a: One way between groups ANOVA; b: Chi Squared test for Independence; c: Kruskal-Wallis Test Abbreviations: SD, Standard deviation; WIS; Walking Impact Scale; TUG, Timed up and go; FES, Falls Efficacy Scale FRT, Functional Reach Test; mm/s, millimetres per second; cm, centimetres Postural sway as measured by mean COP<sub>velocity</sub> did not differ significantly across the three groups (Kruskal-Wallis test, p=0.07) although repeat fallers had a larger postural sway than non- and single fallers did.

One way between groups ANOVA indicated the mean FRT score of 21cm (SD=11cm) in the repeat fallers was significantly lower than non-fallers (mean =26cm; SD=9cm) and single fallers (mean =23cm, SD=11cm) and was statistically significant when adjusted by Bonferroni correction (p=0.008).

A Kruskal-Wallis test indicated there were no significant differences in fear of falling as measured by the Falls Efficacy Scale (FES) between the three falls groups although repeat fallers did score higher on the measure (indicating lower confidence), than both non- and single fallers. When adjusted with a Bonferroni correction (p=0.0083) these differences were not significant (p=0.013).

Follow up analysis carried out between no falls and single falls, and no falls and repeat fallers with respect to the FRT were adjusted with a Bonferroni correction (0.05/2 = 0.025) to account for the two group comparisons. Post hoc comparisons using the Tukey HSD indicated there were no significant difference in FRT scores between the no falls group (mean =26cm, SD=8.8) and single fallers (mean =23cm, SD=11cm; t(140)=2.23, p=0.027). There were however significant differences in FRT scores between no-fallers (mean =26cm, SD=8.8cm) and repeat fallers (mean = 21cm, SD=11cm; t(134)=2.814, p=0.006, two tailed).

# Sensory and motor performance and falls

Further exploratory analyses investigated sensory performance in the EmNSA and

composite ankle strength and falls (table 3-10). A Bonferroni correction was made with

statistical significance adjusted to 0.00625 to account for the eight sensory

comparisons made between falls groups.

Measure	No Falls (n=104)	Single fallers (n=38)	Repeat fallers (n=31)	p value
EmNSA Score (IQR,				
Range)				
Tactile Sensation				
Тое	7 (1, 8)	7 (3,8)	7 (2,6)	0.07 <sup>a</sup>
Foot	7 (1,5)	7 (3,8)	7 (2, 6)	0.06ª
Shin	8 (1,5)	7 (2, 8)	8 (1,6)	0.02ª
Thigh	8 (1,4)	8 (1,6)	8 (1,6)	0.14ª
Proprioception				
Тое	2 (0,2)	2 (1,1)	2 (1,1)	0.006ª*
Ankle	2 (0,1)	2 (1,1)	2 (1,1)	0.04ª
Knee	2 (0,1)	2 (0,1)	2 (0,1)	0.008ª
Нір	2 (2,2)	2 (0,1)	2 (0,1)	0.006ª*
Ankle Composite strength, mean KG	49.6 (24)	46.2 (26)	44.9 (25)	0.462 <sup>b</sup>

**Table 3-10.** Comparison of sensory and strength performance between non fallers, single fallers and repeat fallers (stroke participants)

a; Kruskal Wallis; b One way between groups ANOVA

\* significant at adjusted level of 0.00625 accounting for bonferroni correction (0.05/8=0.00625)

Kruskal Wallis tests indicated no statistically significant differences in tactile sensation between the three falls groupings at the toe (p=0.07), foot (p=0.06), shin (p=0.02) or thigh (p=0.14). Similarly, whilst repeat fallers did show lower scores on ankle composite strength compared to single and non-fallers, a one way ANOVA indicated these differences were not statistically significant. In contrast, statistically significant differences in proprioception between the three falls groups were found at the toe (p=0.006) and hip (p=0.006). Ankle and knee proprioception scores were not statistically significant when adjusted.

Follow up Mann Whitney U tests between no falls v's single falls and no falls v's repeat fallers across total proprioception scores (i.e. all lower limb joints) with a Bonferroni adjustment (0.05/2 = 0.025) to account for the two comparisons (i.e. No falls v's Single falls and No falls v's Repeat falls). There was a significant difference in lower limb proprioception score between the no falls group (Md =8, n=104) and single fallers (Md = 8, n=38) *U* = 1548, z=-2.613, p=0.009, r=0.22). Comparing non-fallers with repeat fallers a Mann Whitney U test also revealed significant differences in lower limb proprioception scores (*U* =1210, z=-2.766, p=0.006, *r*=0.24).

#### 3.5.9. Logistic regression analysis

From the above exploratory analyses, potential predictor variables WIS score, FRT score, and lower limb proprioception scores were all significantly different between no falls/single falls/repeat falls groups with follow up analysis identifying significant differences within the three groups. The inclusion of these variables is also supported by the literature in which perceived walking ability, dynamic balance and lower limb proprioception have been associated with falls and/or functional (dis)ability in neurological populations (Holland et al, 2006; Bladh et al, 2010; Acar & Karantas, 2010; Tyson et al, 2013). Despite a lack of significance between the falls groups in this study, age and time since stroke have been linked with falls incidence (Batchelor et al, 2012) so are also included as predictor variables. In addition, ankle strength, particularly dorsiflexion, has been linked to falls and functional balance (Macrae et al, 1998; Lord

et al, 1991; Kludig & Gajewski, 2009). In this study, composite ankle strength showed strong correlations with the FES, with low falls efficacy linked with increased falls incidence in studies of the elderly (Delbaere et al, 2010) and stroke (Belgen et al, 2005).

The six potential predictor variables included in logistic regression are therefore: Age, time since stroke, Walking Impact Scale (WIS); the Functional Reach test (FRT); and at impairment level, the EmNSA lower limb proprioception score, and ankle composite strength.

Further analysis of single fallers and repeat fallers for each of the variables was carried out with no statistically significant differences identified (unpaired t test, p>0.05) suggesting single fallers and repeat fallers share similar predictor variable characteristics (table 3-11). In light of this, and in line with falls studies in stroke (Batchelor et al, 2012; Schmid et al, 2013; Weerdsteyn et al, 2008), single fallers and repeat fallers were recoded and categorised as "fallers" and non-fallers categorised 'non-fallers. The dichotomous dependent variable for use in logistic regression analysis was thus faller/non-faller. **Table 3-11.** Comparison of single fallers and repeat fallers in predictor variables (stroke participants)

Variable	Single fallers	<b>Repeat fallers</b>	p value
	(n=38)	(n=31)	
Age, years mean (SD)	65.5 (11.5)	70 (12)	0.128ª
Time post stroke, months mean (SD)	25 (44)	39 (58)	0.224 <sup>b</sup>
EmNSA Total Proprioception score, median (IQR, Range)	8 (2,4)	8 (2,4)	0.909 <sup>b</sup>
Functional Reach Test cm , mean (SD)	23 (11)	21 (11)	0.619ª
Walking Impact Scale, mean (SD)	41 (12)	43 (12)	0.445 <sup>b</sup>
Ankle Strength, kg, mean (SD)	46.2 (26)	44.9 (25)	0.72 <sup>a</sup>

a: Independent samples t-test; b Mann Whitney U test. Abbreviations: SD, Standard deviation; EmNSA; Erasmus MC Nottingham Sensory Assessment; IQR, Inner Quartile Range; cm, centimetres; kg, kilogrammes.

# Analysis of predictor variables

Values for the six potential predictor variables are summarised in table 3-12 with falls

classification recoded and categorised as fallers or non-fallers. Three of the six

predictor variables show statistically significant differences between fallers and non-

fallers.

 Table 3-12. Differences between fallers and non-fallers in predictor variable performance

I

(stroke participants)

Predictor	All participants (n=174)	Non Fallers (n=104)	Fallers (n=70)	p value
Age, mean years (SD)	67(11)	66(12)	67 (11)	0.648ª
Time Since stroke, mean months (SD)	33 (48)	34.5 (47)	31(50)	0.909 <sup>b</sup>
Lower limb proprioception, median (IQR, range)	8 (1, 4)	8 (0,3)	8 (2, 4)	0.001 <sup>b</sup>
Walking Impact Scale, median (IQR)	37 (14)	33 (23, 48)	44 (18, 47)	<0.001 <sup>b</sup>
Functional Reach Test, mean cm	24.6(10)	26.4 (8.9)	22.2 (11)	0.003ª
Ankle Composite Strength, mean, kg	47.6 (25)	49.6 (24.4)	45.1 (25.2)	0.235ª

a: independent samples t-test; b Mann Whitney U test. Abbreviations: SD, Standard deviation; EmNSA; Erasmus MC Nottingham Sensory Assessment; IQR, Inner Quartile Range; cm, centimetres; kg, kilogrammes

# Logistic regression analysis: full model

Direct logistic regression was performed to assess the impact of a number of factors on the likelihood that stroke participants had reported one or more falls in the last three months. Assumptions of multi-collinearity, normality, and outliers were all met following diagnostics. Pearson product moment correlation coefficient values between independent variables did not exceed r=0.7. Case-wise diagnostics found three cases with standardised residual values greater than +/- 3.3 indicative of outliers. Evaluation of these outliers found a Cook's distance of 0.429, below the 1.0 threshold value suggested by Tabachnick & Fidell, (2013, p.75), indicating they had no undue influence on the regression model overall.

The model contained six independent variables (age, time since stroke, lower limb proprioception scores, WIS score, FRT score and ankle composite strength). The full model containing all predictors was statistically significant  $X^2$  (6, N=165) = 25.20, p<0.001, indicating that the model was able to distinguish between participants reporting falls and those reporting no falls. The model as a whole explained between 14.2% (Cox and Snell R squared) and 19.1% (Nagelkerke R squared) of the variance in falls status, and correctly classified 66.7% of cases. As shown in table 3-13 only two of the independent variables made a unique statistically significant contribution to the model: lower limb proprioception and WIS.

The strongest predictor of falls reporting was lower limb proprioception with an odds ratio of 0.66. As this was less than 1, this indicates that for every point decrease in proprioception score (i.e. poorer proprioception), participants were 0.66 times more likely to report one or more falls, controlling for all other factors in the model. In other words, there is a 34% reduction in the likelihood of reporting a fall with every point increase in the proprioception score.

The WIS had an odds ratio of 1.05. This indicated that for each point increase on this scale (indicating greater perceived impact on walking), participants were 5% more likely to report one or more falls, when all factors are controlled for. Apart from the WIS and proprioception, the 95% CI crossed 1.

		S.E.	Wald		р	Odds Ratio	95% CI for Odds ratio	
Variable	В			df				
							Lower	Upper
Age	0.002	0.017	0.009	1	0.925	1.01	0.98	1.04
Time post stroke	-0.001	0.004	0.11	1	0.740	0.99	0.99	1.01
Proprioception	-0.409	0.172	5.667	1	0.017*	0.66	0.47	0.92
FRT	-0.032	0.024	1.793	1	0.181	0.97	0.93	1.01
WIS	0.044	0.015	8.23	1	0.004*	1.05	1.02	1.08
Ankle Strength	0.010	0.009	1.319	1	0.251	1.01	0.99	1.03
Constant	1.199	2.255	0.283	1	0.595	3.32		

**Table 3-13** Logistic regression of factors predicting likelihood of reporting one or more fallin stroke participants

Abbreviations: FRT, Functional Reach Test; WIS, Walking Impact Scale; CI, Confidence Interval

\*p<0.05

#### 3.6. Discussion

This study investigated the prevalence and distribution of lower limb somatosensory impairments in chronic stroke and the association between these impairments, ankle strength and functional measures of walking, balance and falls. It demonstrated that somatosensory deficits were evident in the majority of the 180 stroke participants who were on average 33 months post stroke onset. Overall, three guarters (74%, n=123/167) of this study sample had absent or impaired tactile sensation in at least one modality, in at least one part of the lower limb, most frequently sharp-blunt discrimination in the toes. It further found absent or impaired proprioception in 28% (n=49/173) of participants in at least one lower limb joint, with proportions of impairment greater in distal joints (toes and ankle) than proximally. Applying a previously used, albeit arbitrarily defined impairment cut off (i.e. ≤6/8 in any one modality), this study indicates that 59% of chronic stroke survivors experience some form of lower limb tactile deficit, with 21% having impaired lower limb proprioception. This study identified significant but weak associations between lower limb sensation, balance and fall. Worse toe and hip proprioception and distal (toe and foot) tactile sensation was associated with an increased incidence of reported falls, with reduced distal tactile sensation further associated with a greater fear of falling. Poorer distal proprioception was also associated with an increased postural sway. These associations, whilst statistically significant, were all weak (r=0.12-0.24). In contrast, greater ankle strength was strongly and significantly associated with better performance in all measures of mobility and balance, but was not significantly associated with fewer falls. That ankle strength was related to such functions was

unsurprising and adds to previous findings (van Swigchem et al, 2013; Kluding & Cajewski, 2009) so was not pursued further in this thesis, either independently or as a composite measure with sensation.

Correlational analysis and logistic regression analysis further identified a significant predictive value of lower limb proprioception and perceived impact of stroke on walking ability and falls. Lower limb proprioception and the Walking Impact Scale (WIS) were significant factors in predicting whether a fall was reported or not when other predictor variables were controlled for. Age, time since stroke, dynamic balance and ankle strength did not contribute significantly to the logistic regression model. Despite the significance, lower limb proprioception and WIS accounted for just 13%-19% of the variance suggesting other variables impact falls incidence and reporting. What this study did highlight is an association, albeit weak, between sensation (proprioception) and falls reporting. Whilst a focus on sensation may be seen as somewhat reductionist, the role of several other variables and in particular strength is recognised and should therefore be evaluated using a comprehensive assessment to examine these multiple factors. The purpose of this thesis however was to focus on the less explored area of sensation.

The demographic profile of the stroke group in this study is similar to that of other studies in which ambulatory chronic stroke survivors have been investigated (Durcan et al, 2016; Robinson et al, 2011; Lee et al, 2015) indicating it is largely representative of chronic ambulatory stroke survivors. This stroke sample had similar levels of walking ability and walking aid use compared to stroke populations in other studies (Blennerhasset et al 2012; Lee et al, 2015) and had levels of falls in line with previous

studies (Hyndman et al, 2002; Mackintosh et al, 2005; Blennerhasset et al, 2012). The control group reported substantially lower levels of falls than other studies of elderly groups (Lord et al, 1991; Rubenstein et al, 2006) so were perhaps not representative of the healthy population aged 65+ in relation to falls. Minimal walking aid use in the control sample, with no single participant using a walking aid indoors and only 11% using an aid whilst walking outdoors, suggests they were active, able elderly.

The prevalence and distribution of somatosensory deficits found in this study are broadly in line with that of other studies, which suggest for the most part, somatosensory impairments in approximately 50-60% of acute/sub-acute stroke survivors (Carey & Matyas, 2011; Tyson et al, 2008; Connell et al, 2008). A large range of prevalence rates have been reported in studies of somatosensory deficits among different cohorts of stroke participants. At one extreme, Kim & Choi-Kwon (1996) found 57 out of 67 (85%) of their sample of acute stroke (7 days post onset) had impaired texture discriminative function in the hand. Conversely, Schmid et al (2013) found sensory loss in the feet of their chronic stroke sample (mean 7 years post onset) as low as 7% using the National Institutes of Health Stroke Scale (NIHSS). The different populations studied and the different body parts assessed could explain such variability, but a proportion of variance may be due to the properties of the sensory tests used and the modality assessed. Kim & Choi Kwon's study, for example, involved a series of challenging higher-level sensory discrimination tasks such as stereognosis, texture discrimination, two-point discrimination, and graded position sense discrimination. A battery of tests such as this will arguably identify very mild and subtle sensory deficits and thus report higher prevalence levels. In contrast, Schmid et al (2013) employed the sensory subtest of the NIHSS, which assesses detection to pain

through pinprick. Cross study comparisons of prevalence rates are therefore likely to be of limited value, as variations in assessment methods and population demographics influence prevalence variance.

The results of this study indicate that in the chronic phase of stroke, deficits in tactile sensation are more common than deficits in proprioception. As with overall prevalence figures, the findings from other studies report marked differences in the relative proportions of tactile and proprioceptive deficits with higher number of proprioceptive impairments reported (Carey & Matyas, 2011; Connell et al, 2008) alongside other studies showing higher number of tactile deficits (Tyson et al, 2013; Tyson et al, 2008; Winward et al, 2007). Further still, reports of the relative proportions of tactile and proprioceptive impairments can vary substantially in the same sample depending on the sensory measure used (Meyer et al, 2016).

Similar to this study, Tyson and colleagues (2008; 2013), Connell et al (2008), Meyer et al (2016) and Winward et al (2007) used multimodal standardised sensory tests in acute/sub-acute patients post stroke. Tyson et al (2008) using parts of the Rivermead Assessment of Sensory Perception (RASP), found very similar prevalence levels to this study with absent/impaired tactile sensation in the lower limbs evident in 63% of their acute/sub-acute participants. Distinguishing between tests of tactile detection and tactile discrimination (localisation of stimulus), they found 62% of their sample impaired in lower limb sensory discrimination and 41% absent or impaired in lower limb tactile detection. Similar to this study, proprioceptive deficits were much lower than tactile deficits with absent or impaired proprioception occurring in 24% of their sample (Tyson et al, 2008).

More recently a pooled analysis of lower limb sensory data from five studies comprising 459 acute/subacute stroke (mean =19 days post onset; SD=35 days) (Tyson et al, 2013) found lower limb tactile and proprioception detection and discrimination was absent or impaired in 45% of participants overall. Tyson et al (2013) found tactile sensation was impaired in 39% of their sample whereas proprioceptive impairments were reported in 24%, levels similar to this study. Winward et al (2007) found substantial variations in tactile and proprioceptive ability but overall most patients had recovered most somatosensory abilities by six months. They assessed nine patients at six months post stroke using the RASP and found six out of nine (67%) scored between 97-100% on proprioception with all nine scoring at least 80%, and deemed as having intact proprioception. Five of the nine patients scored 100% on pressure sensation with only one of the nine deemed to have demonstrable sensory loss of surface pressure. Similarly, five out of nine scored >80% on tests of sharp blunt discrimination. Drawing comparisons and conclusions from such a small sample, however, should be undertaken cautiously.

Differing levels of tactile and proprioceptive impairment in chronic stroke may have various interpretations. Firstly, lower reported levels of proprioceptive deficit may be due to lower levels of proprioceptive deficit. There are multiple conscious and subconscious afferent inputs, which provide proprioceptive information, so the degree of sparing of some proprioceptive pathways may be greater than in tactile sensation. Despite sharing a common pathway of the dorsal column, differing levels of impairment between light touch and proprioception also suggest impairment in one does not necessarily result in impairment in the other. Secondly, recovery of proprioception over time may differ compared to tactile sensation. Longitudinal

studies have shown greater recovery of proprioception six months after stroke (Connell et al, 2008; Winward et al, 2007). This could reflect differences in adaptive changes in the two systems. It could also reflect the growing belief that active movements contribute to proprioceptive inputs (Goble et al, 2010; Proske & Gandevia, 2012), so movement occurring during ambulation may naturally facilitate lower limb proprioceptive recovery.

In contrast to this study, Connell et al (2008) in their study of 70 acute (median 15 days post stroke onset) using the Nottingham Sensory Assessment (NSA) (Lincoln et al, 1991) found proprioceptive impairment overall was (marginally) more common than tactile sensation. Exteroceptive deficits in the lower limb ranged from 25%-51% of participants whereas lower limb proprioceptive deficits at the ankle, knee and hip were 34%, 52% and 51% respectively, much higher than in this study. One plausible explanation may be the increased sensitivity of the proprioceptive component of the original NSA, which assesses several aspects of proprioception such as appreciation of movement, direction of movement and joint position sense. The proprioceptive component of the EmNSA and the RASP, used in Tyson et al's (2008) and Winward et al's (2007) study, assess movement detection and movement direction, but not joint position sense. Movement detection/direction and position sense are distinct and separate constructs of proprioception (Goble, 2010; Proske & Gandevia, 2012; Han et al, 2016) so by assessing both JPS and movement, the original NSA is possibly identifying impairment in both constructs with greater sensitivity than the EmNSA and RASP.

Whilst cross study comparisons are often confounded by differences in sample characteristics, the differing reports of "impairment" prevalence can also be illustrated by a recent study of upper limb somatosensation in sub-acute stroke (n=122, median 82 days post stroke, IQR 57-132 days) by Meyer et al (2016). The authors assessed their cohort using two standardised measures of tactile sensation (the EmNSA and Perceived Threshold to Touch test), two measures of proprioception (EmNSA and the Thumb Finding Test - TFT) and three measures of higher cortical sensory tests. Impairment prevalence levels between the different tactile and higher cortical measures were not substantial. In contrast, upper limb proprioception, assessed with the EmNSA, categorised 23% of their sample impaired. By comparison, the TFT categorised 54% of the sample had impaired proprioception.

It is clear that varying levels of proprioception reported may, in part, be due to both measure accuracy and interpretation of measure score. The EmNSA assesses passive movement detection and direction discrimination at each of the four lower limb joints. In this test, participants indicate whether they feel the limb moving, and if so, the direction in which the limb was moved. The manual application of this approach exposes it to unquantifiable and non-standardised movement speeds, varying tactile input through handling, and questionable accuracy due to the (often visual) estimation of the degree of movement occurring before detection is reported. Further, the use of an ordinal scale in the EmNSA such as absent/impaired/normal, means it is potentially less responsive to change (Hicks, 2004), prone to ceiling effects (Lin et al, 2004) and the summation of ordinal data to represent a total score does not provide an indication of severity (Fawcett, 2007; Hicks, 2004). Inevitably, such methods and the use of their scoring have drawn widespread criticism in both research and clinical

reviews (Elangovan et al, 2014; Hilier et al, 2015; Han et al, 2016; Suetterlin & Sayer, 2014). The upshot is that they are postulated as somewhat crude screening measures, which may detect profound proprioceptive deficits but are unlikely to detect mildmoderate impairments. They are suggested as unsuitable for research purposes or to detect the impact of rehabilitation interventions (Elangovan et al, 2014). In this study, 72% of stroke participants and 100% of control participants scored the maximum 8/8, suggestive of significant ceiling effects and poor sensitivity in the proprioceptive component of the EmNSA.

Whilst the above studies provide some comparative illustration regarding the extent of somatosensory dysfunction, presenting single figures to represent "somatosensory impairment" should be viewed with caution. Most standardised measures assess several modes or aspects of tactile sensation and proprioception using an ordinal scale, so summing ordinal scores to provide a single figure, to represent "impairment" overall is potentially misleading. Whilst tactile modalities have been shown to be quantifiably distinct (Winward et al, 2007; Connell et al, 2008) and highly inter-related (Tyson et al, 2008; Stolk-Hornsveld et al, 2006), the summation of several ordinal scores to provide a total tactile sensory score does not indicate the nature or severity of somatosensory impairment. Further, it is not statistically robust. For example, a summed score of 35/40 on the EmNSA may result in a "normal" classification overall, yet substantial impairment in one or more modalities or body areas could still be present.

Secondly, describing a sample using dichotomous categories of impaired/not impaired requires the determination of a cut-off point. Any cut-off score should be established

through robust psychometric analysis not arbitrarily defined, as the relative proportions of those falling above and below the cut off, will determine the reported extent and prevalence of somatosensory deficits. If arbitrary cut off scores are employed, the concern is that individuals with impairment in a single modality in single or multiple areas, may be excluded from analyses and prevalence figures distorted. For example, a cut-off score could be derived from the healthy age matched control data (n=46) in this study in which no one control participant scored lower than 34/40 on the EmNSA. This score could arguably be an appropriate cut off. Using this cut-off, 19% (n=31/163) of this study sample could be categorised "impaired", much lower than the 74% (n=123/163) who had absent or impaired sensation in at least one sensory modality in one body part. Clearly, a measure in which sensitivity and specificity has not been established may inaccurately report impaired/not impaired. Such difficulties are inherent within the EmNSA in which sensitivity and specificity have not been established so whilst an arbitrary cut of point of  $\leq 6/8$  for each modality has been used previously (Meyer et al, 2016) this is not universally agreed or psychometrically established. One of the ironies of measures such as the EmNSA, is that for the large part, they are clinically feasible and easy to use, yet interpreting their results is less than straightforward. Whilst they continue as the mainstay for somatosensory assessment, it appears important to clarify the modality (type) and the body area (location) assessed rather than simply presenting an overall figure to inform treatment-planning decisions.

Results of this study indicate that the sensory modality most affected by stroke is sharp-blunt discrimination with 56% of the study sample scoring ≤6/8 across the lower limbs. By comparison, impairment in other tactile modalities was much lower, with
between 15%-25% of stroke participants impaired in light touch, pinprick and pressure. There are several possible explanations for these results. Firstly, success in a test of tactile discrimination requires at the very minimum, intact detection. Impairment levels in discrimination tests should theoretically be at the very least the same as detection, or higher as is demonstrated in most studies (Tyson et al 2008, 2013; Meyer et al, 2016; Carey & Matyas, 2011; Connell et al, 2008). Borstad & Larsson (2014) propose a somatosensory hierarchy whereby tactile detection requires lower level processing and tactile discrimination requiring higher level cortical processing. Most notably Carey and colleagues, who have observed the neural correlates of upper limb tactile discrimination and demonstrated the association with functionally relevant outcomes (Carey & Matyas, 2005; 2011; 2016), have demonstrated this in multiple studies. The implication being that impairment to sharp-blunt discrimination is higher in this stroke population compared to exteroceptive detection tests such as light touch etc., because tests of discrimination place greater emphasis on higher cortical processes. However, it must also be recognised that tests of discrimination are more susceptible to other factors, which may influence the outcome, particularly when the outcome is based on subjective reporting of somatosensory perception. Factors such as comprehension, attention, recall and fatigue are intrinsic to the accurate processing of subjectively reported sensation, and are frequently reported sequelae of stroke (Makin et al, 2013). Separating the relative contribution of attention, for example, in poorer performance in a test such as sharp-blunt discrimination, was not possible in this study where a standardised test of attention was not administered.

Whilst the higher cortical processes required for sharp-blunt discrimination may explain in part why it was impaired in more participants, this study also found greater

impairment levels distally than proximally, which is broadly in line with other tactile modalities (Meyer et al, 2016; Busse & Tyson, 2009; Tyson et al, 2008; Connell et al, 2008), and somatosensory cortex somatotophy (Holmes 1927; Kandel et al, 2013). However, the distal-proximal difference in sharp-blunt discrimination was much greater than other modalities. Seventy-one percent of participants had absent or impaired sharp-blunt discrimination in the toes, with 32% absent or impaired at the thigh. Conversely, the difference in proportions of absent/ impaired sensation distally (toes) to proximally (thigh) were much smaller in the other tactile modalities. Light touch was absent/impaired at the toes in 25% and at the thigh in 11%. Similar differences were found across pressure (17% and 10%) and pin prick (15% and 10%) for toes and thigh respectively.

The proximal-distal differences in sharp-blunt discrimination may be explained in simple terms related to both the validity and reliability of sharp-blunt testing, particularly in the toes. Testing sharp blunt in the toes is less reliable than in other parts of the lower limb. Stolk-Hornsveld et al (2006) reported intra-rater reliability of sharp-blunt testing in the toes with a weighted kappa value of 0.58-0.83, the foot (0.82-0.90) the shank (0.69-1.00) and the thigh (0.71-0.89). Measurement error may contribute in two ways. Firstly, there is potential for the force of application of the sharp and blunt stimuli to vary over the three trials as it is manually applied. Secondly, and more pertinently, the functional wear-and-tear and day-to-day shearing forces at the plantar aspect of the toes is different from that of the rest of the lower limb and upper limb. The formation of calloused, thick hard skin on the plantar aspect of the toes is different from that skin on the plantar aspect of the toes is different from that skin on the plantar aspect of the toes is not uncommon. The thick skin is likely to mean that the sharp stimulus becomes

imperceptible. Random error and incorrect responses to sharp-blunt are possibly confounded by peripheral dermal changes, not stroke related sensory deficits. The scoring system of the EmNSA is such that just one wrong answer from three trials results in a submaximal score and two wrong results, in a classification of impaired. False positives may therefore arguably be due to random error and poor reliability due to hard skin and/or non-uniform application of the stimulus. It may explain why 29% of participants in this study had impaired sharp-blunt discrimination only, much higher than recent study of the hand in which 13% had sharp-blunt impairment in isolation (Meyer et al, 2016). It may also explain why 50% (n=23/46) of controls in this study scored sub-maximally in sharp-blunt testing with the vast majority of these (n=21/23) showing deficit in the toes only. Whilst ageing can result in a deterioration in somatosensory function, performance disparity on tests of touch detection and discrimination is not significant (Dunn et al, 2015). The almost exclusive sub-maximal scoring in distal sharp-blunt discrimination and not exteroceptive or proprioceptive modalities in a healthy population challenges the validity of sharp-blunt testing in the feet/toes. The use of sharp-blunt discrimination test as a measure of higher cortical somatosensory processing may be more suited to the hand and upper limb where it corresponds with other measures of higher cortical processing (Meyer et al, 2016).

Difference was also found between distal and proximal proprioception with 30% absent/impaired in the toes and just 3% impaired proximally at the hip. Some have found greater deficits in hip proprioception than ankle proprioception (51% v's 34%) (Connell et al, 2008) whereas others report greater impairment distally than proximally (Stolk-Hornsveld et al, 2006; Lincoln et al, 1998). Clinical convention suggests that if toe proprioception is intact, it is assumed that larger, more proximal joints will also be

intact. The theoretical underpinnings behind this proximal-distal disparity are multifaceted. One explanation is underpinned by the bilateral projections of sensory ascending pathways, which transmit proprioceptive information. It has been demonstrated that bilateral premotor cortices, cerebellum and putamen are involved in the processing and integration of somatosensory afferents (Amaral, 2013; Pearson & Gordon, 2013; Preusser et al, 2015) with bilateral deficits occurring in 16-20% of stroke survivors following contralateral stroke (Carey & Matyas, 2011; Yalcin et al, 2015; Connell et al, 2008). Given these bilateral pathways, Lu et al (2000) further demonstrated that proprioceptive information is not processed bilaterally for all parts of a limb with proprioceptive afferent inputs from proximal musculature processed bilaterally whereas afferents from distal segments are processed in the contralateral (affected) hemisphere only (Lu et al, 2000). A second potential explanation relates to the mechanical properties and proportional changes in the muscle fascicle lengths. Refshauge et al (1995) reported that the stimulus threshold for muscle spindles, which indicates fascicle length changes, are much higher (i.e. poorer) at the toe, than those of the more proximal joints, resulting in poorer proprioceptive acuity distally compared to proximally.

This study also demonstrated that the somatosensory profile and distribution of deficits in the lower limb were split almost equally between single modality and multiple modality deficits. In the 96 stroke participants that had some form of somatosensory deficit, 49% (n=47/96) had a deficit in two or more sensory modalities (i.e. exteroceptive/sharp blunt/proprioception). The remaining participants (51%, n=49/96) had a deficit in just one sensory modality (i.e. proprioception or exteroception or sharp-blunt) with only two participants having a pure proprioceptive

deficit and one participant having a pure deficit in exteroception. The vast majority of deficits in a single modality (i.e. n=46/49), occurred in sharp-blunt discrimination, and as discussed earlier, mostly occurred in the toes. In comparison, Meyer et al (2016) found broadly similar proportions of multiple v's single deficits with 43% demonstrating deficit in one modality only and 57% having deficits in two or more modalities.

This study also found that most chronic stroke survivors experience a combination of proprioceptive and tactile deficits with just two of the 35 participants recording a proprioceptive deficit in isolation. It suggests that tactile and proprioception impairments are closely linked and often experienced in tandem. It also indicates that those with proprioceptive deficits are also likely to have tactile deficits whilst those with tactile deficits will not necessarily have proprioceptive deficits. This has clear implications to the assessment of somatosensation in clinical practice. The administering of just light touch and proprioception to gauge somatosensory ability has been used in other studies (Tyson et al, 2008; Lin et al, 2005) and appears to be mirrored in current clinical practice with the majority of physiotherapists and occupational therapists assessing light touch and proprioception only (Pumpa et al, 2015). This practice fits with anatomical and neurophysiological understanding of the mechanisms that underpin somatosensation. Both light touch and proprioception are transmitted via the dorsal column medial lemniscus into the primary somatosensory cortex via the thalamus. Whilst they project into different Broadmann's areas of the somatosensory cortex, it is easy to understand how an infarct affecting the cortex, which is supplied by the middle cerebral artery (MCA), could affect aspects of both tactile sensation and proprioception. However, anterior and posterior spinocerebellar

pathways also project proprioceptive information into the cerebellum (Amaral, 2013; Bosco & Popple, 2001) so an infarct that affects the somatosensory cortex and thus tactile sensation, may not necessarily affect proprioceptive afferents (Maschke et al, 2003). A deficit in proprioceptive ability on its own due to a central cause is thus difficult to envisage due to the multiple combined and isolated pathways and projections of both tactile and proprioception afferents. It may also explain why proprioception was less impaired compared to tactile sensation.

A further objective of this study was to compare lower limb sensory performance between stroke participants and age matched healthy controls. Lower limb somatosensory ability declines with age, with deterioration demonstrated in peripheral nerve function (Ward et al, 2016), plantar tactile sensitivity (Qui et al, 2012), tests of texture discrimination (Carey et al, 1997; Miller et al, 2009), and lower limb proprioception (Goble, 2010; Ko et al, 2015; Deshpande et al, 2010; Wingert et al, 2014). Age related decline in somatosensory ability has been associated with reduced standing and dynamic balance performance, gait speed and falls (Deshpande et al, 2010; Lord et al, 2003). In line with expectation, this study found statistically significant differences in overall tactile and proprioceptive ability between stroke and healthy control participants. Somewhat surprisingly, the differences in light touch, pin prick and pressure sensation were not significant when allowing for the multiple comparisons and a Bonferroni adjustment. Once significance levels were adjusted, only sharp-blunt discrimination at each body part and proprioception at the toe was significantly different between stroke and controls. Part of this explanation may lie in the higher cortical demands of sharp-blunt discrimination discussed earlier, with the sequalae of stroke more likely to impact on such processes. Secondly, differences in

the recovery of individual sensory modalities may lead to stroke and control participants being similar in certain sensory abilities, particularly in a chronic cohort as used in this study. Whilst such differences in recovery have been demonstrated, there are insufficient studies of chronic stroke and somatosensation in which to compare these results and draw conclusions.

A further objective of this study was to investigate the association between lower limb somatosensory and functional measures in ambulatory stroke. This study identified several statistically significant, but weak correlations between lower limb somatosensation and measures of balance and falls, but not gait.

Tactile sensation at the toes and foot were significantly, but very weakly correlated (r=0.16-0.20) with falls reporting and fear of falls. Most notably, lower limb proprioception impairment, distal from the knee, was associated with falls reporting. Intuitively, impaired somatosensation, particularly proprioception, should play a key role, in falls and falls risk in a community dwelling population. The findings from the qualitative study (study 1) support this, with reports of not knowing foot position and misjudging step heights implicated in catching toes, tripping and falling. In community dwelling people with stroke, falls differ from those occurring in inpatient and/or rehabilitation settings with, for example, falls tending to occur during dynamic activities such as walking, and obstacle avoidance (curbs, uneven pavements, thresholds) rather than during transfers (Schmid et al, 2013; Batchelor et al, 2012). The implication being that lower limb JPS awareness should play a greater role in falls in an ambulatory community dwelling stroke population than tactile sensation.

disturbance, 1A afferent (proprioceptive) muscle spindles are excitated, triggering a stretch reflex, and a subsequent corrective motor response (Grey et al, 2004). It is proposed that such feedback mechanisms from stretch sensitive proprioceptive mechanoreceptors provide not only sense of joint position, so may be implicated in avoiding potential trips, but they are also key in detecting sudden perturbations during a trip or balance disturbance (Grey et al, 2004). Impairment to this neural pathway is implicated in slower responses to perturbation, and suggested to be an unrecognised falls determinant (Marks, 2015).

Empirically, hip and knee proprioception performance error is moderately correlated with precision obstacle crossing (Qaiser et al, 2016) and poor hip JPS in the elderly is related to lower performance on dynamic measures of balance but not static balance (Wingert et al, 2014). People with stroke commonly report 'losing balance' or 'misjudgement' (e.g. misjudging step height) as being the reason for a fall (Hyndman et al, 2002; Batchelor et al, 2012). For example, studies have shown that even when people with stroke are able to walk without physical assistance, complex walking tasks such as obstacle crossing are impaired (Den Otter et al, 2005; Said et al 2008) and those who fail such task have a higher incidence of falls (Said et al, 2013).

In contrast to the findings from this study, lower limb somatosensation is rarely demonstrated as a factor in falls studies of chronic stroke. Multiple factors are implicated in falls, such as polypharmacy, environment, fear avoidance, with physical impairments not necessarily associated with falls at all (Schmid et al, 2013; Robinson et al, 2011; Durcan et al, 2016; Hyndman et al, 2002). Falls are complex in terms of how they are measured, reported and in terms of the factors which contribute to them

(Batchelor et al, 2012). A lack of association could, at least in part, be explained by the accuracy/sensitivity of measures used to assess both falls and sensory function. Schmid et al (2013) for example, investigated 160 chronic stroke participants using amongst other measures, the National Institutes of Health Stroke Scale (NIHSS). They report no significant difference (p=0.75) in tactile sensory function between those who reported falling at least once (n=53) and those who reported they had never fallen (n=107). The implication being that sensory function is not a factor in falls. The impairment-focussed scale provides categorical classifications of no sensory loss, mild-moderate loss or severe loss, to pin prick alone. It is a crude screening measure of protective sensation (pain) predominantly used in the acute setting. It is unsurprising, therefore, that somatosensory function was not a significant predictor. A further study by Robinson et al (2011) investigated the physical factors related to community ambulation and falls in 30 chronic stroke participants (time since stroke= 39 months, SD = 26 months). Lower limb somatosensory function was assessed using a Q-tip (cotton bud) to assess tactile sensibility and passive movement detection sense at the 1st metatarsal joint. Sensory function again was not significantly associated with falls and was not considered a significant factor in community ambulation. In contrast, Soyuer & Ozturk (2007) investigated the relationship between stroke lower limb proprioceptive impairments and falls in 100 chronic stroke participants. Knee JPS error, measured using contralateral reproduction of JPS, was not significantly different between nonfallers and single fallers but was significantly worse (p=0.001) in repeat fallers compared to non-faller/single fallers.

Whilst lower extremity somatosensory impairment has been implicated in falls of the elderly (Ward et al, 2016; Lord et al, 1991), its role in stroke, MS and Parkinson's is

equivocal (Carpenter and Bloem, 2011; Schmid et al, 2013; Hoang et al, 2016). Stroke severity or related impairments, for example, do not necessarily translate into increased falls. Schmid et al, 2013, found neither stroke severity nor any of the individual components of the neurological examination (such as leg weakness, sensation or ataxia) were associated with fall risk. Similarly, Hyndman et al (2002), found no differences in mobility or motor control, between fallers and non-fallers. Such findings may for example, be explained by factors such as self-imposed reduced activity levels, irrespective of physical ability. Several studies have suggested that the incidence of falls may be reduced due to participants 'shrinking their life-space' (Ward-Griffin, 2004), limiting their activities (Schmid et al, 2009) and through social isolation (Salter et al, 2008). Through behavioural modification, it is plausible that those with greater levels of physical disability may experience fewer falls. In contrast, improved physically ability and greater activity levels may increase falls, as has been shown in elderly men (Chan et al, 2006). Furthermore, factors such as impulsivity and risk-taking behaviour, have been demonstrated to be an independent risk factor for falls in the elderly (Butler et al, 2015) and are implicated in those with Parkinson's who fall (Smulders et al, 2014), but have yet to be substantiated in stroke. Such factors would potentially confound the association between physical impairments and falls further. Other non-physical factors such as cognitive functioning have also been implicated in falls, as individuals with stroke are more likely to fall when walking, particularly when increased cognitive control is required. Studies of cognitive-motor interference have shown that following stroke, those who fall are more often unable to walk and talk at the same time or tend to slow down when performing a concurrent mental task (Hyndman et al, 2006; 2004).

The definition of what constitutes a "faller" is further open to interpretation with the suggestion that single fallers share similar characteristics as non-fallers and should be categorised as non-fallers (Gunn et al, 2013; Soyuer & Ozturk, 2007; Belgen et al, 2006). In contrast, single fallers have also been grouped together with repeat fallers forming a falls group in various studies (Batchelor et al, 2012; Schmid et al, 2013; Weerdsteyn et al, 2008) so there is inconsistency in the literature. In this study, exploratory analysis as part of the logistic regression analysis found that single fallers and repeat fallers did not differ significantly in terms of age, time since stroke, lower limb proprioception, Functional Reach Test, Walking Impact Scale or ankle strength. Conversely, fallers and non-fallers did differ significantly in their performance on proprioception, the Functional Reach Test and Walking Impact Scale.

That gait speed was not significantly related to lower limb somatosensation in this study is not surprising as reports of associations between gait speed and lower limb somatosensation are limited or certainly tenuous. Lee et al (2015) found in their cohort of chronic, community ambulatory stroke participants (>6 months post onset) a weak but statistically significant correlation (r=0.29; p<0.05) between lower limb somatosensation and self- paced gait speed. Hsu et al (2003) used the sensory subtest of the Fugl-Meyer Assessment (FMA-S) and found moderate and significant correlations between lower limb sensation scores (tactile and proprioception) and gait velocity (r=0.40; p<0.05). In contrast, (Tyson et al, 2013) pooled the data of 459 acute-6 months post stroke patients from five studies for analysis with only lower limb weakness found to be an independently significant predictor of mobility (p<0.01) and balance (p<0.01). Lower limb proprioception and tactile sensation, combined and independent, did not predict mobility (p=0.12) or balance (p=0.07) but did predict

ADL's (p=0.04). The limited evidence of an association between lower limb sensation and gait speed could not be supported by this study. A lack of association may be partly explained by the use of gait speed as a measure. The ability to generate a reciprocal gait pattern, in a flat, well-lit environment may not necessarily require intact supra-spinal sensory-motor cortical structures. Animal studies indicate that reciprocal lower extremity motor activity is largely automatically driven at a sub cortical, spinal cord level by spinal networks or central pattern generators (CPG's) for locomotion (Guertin, 2009; Whelan et al, 2000). Although compelling, the evidence is mostly limited to animal studies with limited evidence in humans (Dimitrijevic et al, 1998). Despite this, the existence of spinal CPG's for locomotion in humans is highly likely (see Guertin, 2013 for a review) although the unique attributes of human gait may, to some extent, be associated with a slightly different organization of the CPG. For example, the heel-strike at initial contact, a loading response in early stance, and synchronized activity of lower-extremity extensor and flexor muscles, may require greater supraspinal input during walking in humans compared with lower vertebrates (Guertin, 2013).

In addition to the unique biomechanics of human gait, cortical influences are likely more important during real world walking and adaptation. Electroencephalography (EEG) studies of cortical activity demonstrate that gait pattern adjustments necessary to walk in varying conditions require supraspinal input, especially from somatosensory cortices. Bradford et al (2016) recently demonstrated that whilst motor related cortical activity was relatively dormant during flat treadmill walking (suggesting greater spinal CPG activity), during uphill walking, much greater electrocortical activity levels were evident in key somatosensory regions. Such findings, they suggest, indicate the sensory

cortex is at a heightened state for monitoring somatosensory feedback (and feedforward) during more challenging walking conditions. Sensory feedback likely serves the purpose of modulating and adapting CPG-generated motor output for its adaptation to environmental constraints or obstacles. The 10m walk test for many chronic, ambulatory stroke survivors may therefore not represent a sufficiently challenging test and may not require or rely on somatosensory information. In keeping with this, Lin et al (2012) found that proprioceptive interference in the form of vibrations administered to the tendo-achillies of the hemi paretic ankle did not affect gait parameters in their chronic (53 months post onset) treadmill-walking stroke participants.

It is also generally agreed that the neural mechanisms involved in real word tasks involve the CNS developing different strategies of sensory reweighting depending on the task, the environment, the afferents and voluntary movement involved (Saradjian, 2015). Further interpretations as to why gait speed may not be strongly associated with lower limb somatosensory function may lie in the ability of the CNS to gate, expected, incoming sensory information during volitional movements. Here, internal models of the limb within the brain are felt to predict sensory information associated with movements and "gate" it out. This is shown by a lack of response to expected sensory stimuli in the motor area. In contrast, unexpected sensory information (for example associated with a perturbation or trip) is not gated and leads to an appropriate motor response (Saradjian, 2015). Mullie & Duclos (2014) also found that interference of ankle proprioceptors (triceps surae) did not significantly affect balance during gait or posture in stroke participants but interestingly it did significantly affect static and dynamic balance ability in healthy subjects. Their study suggests that ankle

proprioception may normally have an influence on functional balance and gait, but given the difference between groups, proprioceptive information may not be processed or integrated by stroke participants in the same way as by healthy participants. There is thus a different emphasis in that stroke may affect the ability to gate and thus *use* proprioceptive information during gait. Certainly reweighting the sensory integration process following stroke is documented with a reliance and dominance of vision over proprioceptive information (Chien et al, 2014; Bonan et al, 2012, 2006). Such reorganisation may also partly explain why studies of factors influencing community ambulation rarely attribute significance to lower extremity somatosensation (Robinson et al, 2011; Durcan et al, 2016; Lee et al, 2015).

However, walking ability extends beyond speed performance, with the suggestion that gait asymmetry could provide greater insight to understanding paretic leg impairments and the compensatory mechanisms used (Allen et al, 2011; Lauziere et al, 2014). Observations of prolonged swing, shorter stance time and reduced step length of the paretic limb compared with the non-paretic limb are common (Kim and Eng 2003; Patterson et al. 2008). Community dwelling chronic stroke survivors often continue to exhibit such spatiotemporal gait asymmetries, despite good motor control (Patterson et al. 2010). Abnormal tactile and proprioceptive inputs may perpetuate such asymmetries, although the relationship between lower limb somatosensation and spatiotemporal parameters of gait is weak (Hsu et al, 2003; Lin et al, 2006). The clinical measures used to assess sensory deficits, the variability of the equations used to calculate gait asymmetry, and the relative importance of each sensorimotor deficit to gait have been suggested to explain these findings (Lauziere et al, 2014).

This study also found a weak association between balance and somatosensation although this was limited to toe/ankle proprioception and postural sway as measured by COP velocity. In contrast, tactile sensation was found to have no significant associations with either static balance (COP) or dynamic balance (FRT). This weak association between tactile sensation and balance is a little surprising. Theoretical expectation and evidence from empirical studies indicates that reduced tactile acuity of the plantar surface of the foot, through either artificial anaesthetizing or disease, results in increased postural sway (Nurse & Nigg, 2001; Zhang & Li, 2013) whilst enhanced somatosensory input through under foot textured surfaces, may result in decreased postural sway (Qui et al, 2012; Orth et al, 2013). Furthermore, Tyson et al (2006) found sensation, which included both tactile sensation and proprioception combined, had a highly statistically significant predictive relationship (p=0.0001) with dynamic balance. Their study included stroke survivors who were between two and four weeks post-stroke and multiple regression analysis indicated that sensation and weakness accounted for 47% of the variance in balance disability (Tyson et al, 2006). There are several possible interpretations of the weak association with tactile sensation and balance in the results of this dissertation study. The EmNSA assesses passive tactile sensation at three points on the plantar aspect of the 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> toe. In contrast, balance-related postural sway and forward reaching movements when standing involve ankle dorsi-plantarflexion where larger areas of the forefoot and heel are stimulated. As one sways and/or reaches forward tactile sensation at the distal plantar surface of the toes does not necessarily reflect the sensory stimulation placed on the foot/ankle during these movements. Postural adjustments are more likely to occur in response to stimulation of larger parts of the forefoot and heel (Kavounndias

et al, 1998). Tactile acuity at the toes may have little impact on balance. The notion that distal proprioception is involved in postural adjustments is supported by the data from this study suggesting anterior-posterior postural sway is modulated by proprioceptive mechanisms at the foot-ankle complex.

This study also identified a significant, albeit weak, correlation between the perceived impact of stroke on walking ability (Walking Impact Scale) and somatosensory performance (both tactile and proprioceptive sensation). This finding is interesting given that the objective measure of gait speed did not significantly correlate with somatosensory performance. Walking ability is not just about straight-line speed. Walking is a complex and multifaceted activity and walking ability is heavily reliant on individual and environmental context. The Walking Impact Scale potentially provides a contextual and personal reflection with respect to this. The visible symptoms of stroke do not necessarily reflect the experience of stroke, and the experience of stroke is more likely to influence activity levels and result in seeking treatment. It is therefore reasonable to assume that in some individuals relatively minor impairments, whilst not reflected in gait speed performance, may be self-reported as having had a major impact on several aspects of *their* walking ability. This may be particularly true in those individuals who pre-stroke were high performing or for those who expose themselves post stroke to more challenging walking environments. The opposite may of course be true where severely impaired individuals' self-report does not necessarily reflect their performance. Self-report is a very valuable tool to reflect perceived impact, but what must also be considered is the potential impact of stroke related neuropsychological disorders such as abnormal magnitude estimation (Woods et al, 2006), and

indifference to the impact of a deficit (anosodiaphoria), which may confound selfreport.

## 3.7. Study Strengths

This is the first study to map the prevalence and distribution of lower limb somatosensory impairments in a large group of chronic stroke survivors. It attempted to clarify and enhance our understanding of the underlying causes behind the functional difficulties faced by chronic stroke survivors. In targeting this relatively understudied population, who may no longer be involved in rehabilitation services, it provides insight into the sensory impairments that are experienced by them. This study adds to the scant understanding of the sensory function of chronic stroke survivors once they return to their respective communities. It utilised self-report measures to investigate the perceived impact of stroke on functional ability, demonstrating a significant association with sensory performance and a predictor of falls. Using such measures provide insight into the perceived impact of impairments, which may not be fully captured by objective measures of performance.

This study also provides data questioning the validity of using a sensory measure that is largely a screening tool for acute patients. It highlights that the measurement of lower limb somatosensation in its current format is problematic and requires further development and investigation. It further highlights that correlational observational studies that employ measures of mobility and sensation do not corroborate the findings of qualitative and/or laboratory studies in this area.

#### 3.8. Study limitations

This study was not without limitations. Due to the logistics of recruiting chronic stroke survivors who tend to have little contact with formal rehabilitation services, the study design used a convenience sampling approach. This approach may have led to sample bias. Further, assessment centres were limited to the local community hospitals and university laboratory so these results may not be generalizable to very limited community ambulators or those unable to attend outpatient clinics. The need to include multiple measures of impairment alongside the EmNSA, as part of the FAIMIS study, meant the inclusion of more detailed and potentially more precise measures of sensory and mobility/balance function was not possible. For example, quantitative sensory testing of vibration threshold (e.g. Biosthesiometer or Rydell tuning fork), may have provided a more sensitive assessment of large fibre function and proprioception, but was excluded due to time limitations. The inclusion of additional sensory measures may have enhanced the findings from this study, providing a more comprehensive analysis of somatosensory function. In addition, the functional mobility measures used in this study were chosen collaboratively by the FAiMiS team, based on their psychometric properties, and their clinical utility. It is recognised that measures such as the 10 metre walk test and the forward functional reach test, may lack the sensitivity to reflect real life, day-to-day functional activities of walking and balance, particular in chronic stroke participants. Alternative mobility measures such as the Community Balance and Mobility Measure (Knorr et al, 2010), or mini- Balance Evaluation Systems Test (mini-BESTest) (Franchignoni et al, 2010) potentially reflect several aspects of everyday mobility and balance such as changing direction, altering walking speed and dual-task interference. Such measures may have further enhanced

the findings from this study although the use of such measures were not feasible to complete, due to assessment time restrictions and the requirements of the FAiMiS study.

# 3.9. Conclusion

This study demonstrates that impairment in at least one modality of lower limb somatosensation was present in the majority of chronic stroke survivors, with tactile impairment more frequently seen than proprioceptive deficits. Despite the prevalence of these impairments, and in contrast to some studies, lower limb sensory ability was not significantly associated with walking speed. Lower limb proprioception however was significantly, but weakly, associated with both increased postural sway and increased falls incidence in chronic stroke. This study suggests that for the large part, the functional impact of lower limb sensory impairment is minimal in chronic stroke. Where significant relationships were identified, it was predominantly sensory impairment in the foot-ankle complex that was most strongly associated with functional decline, most notably falls and increased postural sway. However, whilst reduced lower limb proprioception was significantly associated with falls reporting and increased postural sway, the strength of this correlation and the nature of the proprioceptive assessment used in the EmNSA, questions the validity and clinical relevance of this association.

This study also highlights the potential drawbacks of using a measure in a research study, which is for the large part, a clinical screening tool. The EmNSA is suggested to be a robust and clinically feasible measure of somatosensation yet this study highlights the difficulties associated with interpreting the results in research, particularly where

prevalence is an objective. The reporting of prevalence is problematic due to the ordinal nature of the data and the arbitrary use of a cut-off score. The validity and sensitivity of the subtests of sharp-blunt discrimination and proprioception are also brought into question and require further validation. This study suggests that the quality of a somatosensory measure largely dictates both prevalence and functional relevance. The determination of prevalence, along with relationship with function are key factors to informing treatment approaches. To date, the clinical relevance of sensory retraining of the lower limb and feet has yet to be established in stroke, and this study indicates it may not always be necessary since somatosensation did not appear to significantly contribute to functional decline in these chronic stroke survivors.

Chapter 4. Measuring tactile sensation and proprioception in the lower limb; a review of current approaches and measures

### 4.1. Chapter Overview

This chapter provides a review of current measures of somatosensation. It reviews several global measures of somatosensation, commonly used in neurological clinical practice, which assess multiple modes of tactile sensation and proprioception. It also reviews several measures and approaches from other clinical areas, most notably the sports and orthopaedic literature. It is intended that this review will provide insight into a diverse range of somatosensory measures, their function, merits and limitations, helping to inform the development and design of novel measures of somatosensation.

#### 4.2. Introduction

In 1888, A Manual of Diseases of the Nervous System was published by W.R. Gowers. In it was one of the first complete sensory examinations detailing tests for tactile, thermal and pain sensation (Gowers, 1888). Forty-one years later, Robert Bing's *Compendium of Regional Diagnosis in Affectations of the Brain and Spinal Cord* (Bing, 1929) detailed the testing of four principle areas of "sensibility": tactile sensibility (using cotton wool); temperature sensation (using hot/cold test tubes); pain sensation (using pin prick), and deep sensibility (using joint movement detection and vibratory sense using a tuning fork). The clinical neurological examination for somatosensory functioning has remained largely static since. Most standardised and non-standardised clinical measures used in neurological conditions continue to assess passive stimulus detection of the four principle areas highlighted above (Gilman, 2002; Connell & Tyson, 2012; Pumpa et al, 2015). The availability and ease of use of such simple equipment

has meant these methods, or variants of, continue to be commonly used in clinical practice. A reported 84-95% of physiotherapists, 87% of doctors and 77-91% of occupational therapists routinely assess somatosensation as part of their clinical assessment of stroke (Pumpa et al 2015; Winward et al, 1999). The most commonly used approach involves assessing light touch and proprioception although 70% of physiotherapists do not using a standardised measure in their somatosensory assessment (Pumpa et al, 2015).

Despite the widespread use of measures that have changed very little, satisfaction with current approaches to somatosensory assessment is low. Recognised concerns include the reliability of the clinical sensory examination, the absence of standardization, poor responsiveness, inappropriate summation of ordinal data, large ceiling effects, and the validity of using an approach which was designed to assess the integrity of the peripheral mechanoreceptors (Lincoln et al, 1991; Sullivan & Hedman , 2008; Connell & Tyson, 2012; Pumpa et al, 2015; Hilier et al, 2015; Han et al 2016; Donaghy et al, 2016). More robust and sophisticated measures designed for research studies address some of these limitations yet tend to lack clinical utility in neurological populations and are often poorly evaluated (Sullivan & Hedman, 2008; Connell & Tyson, 2012; Hilier et al, 2015).

Nonetheless, the assertion that co-ordinated, appropriately scaled movement relies on intact peripheral and central processing of tactile and proprioceptive input is compelling. Clinical treatment approaches (Bobath, 1990; Brunstrom, 1970) neurophysiological studies (Ackerley et al, 2012, 2016; Saradjivan, 2015; Borich et al, 2015;) and laboratory studies (Perry et al, 2001; Chisholm et al, 2016; Zehr et al, 2014;

Collings et al, 2015) support and demonstrate this. However, clear and compelling evidence linking lower limb measures of somatosensation with measures of patient function in chronic stroke is yet to be established and so the contribution of somatosensory input to functional (dis)ability is equivocal (Lee et al, 2015; Schmid et al, 2013; Tyson et al, 2013; Robinson et al, 2011; Lin et al, 2012). In part, the shortcomings of somatosensory assessment methods may have contributed to this position (Lincoln et al, 1991; Elangovan, 2014; Hilier et al, 2016; Suetterlin & Sayer, 2014. Broadly speaking, the most common approach to assessing lower limb tactile and proprioceptive sensation in neurological populations is through the passive application of a given stimulus or movement to a given body part (Kessner et al, 2016; Pumpa et al, 2015; Connell & Tyson, 2012). Measures of somatosensation can be broadly distinguished into two distinct categories. Firstly, there are the measures that are designed to assess several modes of tactile sensation and proprioceptive sensation. These tend to assess global, multi-modal sensation of the entire body. They are simple, clinically feasible, but their accuracy is questionable. Secondly, there are several (seemingly) more sophisticated measures/tools, which tend to evaluate one aspect of tactile sensation or proprioceptive ability, usually in one single joint or body part. Such methods often utilise equipment, ranging from the simple through to the sophisticated, and are mostly employed within research and laboratory environments. They are suggested to possess greater accuracy.

A need to review current assessment methods and develop new methods of assessments is thus required. Whilst lower limb somatosensory measures have been developed across the neurological, orthopaedic and sports science communities, especially within the area of proprioception, the potential learnings, applicability and

relevance of many of these measures to a stroke population has, for the large part, not been investigated. In light of this, a review of the breadth of approaches and methods to measuring lower limb tactile sensation and proprioception, spanning both clinical and research settings within neurological, orthopaedic and sport science populations, was undertaken in order to inform the development of novel measures of somatosensation

#### 4.3. Aim & objectives of review

The aim of this review is to provide a broad overview of the approaches to measuring lower limb tactile sensation and proprioception with examples of methods and tools used within those approaches. Specifically, the objectives were to:

1) Where appropriate briefly highlight the theoretical basis underlying approaches to measuring tactile sensation and proprioception;

2) Report the overall approaches and a selection of specific methods used to measure tactile sensation and proprioception across clinical and/or research settings;

3) Use the findings to consider how current approaches and methods developed in a wide range of populations may inform the development of novel measures in a stroke population

## 4.4. Search strategy

To identify measurement approaches and the methods/tools used within those approaches, a search of the literature was carried out. The search strategy involved two steps. First, an electronic database search was conducted. Then a secondary search was conducted looking at the reference lists from articles that were reviewed in full-text from the database search. The databases searched included Medline (EBSCO & Ovid), AMED, EMBASE, Science Direct, and CINAHL. Search dates were from database inception through to and including August 2016. Search terms used included combinations of "tactile sens\$", "touch sens\$", "somatosens\$", "touch perception", "sens\$ discrimination" and "proprioception", "kinesthesia", "joint position sense", "joint motion", "joint movement" AND "toe", "foot", "ankle", "knee", "lower limb", "leg", "lower extremity" AND "tests", "methods", "approaches", "measures" "examinations". Articles identified were then reviewed to ensure the research article and measures of tactile and proprioception assessment met the following inclusion criteria:

- Described and/or employed an approach and/or method/tool to measure tactile sensation and/or proprioception (or comparable terms) in the lower limb

- In any human population

- Written in English

In many instances, multiple individual methods/tools, which attempt to measure the same construct, were identified. For example, Smith et al (2013) in their systematic review of the reliability of measures of knee proprioception identified 18 different tools that measured knee joint position sense alone. Further measures were excluded from their review because reliability data was not reported. Multiple individual methods have also been developed, especially with regard to proprioception for individual ankle and hip joints. In this instance, it is beyond the scope of this chapter to document and review *every* method, so tools similar in their method/equipment and measuring the same aspect of tactile sensation/proprioception (i.e. joint position sense, movement direction discrimination) were not necessarily reviewed. Where

reported, reliability and/or validity data is included in the review for the measures/tools discussed.

### 4.5. Multi-Modal measures

# 4.5.1. Tactile sensation

The most psychometrically robust and clinically usable "all in one" measures of multimodal tactile sensation include: the original Nottingham Sensory Assessment (Lincoln et al, 1991), the revised Nottingham Sensory Assessment (Lincoln et al, 1998), the Erasmus Medical Center Modified Nottingham Sensory Assessment (Stolk-Hornsveld et al, 2006), the Rivermead Assessment of Somatosensory Performance (Winward et al, 2002), the sensory subtest of the Fugl-Meyer Assessment (Fugl-Meyer et al, 1975), and the Cumulative Somatosensory Impairment Index (Deshpande et al, 2010). These tests are similar in their approach in that they measure multiple modes of passive tactile sensation (except Fugl-Meyer, which assesses light touch only). They use minimal equipment enhancing their clinical usability. Measurement level is mostly ordinal, scoring sensation as normal, impaired or absent, with some method variations in terms of body parts assessed, inter limb comparisons and number of times touched per site. Further details for each measure along with reliability and validity are discussed below and a summary provided in table 4.1.

The Nottingham Sensory Assessment (NSA) (Lincoln et al, 1991) was developed as a standardised scale to assess sensory impairment in stroke patients. It was developed in an attempt to standardise the multiple sensory assessments that were frequently used in clinical practice. Test items include light touch (applied using cotton wool), pressure (applied using the assessor's finger), pinprick (using a Neurotip), and temperature

(using hot and cold water in test tubes). Items also assess tactile localisation, bilateral simultaneous touch, proprioception (by mimicry), two-point discrimination and stereognosis. It uses an ordinal measurement scale, with the face, trunk, upper limb and lower limb assessed for each sensory modality and scored as either absent/impaired or normal. It is a lengthy assessment taking up to one hour to complete. Lincoln et al (1991) evaluated the measure amongst a cohort of 20 hospitalised and community dwelling stroke patients and whilst the NSA was found to have acceptable intra-rater reliability, inter-rater reliability was poor, particularly in kinesthesia and in the lower limb. For example, at the knee, Kappa coefficients were as low as 0.10, 0.14 and 0.13 for movement detection, movement direction and JPS respectively. Reliability of tactile sensation was marginally better than proprioception although remained poor with kappa values of 0.19 (foot light touch), 0.21 (ankle light touch) and 0.14 (ankle touch localisation). The validity of the NSA was not established by the original authors although it was investigated in 2007 (Connell, 2007), with lower limb tactile sensation showing significant correlations with stroke severity (NIHSS, r=0.55, p<0.001), lower limb gross motor ability (RMA, r=0.29, p=0.02) and independence in activities of daily living (Barthel Index, r=0.35, p=0.005).

In light of the poor inter-rater reliability, the revised NSA was developed (rNSA)(Lincoln et al., 1998), which included the addition of assessment instructions, a shortening of the scale, and producing a hierarchy of items so that testing could be discontinued if no impairment was detected in the distal part of the limb. The inter-rater reliability of the rNSA was evaluated and whilst inter-rater reliability improved, it was still not good, with particular items highly unreliable (Lincoln et al, 1998). Most notably, kappa values of tactile modalities at the foot ranged from 0.04 to 0.46 and at the ankle from 0.15-

0.30. Proprioception had better reliability although remained weak to moderate with kappa values ranging from 0.31 - 0.46.

Further changes to the rNSA were implemented to produce the Erasmus Medical Center Modified Nottingham Sensory Assessment (EmNSA). This involved the removal of both temperature and two-point discrimination items due to poor inter-reliability and the addition of sharp-blunt discrimination to assess pain (Stolk-Horsnveld et al, 2006). Further changes to the rNSA included additional standardisation and explicit instruction on body parts tested and assessor handling for proprioception, which was absent from the rNSA. Reliability testing of the EmNSA was conducted in a cohort of 18 neurological inpatients with intra-cranial disorders. Intra-rater reliability for individual tactile modalities of the lower extremity using kappa weighted  $(k_w)$  values were light touch  $K_w=0.77-0.78$ ; pressure 0.93-0.91; pin prick 0.87 - 0.92; and sharp-blunt 0.71-0.90. For inter-rater reliability, light touch 0.81, pressure 0.83, pinprick 0.88, sharpblunt 0.70. Neither the validity nor responsiveness of this measure was established although it is suggested to offer a good balance of robustness and usability in clinical practice (Connell & Tyson, 2012). Whilst the EmNSA is a globalised measure assessing multiple body parts, the lower limb assessment involves testing tactile ability at three points at the anterior thigh, three at the anterior shin, three at the dorsum of the foot, and three at the plantar aspect of the toes. Light touch is assessed initially at each

Table 4.1.	Summary of Muli	ti-Modal Measures of sensation					
					Relia	bility	
Measure	Body Location	Sensory Mode Measured	Authors	Sample	Intra-rater	Inter-rater	Validity
NSA	Lowerlimb	Tactile sensations; JPS/MDD/DPM	Lincoln et al (1991) Connell (2007)	Stroke (n=20) Stroke (n= 70)	+ N RR	+ N	NR +/++
rNSA	Lowerlimb	Tactile sensations; JPS/MDD/DPM	Lincoln et al (1998)	Stroke (n=34)	‡	++/+	NR
EmNSA	Lowerlimb	Tactile sensations; MDD/DPM	Stolk-Hornsveld et al (2006)	Neurological (n=18)	+ + +	+++/++	NR
RASP	Lower limb	Tactile sensations; MDD/DPM	Winward et al (2002) Tyson et al (2008)	Acute stroke/neuro (n=12-100) Stroke (n=102)	++/+++ NR	++/+++ NR	+ ‡
FMA-S	Lower limb	Light touch; JPS	Lin et al (2004) Sullivan et al (2011)	Stroke (n= 176) Stroke (n=15)	NR +++	+ ‡	+ X
CSII	Foot/Ankle	Tactile sensation; JPS	Deshplande et al (2010)	Elderly (n=799)	NR	NR	ŧ
Abbreviat NSA, Nott Sensory A CSII, Cur	ions: ingham Sensory / ssessment; RASP, uulative Somatos	Assessment; rNSA, revised Nottingha , Rivermead Assessment of Somatose ensory Impairment Index; JPS, Joint F	m Sensory Assessment; EmNS nsory Performance; FMA-S, F osition Sense; MDD, Movem	SA, Erasmus Medical Center Modi ugl-Meyer Assessment Sensory S ent Direction Discrimination; DPN	ified Nottingh Subtest; M, Detection o	lam of Passive Mc	vement
key: NR, Not re ++ = Mode	ported; ++++ = Ex :rate reliability/v	ccellent reliability/validity (>0.75); ++- alidity (0.4-0.59); + = Poor reliability/	+ = Good reliability/validity(> /alidity (<0.39)	0.6 - 0.74);			

point stipulated above, and unlike the original version, if participants score normal on light touch, they are automatically assigned a normal score on modalities of pressure and pinprick sensation. The Rivermead Assessment of Somatosensory Performance (RASP) (Winward et al, 2002; 2012) provides a quantitative test using an interval scale and is used in both clinical (Pumpa et al, 2015) and research environments (Tyson et al, 2008). The RASP was designed as a relatively quick clinical screening assessment of sensory impairment for use in people with acute stroke and all types of CNS disorders. The tests used include sharp-dull discrimination, tactile detection and localisation, temperature discrimination, proprioception (detecting movement and discriminating direction), extinction and two-point discrimination. Lower extremity tactile sensation testing involves one point on the dorsum of the foot and one on the plantar aspect. The whole test takes 20 to 30 minutes to complete but the tests can be used individually and each take a few minutes. Reliability was investigated in two separate cohorts of sub-acute patients with 12 participants recruited to assess test-retest reliability and 15 for intra-rater reliability. Pearson correlations for both inter- and intra-rater reliability of the overall score of the RASP was excellent (r=0.92) (Winward et al, 2002). Individual tactile modalities for intra-rater reliability were also excellent with sharp/dull (r=0.84), surface pressure touch (r=0.90), surface localization (r=0.96) and temperature (r=0.84). A breakdown of inter-rater reliability for individual tactile modalities was not reported.

Validity of the measure was investigated amongst a larger sample of 100 acute/subacute stroke patients and 50 controls. Each tactile and proprioceptive modality within the RASP could discriminate between healthy controls and acute stroke patients (p<0.001). The authors anticipated there would be a significant positive relationship

between sensory loss and motor impairment in stroke patients, and so calculated the Spearman correlation coefficients between the Motricity Index scores (Demeurisse et al, 1980) and RASP item scores. The coefficients were weak and not significant (p>0.05) for all modalities: sharp/dull (r = 0.08); surface pressure touch (r = 0.14); surface localization (r = 0.21); and temperature discrimination (r = 0.08). Further, Spearman correlation coefficients between individual tactile modalities and the Rivermead Motor Assessment (RMA – Lincoln et al, 1979) were also weak and not significant (p>0.05) for sharp/dull discrimination (r = 0.23), surface pressure touch (r = 0.21), surface localization (r = 0.25), and temperature discrimination (r = 0.05). Finally, none of the individual tactile modalities of the RASP were significantly correlated with the Barthel ADL index (Wade et al, 1988) with sharp/dull discrimination (r = 0.27), surface pressure touch (r = 0.27), surface localization (r = 0.31), temperature discrimination (r = 0.09). Despite this, validity was deemed acceptable by the authors since the tests were adapted from traditional tests, many of which had been in clinical use for over a century (Winward et al, 2002).

The validity of the RASP was investigated further using parts, rather than its entirety. Tyson et al (2008) in a cohort of hospital inpatients with first time stroke (n=102), investigated detection and discrimination modalities of light touch and proprioception. Moderate and significant correlations were reported with the Barthel Index (BI) (r= 0.541, p<0.000) and Rivermead Mobility Index (RMI) (r= 0.515, p<0.000) in acute patients on admission. Patients were followed up at three months, and using the initial admission sensory data and a postal returned self-reported RMI and BI, weak to moderate yet significant relationships were found between tactile sensation and RMI/BI (r=0.287, p=0.01; r=0.495, p<0.000) and proprioception and RMI/BI (r=0.317,

p=0.005; r=0.496, p<0.000). Whilst this study highlighted significant associations between sensation (tactile and proprioception) and functional ability, there are some considerations that need to be taken. For example, this study investigated the relationship between sensory impairment on admission and functional ability in acute patients. It also looked at functional *recovery* of mobility/ADL and initial admission sensory impairment. At the three month follow up sensation was not assessed, and hence it is not possible to draw conclusions between sensation and function, nor generalise these results to a community based stroke population considering the variability and unpredictability of sensory recovery in the first six months after stroke (Winward et al, 2007; Connell et al, 2008). Further, data was not reported with specific reference to the lower limb, so the degree to which lower limb sensation (as measured by the RASP) is associated with function is not clear.

The sensory section of the Fugl–Meyer Assessment (FMA-S) uses a three point ordinal scale and is part of the widely used Fugl-Meyer assessment of motor control (Fugl-Meyer et al 1975). It contains 12 three-point items; four for light touch and eight for joint position sense (JPS) giving a maximum score of 24. For light touch, the patient is asked whether they can feel light touch on the arms, palms of the hands, legs and soles of the feet on both sides. Joint position sense of the thumb, wrist, elbow, shoulder, big toe, ankle, knee and hip are also tested. Inter-rater reliability in a stroke population has demonstrated to be widely variable, ranging from poor to excellent for individual items, with proprioception scoring more highly than tests of light touch (Kw =0.30-0.55 light touch and 0.71-0.90 proprioception; Lin et al, 2004). Whilst the FMA-S did show adequate inter-rater reliability overall, the authors found significant ceiling effects, and weak to moderate validity and responsiveness at different post-stroke

stages of recovery. For example, The FMA-S was found to be weakly but significantly associated with the Barthel Index (BI) and motor scores of the Fugl-Meyer assessment (FMA-M), at each stage of stroke recovery (r = 0.31, p < 0.001; r = 0.29, p < 0.001respectively) (Lin et al, 2004). In addition, significant ceiling effects at all stages of participant recovery (i.e. 14, 30. 90 and 180 days after stroke) were reported, with between 44.4-72.1% of participants scoring the maximum (Lin et al, 2004). Ceiling effects are indicated if greater than 20% of participants score the maximum on an outcome measure (Andresen, 2000). They concluded that the use of the FMA-S in its (then) current form for measuring sensory function of stroke patients could not be supported (Lin et al, 2004). In an attempt to improve its psychometric qualities, Sullivan et al (2011) produced a standardised training procedure to administer the FMA-S (and motor component) which involved two days of training and one month of practice. In doing so they found substantial improvements in inter-rater reliability of the FM-S (light touch- ICC, 0.87; 95% CI, 0.69–0.95; proprioception sub-score- ICC, 0.96; 95% CI, 0.90–0.99) (Sullivan et al, 2011) suggesting inter-rater reliability can be improved, but requires considerable training in its administration.

Whilst such globalised measures represent the most commonly used tools in clinical practice (Pumpa et al, 2015), the validity and responsiveness of tactile items in respect to the lower limb are not usually evaluated or are reported in isolation. Correlational studies evaluating and utilising these measures, especially in establishing their validity, tend to report associations with an overall score of "somatosensory ability". Such scores include both tactile sensation and proprioception, often combining both upper and lower limbs. Whilst these measures are designed to provide an overall score, the reporting of one figure is suggested to provide little insight into the nature or severity

of somatosensory impairment (Connell et al, 2008) and is therefore potentially of little value in terms of informing the treatment approach. Further, the summation of ordinal data is not a statistically robust method (Fawcett, 2007). Where tactile sensation is reported separately, it often combines upper and lower limbs so the properties and contribution of lower limb tactile sensation subscales are largely unknown. Reporting and evaluating lower limb tactile sensation in these global measures with regard to associations with functional measures thus tends to be the exception (Connell, 2007).

One such exception is the clinically derived Cumulative Somatosensory Impairment Index (CSII) (Deshpande et al, 2010) developed as a measure from the InCHIANTI study (Ferrucci et al, 2000), an epidemiological study designed to understand the factors which contribute to mobility decline in late ageing. This measure is compiled from four clinically derived somatosensory assessments, specific to the lower limb. It includes a test for pressure, vibration sensitivity, graphesthesia and ankle proprioception (Deshpande et al, 2010), combined as an index. It comprises three tests of tactile sensitivity of the feet and one proprioceptive (Joint Position Sense – JPS) test of the ankle. Each test is scored using an ordinal scale (0=normal, 1=reduced, 2=absent) giving a minimum score of 0/8 (normal on all four tests) and a maximum of 8/8 (absent on all four tests). Pressure sensitivity is tested on the external malleolus using 4.31 (2.04g) and 4.56 (3.63g) Semmes-Weinstein monofilaments (SWM). Vibration sensitivity is assessed using a 128Hz tuning fork on the bony prominence of the first metatarsal bone. Graphesthesia is assessed by drawing three simple shapes on the sole of the foot (circle, line, and plus sign) and proprioception is tested through JPS reproduction at the ankle. Reliability of the CSII is not reported although variable reliability has been reported for individual tests (SWM - Collins et al, 2010; Craig et al,

2014), vibration sense (Eek & Engardt, 2003; Hedman & Sullivan, 2011); JPS (Deshpande et al, 2003); graphesthesia (Masanic & Bayley, 1998). Discriminant validity of the CSII was established in a cohort of 799 participants (age 21-91) with the CSII able to discriminate age (p<0.001), those with diabetes (p=0.017), peripheral arterial disease (p=0.006), and stroke (p<0.001). Further, at three year follow up, the CSII predicted standing balance performance (p=0.002), dynamic balance performance (p<0.001) and gait speed (p=0.003). The relative weighting or importance of individual items within the CSII is not reported.

## Thoughts and considerations

Such methods are widely used in clinical practice, require minimal equipment, so are easily utilised in different clinical settings. They can be administered by a single person, and are inexpensive. Whilst individual variations exist in terms of body sites assessed, and number of times, they largely involved a repeated process of assessing different tactile modalities rather than a composite modality so can take between 15 minutes and 1 hour to complete. They largely assess for passive sensation, placing minimal attentional and cognitive demands on the participant. They are administered in supine and/or sitting, so do not necessarily require the ability of the participant to be able to stand. The favourable aspects of these tests which would need reflecting in any novel measures focus around their clinical utility, low expense, portability, and ease of administration (assessor and assessee).

### 4.5.2. Proprioception

Current multi-modal measures that incorporate a proprioception component tend to use one (or more) of three approaches to assess proprioception; assessment of joint
position sense (JPS), movement direction discrimination (MDD), and/or detection of passive movement (DPM) (table 4.1). The standardised clinical measures that use a JPS approach include the sensory subtest of the Fugl-Meyer Assessment (FMA-S) (Fugl-Meyer, 1975), the rNSA (Lincoln et al, 1998) and the Cumulative Somatosensory Impairment Index (CSII) (Deshpande et al, 2010). Both the FMA-S and rNSA were designed as stroke specific measures in which the 1<sup>st</sup> metatarsophalangeal joint (MTPJ), ankle, knee and hip joints are passively moved to produce lower limb positional configurations that are then recreated or matched by the subject. The CSII conversely examines ankle JPS alone and was designed as a global measure of somatosensory ability in the elderly (Deshpande et al, 2010). Lin et al (2004) reporting on the psychometric properties of the FMA-S, demonstrated the eight items of position sense (which also includes four items for the upper limb) were more reliable than light touch with adequate to excellent inter-rater agreement (Kw 0.71 to 0.90). Lower limb proprioception was not distinguished from the overall score of proprioception scores or in validity testing from the overall sensation score (light touch and proprioception). Whilst the FMA-S showed good inter-rater reliability, the authors found significant ceiling effects and poor to adequate validity and responsiveness at different post-stroke stages of recovery. They concluded that the use of the FMA-S in its (then) current form for measuring sensory function of stroke patients could not be supported (Lin et al, 2004). As with the tactile tests, Sullivan et al (2011) attempted to reinvigorate interest in the use of the motor and sensory subscales of the FMA by designing a framework of administration in order to improve its reliability and agreement for use in multiple site research trials. The framework involved the production and standardisation of detailed instructions, an intensive two-day training

course and competency assessment for assessors, and recommended practice of one month. In doing so, reliability and agreement of both motor and sensory measures were improved as highlighted earlier with the tactile tests. The validity of the measure and its sensory substrates of light touch and proprioception however have yet to be established.

The revised Nottingham Sensory Assessment (rNSA)(Lincoln et al, 1998) also represents a clinically oriented and standardised measure of global somatosensory function that includes a proprioception subtest. Similar to the FMA-S, the approach to measuring proprioceptive ability includes JPS but differs in that passive movement detection (DPM) and passive movement direction discrimination (MDD) are also incorporated into an ordinal scale of measurement. Lower limb proprioceptive ability is assessed at the great toe (1<sup>st</sup> MTPJ), ankle, knee and hip. Specifically, JPS is recorded as an extension of MDD in that the blindfolded subject is simultaneously assessed in their ability to both appreciate and mirror the direction of the test movement taking place and the test position. The accuracy of the "match" to the test position is considered normal if it is within 10° as deemed through visual observation. No equipment is stipulated nor are detailed instructions included regarding handling and the assessor is required to handle the limb with both hands. Inter-rater reliability was variable, as indicated by kappa coefficients for the proprioception items, with hip (0.31-0.73), knee (0.32-0.68), ankle (0.38-0.77) and toe (0.46-0.62).

Unlike other global measures, the proprioceptive component of the clinically derived CSII involves the testing of just one lower limb joint – the ankle, using one approach – passive-active JPS. Participants are tested in supine with eyes closed whilst an

examiner positions the reference ankle randomly in either 10° of dorsiflexion (DF) or 20° plantarflexion (PF) relative to neutral. The participant is instructed to actively position the test ankle to match the reference ankle. The examiner visually estimates mismatch or error. Scoring is on a three-point ordinal scale: proprioception is scored as normal if the participant repositions the test ankle in both DF and PF conditions to within 5° of the reference ankle; reduced if the ankle is repositioned within 5° in just one of the two conditions (i.e. DF or PF); and absent if matching is greater than 5° in both DF and PF conditions. As discussed earlier, there was strong evidence to support the validity of the CSII overall score. As with the tactile components of the CSII, however, reliability or validity for ankle JPS is not reported, nor is its weighted contribution to the validity of the overall measure.

The assessment approaches involving the DPM and MDD are perhaps more widely used in the clinical environment compared with JPS, and form the proprioceptive component of the EmNSA (Stork-Horsnveld, 2006) and RASP (Winward et al, 2002). In the EmNSA, an assessor administers passive movement of the toe/ankle/knee/hip manually, whilst in the RASP just toe and ankle are assessed. In both measures, the recipient indicates *whether* movement is detected (DPM) and if so, in which direction is that movement (MDD). In both the RASP and EmNSA, threshold to detection is not obtained or estimated i.e. *the point* at which movement is felt. Movement detection is simply whether or not subjects detect the limb being moved (yes/no). The assessor thus estimates proprioceptive impairment using an ordinal scale of absent/impaired/normal based on a yes/no response from the subject. Classification of proprioceptive ability is dependent on the number of incorrect responses given over a series of trials (three in the EmNSA and six in the RASP) per area/joint tested. Such

methods used to establish DPM and MDD *per se* have been shown to have variable reliability, although the precise properties of the lower extremity component is often not reported.

In a cohort of 12 sub-acute stroke patients, Winward et al, (2002) investigated testretest reliability and in a further 15 (different) patients, inter-rater reliability of the measure. For the upper and lower limbs, movement detection (DPM) Pearson correlation coefficients were r=0.83 and for proprioceptive movement direction discrimination (MDD) r=0.50. Inter-rater reliability was not reported for the proprioceptive components but overall reliability of the RASP was reported as (r=0.92). With specific reference to validity, as with the tactile components discussed earlier, the authors investigated the RASP's association with three measures of motor ability and independence (Motricity Index - MI, Rivermead Motor Assessment - RMA and the Barthel ADL index) in sub-acute stroke patients (n=100). As discussed earlier, the tactile components had weak and non-significant relationships with each of the three functional measures, yet the proprioception subtests of DPM and MDD had marginally stronger and statistically significant associations. Detection of passive movement demonstrated weak but significant correlations with the MI (r = 0.31, p < 0.01), and the Barthel Index (r=0.35, p=0.01) but not the RMA (r=0.25, p>0.05). Movement direction discrimination was weakly yet significantly correlated with the MI (r = 0.36, p = 0.01), the RMA (r=0.32, p=0.01) and moderately correlated with the Barthel Index (r=0.41, p<0.01).

The proprioceptive component of the rNSA was modified and evaluated by Stolk-Hornsveld et al (2006) in a cohort of 18 neurological patients with the explicit aim of improving inter-rater reliability through further standardization of the testing procedures. The assessment of JPS within the proprioceptive component was removed with DPM and MDD retained. Further modifications included greater standardisation of verbal and handling instructions during proprioceptive testing. Both DPM and MDD are assessed at the hip, knee, ankle and great toe (1<sup>st</sup> MTP) joints with the patient in supine and vision occluded. Initial screening for MDD is completed with participants required to indicate the *direction* of movement at that joint followed by, if unable to discriminate movement direction, movement detection. Scoring, is on a three-point ordinal scale (absent/impaired/normal) with correct responses required in each of the three trials in each joint tested to score "normal". Reliability testing of the measure was undertaken in a cohort of 18 hospitalised patients with a variety of inter-cranial disorders. In light of the greater standardisation of instructions and assessor handling, both inter- and intra-rater reliability of the proprioceptive subtests was improved compared with the rNSA. Using kappa weighted values, intra-rater reliability in two raters was 0.80 and 0.91 respectively. Inter-rater reliability between two raters, assessing patients at least one hour apart was  $k_w = 0.66$ . Validity of the EmNSA per se has not been established although weak to moderate and statistically significant relationships between the overall proprioception score of the original NSA and measures of stroke severity (NIHSS r=0.47, p<0.01) mobility (RMA, r=0.32, p=0.01) and independence in daily activities (BI r=0.43, p<0.01) have been demonstrated in acute stroke patients (Connell, 2007)

Whilst such globalised measures represent the most commonly used tools in clinical practice (Pumpa et al, 2015), their validity and responsiveness has not been fully established as most research efforts have focussed, quite understandably, on

establishing their reliability. The psychometric properties of the proprioception items in respect to the lower limb are rarely evaluated or reported in isolation. Correlational studies evaluating and utilising these measures, especially those investigating their validity, tend to report associations with *overall* "somatosensory ability" which includes both tactile sensation and proprioception. Further, when tactile and proprioceptive ability is reported and analysed separately, it tends to include both upper and lower limb proprioception scores combined so the properties, contribution and relevance of lower limb proprioceptive subscales are largely unknown. When the lower limb is separated out, proprioceptive sensibility has been more strongly associated with measures of functional ability than tactile sensibility (Connell, 2007) although more recently this has been questioned (Tyson et al, 2013).

# Thoughts/considerations

A reliance on the manual application of these methods undoubtedly maximises their clinical utility. However, it also exposes them to unquantifiable and non-standardised movement speeds, varying tactile input through handling, and questionable accuracy due to the (often visual) estimation of either the extent of error (as in JPS mismatch) or the amount of movement occurring (movement detection). The use of dichotomous/ordinal outcomes mean they are potentially unresponsive to change with ceiling effects seen earlier in this thesis with the EmNSA (study 2) and in previous studies with the FMA-S (Lin et al, 2004). They have been criticised in both research and clinical reviews (Hilier et al, 2015; Han et al, 2016; Suetterlin & Sayer, 2014), are largely used as bedside screening measures and capable of detecting only profound proprioceptive deficits, so may not be appropriate for use in research or to detect the

impact of rehabilitation interventions. Inevitably, they share many similarities with the tactile subtests, so favourable aspects from these methods for consideration in a novel measure include clinical utility, low cost, portability, and ease of administration (assessor and assessee).

#### 4.6. Measures assessing single modes of tactile sensation

Such measures arguably represent an attempt to improve accuracy, involving the quantification of detection and discrimination thresholds to touch, vibration, texture or shear. Measures include for example, the Semmes-Weinstein Monofilaments Test (SWMT) (Semmes & Weinstein, 1960), the clinician administered 128Hz tuning fork, or specialist high-frequency transcutaneous electric nerve stimulation (Eek and Engardt, 2003; Deshpande et al, 2008; Hedman & Sullivan, 2011). Further methods/tools have assessed cutaneous texture discrimination in which the physical properties of a surface are distinguished through active and passive applications (Sato et al, 2015; Carey et al, 1997; Miller et al, 2009; Morioka et al, 2003, 2009) (table 4.2).

The use of SWMT is reported in a variety of clinical populations including the elderly (Ward et al, 2016), diabetic peripheral neuropathy (Craig et al, 2014) and multiple sclerosis (MS) (Uszynski et al 2016). The testing target of cutaneous sensation intended by the SWMT monofilament is not sense of touch, but protective sensation to noxious stimulation with skin deformation hence its predominance in the diabetic peripheral neuropathy literature and prediction of ulceration risk (Feng et al, 2009; Craig et al, 2014). Its origins however are in establishing sensory ability in the hand following traumatic brain injury (Semmes & Weinstein, 1960) and it is reportedly one of the most commonly used standardised clinical tests of tactile sensation in stroke (Pumpa et al, 2015). The SWMT consists of using a series of calibrated nylon monofilaments, which vary in diameter and provide a known target force. They are applied perpendicular to predetermined body parts and pressed until bending to a Cshape. Recipients are required to indicate if they feel the stimulus. The point at which the stimulus cannot be felt is then recorded. Standard 10-g monofilament testing is used clinically to predict diabetic foot ulceration, with loss at this level suggested to be indicative of impaired protective sensation (Boulton et al, 2005) although light-touch detection using 1.4-g and 2-g monofilaments have been suggested to detect subclinical neuropathy (Thomson et al, 2008; Craig et al, 2014). To date, there has been no consensus regarding the standard technique for monofilament mapping locations and the number of sites tested per foot varies although up to 10 locations on the plantar sole have been suggested (Craig et al, 2014). Further studies suggest measurement error and reliability of the SWMT can be confounded by repeated monofilament mechanical stress (Yong et al, 2000) and significant force differences between unused and calibrated monofilaments have been found (Smith et al, 2000). Reliability data is varied with good intra-rater reliability (ICC 0.78, 95%CI 0.68-0.83) reported in healthy populations (Collins et al, 2010) but moderate inter-rater reliability in healthy (ICC = 0.43, 95%CI 0.16 – 0.61) and MS populations (Kw 0.48, 95% CI 0.18 – 0.7) (Collins et al, 2010; Uszynski et al, 2016).

Further approaches to assessing tactile sensibility in the feet have involved applying high frequency oscillations (vibration) to the skin and quantifying detection thresholds of touch vibration. Sense of vibration results from sinusoidal oscillations of objects placed against the skin with specific mechanoreceptors known to respond maximally at different frequencies (Hz). Merkel disk receptors respond maximally to low frequencies (5–15 Hz), Meissner's corpuscles to mid-range frequencies (20–50 Hz), and Pacinian corpuscles to high frequencies (60-400 Hz) (Gardner & Johnson, 2013). Humans are most responsive to vibration at frequencies of 200–250 Hz (Gardner & Johnson, 2013) so vibration sense is largely mediated by the activation of the fast adapting (FA2) Pacinian mechanoreceptors. It is felt that the physiologic properties of the peripheral neural circuitry involved in vibration sensation play a role in modulating reflex responses in lower limb muscles in response to perturbation or changes in terrain (Fallon et al, 2005). Further, a higher threshold to vibration sense in the sole of the feet has been associated with slower gait speed in the elderly (Deshpande et al, 2008). This may in part also be explained by the close links between vibration sense and JPS as the pathways mediating joint position sense (proprioception) and vibration sense are, to the point of the thalamus and cerebellum, identical (Amaral, 2013). Impairment in cutaneous vibration sense can thus be linked to impairment in JPS. However, whilst this is true of acute or demyelinating polyneuropathies, because they terminate upon different thalamic and cerebral cortical neurons, in neurological disorders of central origin such as stroke, one of these sensory functions can be substantially affected while the other is partially or completely spared (Proske & Gandevia, 2012; Gilman, 2002).

Traditionally, vibratory sensation is tested with a 128-Hz tuning fork at the interphalangeal joint of the hallux. It is designed to assess perception of threshold to touch through a graded and self-diminishing vibration. An abnormal result occurs when the patient cannot perceive the stimulation from the tuning fork, while the clinician can simultaneously detect the vibration. It is one of the least commonly used methods of testing tactile sensibility in stroke patients amongst therapists with between 5-9% reportedly using it (Pumpa et al, 2015; Winward et al, 1999). Conversely, three-quarters of doctors (74%) use it as part of their clinical neurological examination of stroke patients (Winward et al, 1999). Critics suggest such methods are unreliable as the vibratory tone generated is a function of how hard the examiner manually strikes the tuning fork to stimulate the vibratory resonance with inevitable inter-tester variance (Craig et al, 2014).

In response, methods in which controlled and graded vibrations are applied to the skin have been developed (Deshpande et al, 2008; Eek & Engardt, 2003; Hedman & Sullivan, 2011). Eek & Engardt (2003) completed a reliability study of a tool designed to standardise and quantify the threshold of "light touch", the perceptual threshold test (PTT). Driven by the unquantifiable and widely used "cotton wool dab", the authors used high frequency (40Hz) transcutaneous electrical nerve stimulation (Hf TENS) of varying amplitude (milliampere - mA) to imitate light touch and thus quantify the point at which touch is perceived. In a cohort of 32 hospitalised, elderly acute stroke patients, electrodes were attached to the tip of the 'bulb' of the big toe and the front arch of each foot. The frequency was set at 40Hz and the intensity i.e. amplitude of the 40Hz vibration increased by 0.5mA steps until the patient reported feeling the tingling sensation in the toe. The authors reported higher thresholds in the toe,

compared to the finger and despite high mean ICC values for the foot across both inter- and intra- rater conditions (ICC=0.96 and 0.99) respectively, wide limits of agreement suggest either systematic error or the occurrence of real variability of tactile function between testing sessions. Given testing sessions were conducted between 10 minutes and one day apart, variability in tactile function is unlikely due to recovery. Further, agreement for the measurement in the hand was good; suggesting the presence of confounding factors more prevalent in the foot may be influencing reliability and agreement. They noted that those participants who fell outside the 95% limits of agreement had the common feature of impaired peripheral circulation, suggesting circulation may cause variability of tactile function. Whilst this is reasonable, this suggestion was not supported by the quantification of peripheral circulation so is likely based on examiner observation/palpation. No aspect of validity of this measure against other sensory tests was established and the ability to perceive a tingling sensation produced by transcutaneous nervous stimulation was assumed to be akin to perceiving a cutaneous tactile sensation.

More recently, Hedman & Sullivan (2011) investigated the viability of the PTT as a clinically relevant measure of sensation in the hand in stroke survivors. They concluded from their study of 29 chronic stroke survivors (mean time since stroke, 8.9 years, SD=6.5 years) that whilst a PTT using electrical stimulation is a reliable and clinically feasible test, it only has the potential to identify sensory capacity in stroke survivors with substantial sensory loss. In addition, in their cohort, the PTT was not associated with overall sensory function, as measured by stereognosis in the NSA and light touch and JPS in the FMA-S. Further, it did not reflect upper limb motor or functional capabilities, with significant yet weak correlations found between PTT and the Action

Research Arm Test (ARAT), the motor activity log (MAL) and the Stroke Rehabilitation Assessment of Movement (STREAM) (r=0.18 - 0.39; p<0.05).

Deshpande et al (2008) found a statistically significant association between vibration perception threshold (VPT) and function in the elderly. In their correlational study which formed part of the wider Health, Aging and Body Composition (Health ABC) study (n=1721), they developed a device to investigate VPT in the great toe in which a vibrating rod, 1.25cm in diameter, was positioned under the distant phalanx and produced a vibratory stimulus of 100Hz. The amplitude of this stimulus was gradually increased in increments of 0.8µm/sec until participants through pushing a hand held clicker perceived the vibration. They found those with slower gait speeds had significantly higher VPT (p<0.01) with multiple regression analysis indicating that VPT and monofilament sensitivity were independently associated with self-selected normal gait speed in their elderly cohort. Reliability of this approach was not reported.

More recently, testing the tactile acuity of the plantar aspect of the foot has attempted to recreate in part, the mechanical forces and functional conditions in which the plantar surface of the foot is exposed. Sato et al (2015), recognising the shearing forces the plantar surface of the foot is exposed to, and its impact on skin integrity, especially in diabetic neuropathy, developed a plantar foot sense-testing instrument (PFSI). The PFSI is a novel device, which applies an automated single shear movement horizontal to the surface of the skin, to provide the sensory cue of shear deformation. A textured mechanical probe (measuring 1cm x 1cm) in which range of movement provided the shearing force and speed could be manipulated. With the probe positioned under the great toe, participants indicated, with a hand held push

button switch, when movement was detected. Reporting of psychometric properties of the testing procedure was limited. Concurrent validity with the Semmes Weinstein Monofilament test was reported although the strength of correlation varied depending on anatomical site (r=0.367 – 0.954; p<0.001). The automation of the device also suggested that repeatability (test-retest) was better than the manual SWMT with the coefficient of variation ranging from 0- 0.1. Further, reliability scores or agreement was not reported. The association between detection of shear forces with functional ability was also not reported although the intuitive link between the shear stress imposed upon the plantar skin during most dynamic weight-bearing activities is intriguing. Footground or foot-shoe interactions rarely occur in the perpendicular, so tests aiming to measure shearing force thresholds may represent such interactions.

Measures reviewed thus far largely involve the passive receiving of stimuli (touch and movement) and thus require "simple" detection processing (Borstad & Nichols-Larsen, 2014). Given cortical activity within primary somatosensory regions differ when a stimulus is actively touched compared with passively received (Romo & Lafuente, 2013; Simoes-Franklin et al, 2011), the use of passive detection tests may fail to examine the integrity of the somatosensory system in its entirety, especially with regard to higher level somatosensory processing. Active or haptic sensation is the active exploration of an object or surface for the express purpose of somatosensory perception (Lederman et al, 1997). The movements selected optimize the relevant somatosensory receptors to gather the pertinent sensory qualities of the object or surface being explored (Lederman et al, 2009). The manual exploration of a stimulus for the purpose of sensory information thus combines tactile and proprioception inputs to form a sensory perception (Blanchard et al, 2011) and is more strongly

associated with measures of motor function in the upper limb (Meyer et al, 2016; Carey et al, 2005).

The area of active/haptic sensation that has arguably received the most recent attention is texture discrimination. The discrimination of texture is suggested to examine both the limitations and the capabilities of the tactile sensory system (Lamb, 1983; Carey et al 2011; Bourgeon et al, 2016). This is considered important in hand function (Carey et al, 2012; Williams et al, 2006; Miller et al, 2009) and readily available materials such as plastic, leather, silk, sandpaper, cloth are reportedly used as texture stimuli within clinical environments despite an absence of quantification and standardisation (Carey et al, 2002; Pumpa et al, 2015). In response, quantifiable, reliable and valid texture discrimination tests have been developed in the hand (Carey et al, 1997; Miller et al, 2009; Williams et al, 2006). The notion of what represents "texture" has been suggested by multidimensional scaling studies to comprise three perceptual dimensions; 1) roughness-smoothness; 2) hardness-softness; and 3) compressional elasticity\springiness (Hollins et al, 1993; Okamoto et al, 2012).

Most commonly, gratings of specific spatial intervals are used to replicate roughness perception and have been used in previous research in which tactile ability has been quantified in the fingertips of people with stroke (Carey et al, 1997; Miller et al, 2009) and improved following retraining (Carey et al, 2011). Carey et al (1997) developed a test designed to assess roughness discrimination in the fingertip through active exploration. The authors developed sets of gratings made from plastic sheets with indented ridges set at finely graded spatial intervals (1500µm to 3000µm) to represent varying degrees of roughness. By providing stimuli of differing roughness, roughness

discrimination thresholds, i.e. the point at which participants could not distinguish between stimuli, were established. The authors reported the test to be reliable across three testing sessions (r=0.92). The test also highlighted significant differences in discrimination thresholds between stroke (n=50) and control (n=50) participants (p<0.001) and has shown greater sensitivity in identifying sensory impairment compared with existing clinical measures of texture discrimination (Carey et al, 2002). Miller et al (2009) developed the AsTEX<sup>®</sup>, a single plastic sheet comprising a continuum of spatial gratings running from "rough" to "smooth". Participants were required to run their fingertip along the gratings, indicating the point at which the surface felt "smooth". Intra -rater reliability was excellent (ICC = 0.98; 95% CI =0.97–0.99) as was inter-rater reliability (ICC= 0.81; 95% CI= 0.73–0.87). Further, the tests took five minutes to administer, were well received and judged clinically feasible although motor impairment of the arm and hand following stroke presents a unique challenge to the administration of the AsTex<sup>®</sup>. They were able to distinguish between subacute and chronic stroke patients (p=0.001) and stroke and control participants (p=0.001) (Miller et al, 2009)

Precisely machined gratings as a measure of roughness perception are based on several neurophysiological studies (Blake et al, 1997; Connor & Johnson, 1992; Weber et al, 2013; Hollins & Bensmaia, 2007). In these studies, the tactile exploration of textured gratings (and raised dots) with defined spatial intervals has been shown to activate impulse patterns of specific slowly adapting type 1 (SA1) Merkel corpuscles mechanoreceptors. That is, spatial gratings result in the displacement of glabrous skin as it is depressed either by ridges or by bulges into grooves. This volumetric skin displacement activates these cutaneous mechanoreceptors. This is further extracted

by specialised cortical neurons, most apparent in Brodman Area 3b and Area 1 (part of the primary somatosensory cortex or S1) (Hollins & Bensmaia, 2007; Bourgeon et al, 2016; Gardner & Johnson, 2013). A grating with a spatial interval greater than 1mm (1000µm) is reported to provide a surface in which roughness perception is dependent on spatial neural coding (of SA1) and produces the best match to psychophysical data of roughness perception (Weber et al, 2013; Morley, 1983; Gardner & Johnson, 2013; Hollins & Bensmaia, 2007).

Functional imaging studies of healthy and stroke participants have further identified multiple neural correlates of higher level processing during texture discrimination tasks. Primary (post central gyrus) and secondary somatosensory (parietal operculum) cortices (S1 & S2) have been linked with additional activity within the posterior parietal cortex (Hartman et al, 2008) precuneus (Borstad et al, 2012), insula (Dijkerman & de Haan, 2007; Carey et al, 2016) and putamen (Preusser et al, 2015) during texture discrimination tasks. Furthermore, cortical activity within primary somatosensory regions differ when a stimulus is actively touched compared with passively received (Simoes-Franklin, et al, 2011). These studies highlight the greater level of resource required during tasks involving active texture discrimination tasks.

A further area of texture discrimination is distinguishing the compliance of an object or surface into percepts of "softness" and "hardness". It is crucial to the ability to grasp and manipulate an object in the hand (Carey et al, 2011) and may be an important component of postural control in the feet (Lynch et al, 2007). We derive the percept of softness through the spatial distribution of pressure on the skin, likely through the dynamic change in pressure distribution over time. More specifically the slowly

adapting type I (SAIs) cutaneous mechanoreceptors are mainly responsible for the discrimination of surface compliance (Hu et al, 2009, 2013; Liu & Song 2008; Srinivasan & LaMotte, 1995). Bergmann-Tiest and Kappers (2010) found that subjects could differentiate object surface compliances with a Weber fraction of  $\sim$ 15%, that is, a discrimination threshold or just noticeable difference of 15% when comparing two compliant materials in the fingertips. There has however been little progress in the relationship between neurophysiological and psychophysical responses and texture discrimination beyond surface roughness (Bergmann-Tiest, 2010). The majority of research to date has focussed on the peripheral neuro-mechanics underlying softnesshardness perception with scant data available on the central processes occurring during discrimination of surface compliance. Whilst the neural correlates underpinning texture discrimination are largely derived from fMRI studies using finger surface roughness, it could be inferred that the discrimination of surface compliance and the perception of hardness-softness is processed, interpreted and integrated in the CNS in a similar way to that of roughness. As discussed earlier, the predominant mechanoreceptors involved peripherally in the coding of both roughness and softness are the slow adapting type 1 mechanoreceptors (SA1) (Weber et al, 2013; Hu et al, 2013). Ultimately, however, their signal patterns must be interpreted perceptually to allow different textures to be compared, interpreted and distinguished. For example, discriminations of texture-roughness may predominantly involve representations of the temporal and spatial features, whereas discrimination of softness perception may involve representations of kinaesthetic, spatial, and intensive cues (Skedung et al 2013).

Cutaneous and pressure sensation on the soles of the feet are critical for maintenance of standing (Kavounoudias et al, 2001) and stepping (Perry et al, 2000) with standing and walking on surfaces of varying compliance naturally eliciting unique postural responses (Thies et al 2005; MacLellan 2006). Despite this, there is little research looking into the ability of the plantar surface of the human foot to perceive and distinguish the compliance of the surface upon which it actively places itself. A limited number of studies investigating the efficacy of sensory retraining in the lower extremity have included hardness-softness perception amongst a battery of tasks intended to retrain plantar sensory deficits in stroke populations (Hilier & Dunsford, 2006; Morioka et al, 2003; Lynch et al, 2007) and elderly populations (Morioka et al, 2009). There are limited reports, however, as to the reliability or validity of such approaches, which is important given that interventions include a variety of floor surfaces and textures with little standardisation of the stimulus properties (Lynch et al, 2007; Hilier & Dunsford, 2006). Morioka et al (2003, 2009) in two randomised controlled trials involving elderly and stroke participants, did however partly define the physical qualities of the foam/rubber mats used in their hardness-softness perceptual learning intervention task. They employed a forced choice design in which participants had to rank five foam/rubber mats based on their perceived hardness. They reported the hardness of these mats as 2425mN, 1875mN, 1500mN, 1125mN and 750mN where mN is milliNewtons (mN). These five mats convert to respective Shore A values of A30, A25, A20, A15, and A10 (Kobunshi Keiki Co.,Ltd, Japan) which is typically the scale used to measure soft foam/rubber hardness across Europe and the U.S.

## Thoughts/considerations

Measures reviewed in this section represent interesting and novel approaches, albeit with further validity and reliability evaluation required. Those that aim to quantify tactile detection thresholds (e.g. SWMT, PTT and Shear Test) have largely been utilised within peripheral neuropathy populations. They establish the presence of protective tactile sensation, but are passive tests of threshold detection, positioning the participant as a passive receiver of stimuli. Arguably, they involve less perceptual or higher level processing of the sensory stimuli, compared to tests of texture and hardness/softness discrimination, which provide a level of sensory quantification whilst assessing "active" sensation. The favourable aspects of these measures which should be considered in novel measure development includes: the importance of quantifying sensory ability using interval/continuous level scales; and the concept that discriminating between stimuli of differing textures/surface qualities places greater emphasis on higher level cortical processing.

### 4.7. Lower limb proprioception: Introduction

Given the complexity, it is unsurprising that a variety of tools and techniques to measure toe, ankle, knee, and hip proprioception have been developed with both clinical and research populations in mind (Hilier et al, 2015; Han et al, 2016). In an attempt to address the reported shortcomings of the manual assessment of proprioception, equipment and measurement tools of varying levels of sophistication, have been developed. Whilst most methods attempt to measure either joint position sense (JPS) or limb movement (kinesthesia), as manual tests do, they tend to employ equipment in order to produce greater accuracy.

# 4.7.1. Measures of single joint proprioception

At perhaps the most simple level, Lord et al (2003) developed a JPS/matching task at the knee as one of the items of the Physiological Profile Approach (PPA) to falls risk assessment. In this matching task, subjects are seated with their eyes closed and are asked to align their lower limbs simultaneously on either side of a large vertical clear acrylic sheet inscribed with a protractor and placed between their legs. Participants actively extend one limb at the knee and are then required to match that limb with active extension of the other limb. Any difference in aligning the lower limbs (indicated by disparities in matching the great toes on either side of the acrylic sheet) is measured in degrees using the transparent protractor. This is a seemingly simple way of measuring matching error whilst potentially reducing measurement error. However, the wide 95% CI values of the ICC indicate that both intra-rater (ICC=0.51, 95%CI 0.19-0.74) and inter-rater (ICC= 0.70 (95% CI 0.17–0.92) reliability of this method is variable (Lord et al, 2003). Despite this, the whole PPA has evidence to support its validity as a quantitative measure of the key physiological risk factors for falls in the elderly (Lord et al, 2003) and has been used widely. The validity of the proprioceptive component in isolation, however, has not been fully established.

Lin et al (2005) in their study investigated gait performance in chronic stroke and the relative impact of ankle/knee JPS. They used a more sophisticated approach in which elements of the clinical measures discussed earlier were combined with some relatively simple equipment. In their test of ankle and knee JPS, the assessor handled the passive limb to a predetermined position, but attached along both the axis of the fibular and the fifth metatarsal were computerised inclinometers. In these tests, the blindfolded patient moved the distal segment of the least affected joint to match the

corresponding joint angle of the most affected side, which had been positioned, to a specific angle by the examiner. For the ankle joint, the patient sat with the leg hanging vertically to the ground whilst the examiner positioned the most affected foot into 10° of either dorsiflexion or plantarflexion. For the knee joint, the examiner moved the affected leg of the seated participant from 90° of knee flexion to 100° or 80° of flexion and then asked the patient to move the least affected leg to match the most affected knee angle. Reliability of this approach was not reported. Validity analysis indicated that participants with impaired knee JPS were significantly older than those with intact knee JPS (p<0.01). Other than the age differences, correlation analysis showed that, knee and ankle joint JPS was not significantly related to any of the gait variables. Although ankle JPS contributed significantly to the variance in gait velocity and stride length (Lin et al, 2005).

Whilst the use of relatively simple equipment enhances clinical feasibility, this may be to the detriment of accuracy (Hilier et al, 2015). In response, measures using specialised, motorised equipment have been developed with the intention of more precisely controlling and evaluating the different aspects of lower limb proprioception sense. Typically, MDD/DPM approaches using specialist equipment involve the passive movement of limbs at varying velocities, with ranges from 0.1°/s to 50°/s (Refshauge et al, 1995) into a given direction. As with the manual tests described earlier, DPM requires the participant to indicate the point at which they detect movement, usually through pressing a stop button. Measurement is usually degrees of movement before detection i.e. threshold to passive movement. MDD is usually also incorporated into these tests, in which the participant is required to indicate the direction of movement. JPS methods tend to involve the reproduction of one or more predetermined positions

and/or contralateral limb matching either in a seated, partial or full weight bearing condition with either a passive-active or active-active approach used. The use of motorised equipment thus allows the precise controlling of movement velocity and position accuracy. Several variables can be more accurately calculated in JPS tests with the most common being constant error, variable error and absolute error (Smith et al, 2013). In most methods, potentially confounding factors such as auditory, visual, tactile and vestibular inputs tend to be occluded.

Comparing ankle JPS of the hemi-paretic and non-hemiparetic ankle after stroke, Yalcin et al's (2012) method typifies passive ankle joint repositioning tests in which as many variables are controlled for. In this approach, the prone, blindfolded, non-weightbearing subject has the ankle fixed to a footplate of an isokinetic dynamometer, which provides ankle displacement at a constant speed in the sagittal plane. An electrogoniometer records ankle displacement/matching error. The ankle is passively moved from the starting position to a series of target positions (in this instance 5° and 10° of plantarflexion and 15° of dorsiflexion) at a set velocity, and held for a standardised amount of time (5 seconds) once the target position is reached. The ankle is returned to the starting position, and is again moved passively towards the target position at the same velocity. When the subject perceives the ankle has returned to the target position, they indicate so by pressing a hand held button, which stops the footplate. In these tests, reliability and validity is rarely evaluated (see below for discussion on those that have) although it is generally well accepted that the magnitude of matching errors can be a useful indicator of proprioceptive acuity (Goble, 2010). However, tests that focus entirely on JPS, often using slow movement speeds between positions, are unlikely to activate the velocity dependent 1A afferents within muscle spindles, which

are implicated in dynamic balance and perturbation detection (Cronin et al, 2009; Grey et al, 2004).

Ko et al (2015) developed ankle JPS measurement equipment specifically for their study of ageing and ankle proprioception (Baltimore Longitudinal Study of Ageing). In this test, participants were seated, blindfolded, and had both feet securely strapped into two pedals. A motor moved the right foot pedal and the test subject moved the left freely. Subjects were assessed on three aspects of proprioception: 1) DPM – the point at which they detected passive movement in the right foot; 2) JPS - the accuracy of actively matching the left foot plate position to a position set (passively) in the right foot plate; and 3) Tracking ability - the ability to track movement in the right (motorised) plate with the left (freely moving plate) at different velocities. The tracking and DPM tests had good-excellent intra-rater reliability (ICC 0.88 and 0.65 respectively) although 95% confidence intervals for the ICC were not reported, and both discriminated age (p=0.01). Conversely, intra-rater reliability of the JPS test was moderate (ICC 0.44) yet lacked construct validity, unable to discriminate between old and young participants (p=0.07) (Ko et al, 2015).

Other methods using the JPS approach have used an active-active paradigm (You et al, 2005; Waddington & Adams, 1999; Witchalls et al, 2012; Deshpande et al, 2003). This approach differs from the passive approach in that the participant actively positions the foot/ankle in the first instance, usually into a series of predetermined positions. These predetermined positions when reached can be verbally indicated by the assessor (Deshpande et al, 2003), through an adjustable block (Waddington et al, 1999; Witchalls et al, 2012) or can be self-selected (You et al, 2005). The active-active

JPS paradigm mimics active joint position feedback during functional standing balance and walking tasks that operates in both active feedback and feed-forward modes (Horak et al, 2005).

Waddington et al (1999) assessed the performance of the proprioceptive system during active, functional ankle movements that occur in most daily activities, exercise and sports. The authors developed the active movement extinction discrimination apparatus (AMEDA) in which ankle JPS was established in healthy, athletic and ankle instability populations. With the participant fully weight bearing, they were required to actively achieve predetermined footplate positions in either sagittal or frontal planes. This is crucially different from passive JPS tests. In this method, the participant stood on a freely hinged platform under a single foot, built into the floor. Participants actively familiarised themselves (three times) with five predetermined footplate positions in either frontal or sagittal planes, as determined by an assessor adjusted block. Participants were then presented with a test series involving 50 repetitions, with a change of angle on each repetition randomized to one of the five test angles and were required to indicate verbally which of the predetermined test positions they had just actively positioned their ankle into (i.e. 1, 2, 3, 4 or 5). Between active movements, participants returned the footplate to horizontal and held it for a standardized interval, while the next stop angle was set (Waddington et al, 1999). Reliability has been reported as excellent in young healthy (ICC 0.82 95% CI 0.64- 0.91) and chronic ankle instability populations (ICC 0.78, 95% CI 0.62 -0.88) (Witchalls et al, 2014) and sensitivity/specificity to predict ankle injuries excellent (Witchalls et al, 2012).

Deshpande et al (2003) developed a motorised device in which four aspects of ankle proprioception were investigated: DPM, active-active JPS reproduction, reproduction of movement velocity, and reproduction of movement force/torque. Evaluated in nonpathological participants of varying ages (range 25-75), participants stood weight bearing, eyes closed, with their shod right foot on a footplate attached to a motor and potentiometer. The footplate's axis of rotation was aligned with the lateral malleolus whilst the other foot was placed on a stable platform at the same height as the footplate. Support was provided by a backrest with Velcro<sup>®</sup> belts at the waist, hip, knee, and foot levels. Active-active JPS reproduction assessed the participants' ability to actively reproduce three ankle joint positions (5° of plantarflexion, 10° of plantarflexion, 5° of dorsiflexion). From a neutral start position, participants actively moved their ankle through their available ROM (beginning in either direction) at a selfselected speed and stopped at one of the three test positions on the experimenter's verbal instructions. They concentrated on this position for 5 seconds and then moved the ankle through full range and back to the start position. Subjects were then asked to reproduce the test position actively. Mismatch absolute error (in degrees) was calculated using a potentiometer. Test-retest reliability (n=12) for the JPS approach was excellent (ICC =0.83) and the authors found that active –active JPS using this device was significantly better in middle aged adults (n=8, aged 40-59, p<0.05) compared with young adults (n=8, aged 20-39) and older adults (n=8, aged >60). In the DPM approach, again in weight bearing, from a neutral ankle position, a torque motor rotated the footplate at 0.25°/s, three times in a dorsiflexion and three times in a plantarflexion direction, in random order. Participants were instructed to press a hand held switch when they perceived ankle joint movement and its direction. The angular

displacement of the footplate required for perception of movement was recorded in degrees. Test-retest reliability for this approach was excellent (ICC=0.95) and detection thresholds (i.e. amount of movement before detection) were significantly higher in adults aged 60+ compared to middle aged (40-59) and young adults (20-39). In addition, the device allowed the evaluation of two further components of proprioception: reproduction of movement velocity and reproduction of movement force. In the assessment of velocity reproduction, from a predetermined position participants move at a self-selected speed within a set range from 20° ankle dorsiflexion to 22° plantarflexion, while concentrating on the speed of movement. After a pause of five seconds, the same movement is attempted at the same velocity. The outcome measure is the difference between average test velocity and the corresponding reproduced velocity. This approach had excellent test-retest reliability (ICC=0.79) but evidence to support its construct validity was lacking in that there were no significant differences between the three age groups (young, middle aged, old) and velocity reproduction error. The reproduction of torque test followed a similar principle to the velocity test but participants were seated and had to recreate a test torque of 10Nm (standardised through verbal feedback) over the course of six trials (three into DF and three PF). Again, the ability to recreate the test force/torque was calculated. Test-retest reliability of this aspect of the measure ranged from good to excellent (ICC=0.72-0.86) but again did not significantly differ across the three age groups. The small size of each age group (n=8) make generalisations to the wider population difficult.

Table 4.3. Summary of	measures of sing	le and multi-joint lower limb pro	prioception				
					Relia	ability	
Measure/Description	<b>Body Location</b>	Aspect of proprioception	Authors	Sample	Intra-rater	Inter-rater	Validity
Persnex Protractor	Knee	Active IPS reproduction	l ord et al (2003)	Flderlv (n=31)	+	+	NR
Digital Inclinometer	knee Ankle	Dassive - Active IPS reproduction	linetal (2005)	Stroke (n=21)	NR	NR	+
Custom Built device	Ankle	DPM/JPS/Movement Tracking	Ko et al (2015)	Elderly (n=289)	++++/++	NR	• +
SenseRite	Ankle	Active-active JPS	You et al (2005)	Adults (n= 46)	++++	NR	*
AMEDA	Ankle	Active-active JPS	Witchells et al (2012, 2014	) YH (n=25); CAI (n= 36)	++++++	NR	**+++
	Knee	Active-Active JPS	Han et al (2013)	YH (n=12)	+ + +	NR	***+++
Custom Built device	Ankle	DPM/JPS/velocity & force	Deshplande et al (2003)	Adults (n= 24)	+++++	NR	+
Slope Box Test	Ankle	JPS	Robbins et al (1995)	YH (n=40); Elderly (n=15)	++++	NR	****++
Custom Built device	Ankle	DPM	Sun et al (2015)	YH (n=21)	‡ + +	NR	NR
Robotised AFO	Ankle	DPM	Fournier et al (2016)	YH (n=30)	‡	NR	‡ ‡
Lokomat Exoskeleton	Knee, Hip	JPS	Domingo & Lam (2014)	SCI (n= 23), Controls (n=23)	++++/++	NR	+++/++
		DPM	Chisholm et al (2016)	SCI (n= 17), controls (n=17)	++++/++	NR	*****+++
Shuttle MiniClinic	Knee, Hip	JPS	Lin et al (2006)	YH (n=62)	NR	NR	‡
Biodex Dynamometer	Knee, Hip	DPM/MDD	Brindle et al (2010)	YH (n=30)	NR	NR	NR
Custom Built device	Hip	M9DPM	Wingert et al (2009)	CP (n=38); controls (n=21)	NR	NR	‡
Video Imaging	Ankle, Knee, Hip	JPS	Stilman et al (2001)	YH (n=20)	NR	NR	*****++
Abbreviations:							
AMEDA, Active Movem	ient Extinction Di	scrimination Apparatus; AFO, Anl	kle Foot Orthosis; JPS, Join	: position sense; DPM, Detec	tion of Pass	ive Moveme	ent;
MDD, Movement Direc	tion Discriminatio	on; YH, Young Healthy; SCI, Spinal	l Cord Injury; CP, Cerebral F	alsy.			
Key:							
NR, Not reported; ++++	Excellent reliable	bility/validity (>0.75); +++ = Good	reliability/validity(>0.6 - 0	74);			
++ = Moderate reliabili	ity/validity (0.4-0	<pre>.59); + = Poor reliability/validity (.</pre>	<0.39)				
* Discriminant validity	(young v old falle	er, p<0.05); ** Discriminant validit	ty (ankle instability v stable	<pre>c, p&lt;0.01); *** Discriminant v;</pre>	alidity (limb	o dominance	e, P<0.05)

\*\*\*\* Dicriminant validity (young v old, p<0.05); \*\*\*\*\* Discriminant valiidty (SCI v healthy, P<0.01); \*\*\*\*\*Face validity

You et al (2005) developed the SENSErite system in which they investigated the relationship between active-active ankle JPS and falls across a cohort of three populations (young, elderly non-fallers and elderly fallers). The system involved participants fully weight-bearing, with a single foot positioned on a hinged platform, which was connected to a potentiometer. The longitudinal axis of the platform and potentiometer was aligned with the lateral malleolus. From a starting position participants were required to actively move (invert/evert/dorsiflex/plantarflex) the ankle to a series of five self-selected target joint positions (within a set range), hold and concentrate on that position for three seconds, return to the start position and then attempt to recreate the target position. This was repeated across five positions and across the four different planes of movement. Mismatch was then recorded by bespoke hardware and software. Test-retest reliability was evaluated across the different planes of movement and was reported as excellent (ICC 0.88 – 0.98) although 95% CI, agreement or inter-rater reliability were not reported. The device showed a strong correlation with clinical goniometry but JPS acuity at the ankle was not significantly different between elderly fallers and non-fallers (p>0.05). The SENSErite system could however discriminate age (p<0.05).

Using a weight bearing set-up has clear real life merits. Most notably, significant correlations between active ankle proprioception scores and functional ability and performance have been demonstrated which is often lacking with JPS/DPM/MDD measures. Han et al (2014) for example found that ankle proprioception scores using the Active Movement Extinction Discrimination Apparatus (AMEDA) were predictive of sport performance across a range of sports, including badminton, swimming, football and gymnastics up to Olympic level. In a subsequent study the relative proprioceptive

importance of three body sites – ankle, shoulder and spine were compared, with ankle proprioception the most significant predictor of sporting performance and most strongly correlated with competition level (Han et al, 2015).

A further test in which ankle JPS was tested but did not rely on the *reproduction* of test joint position and was conducted in full weight bearing, was the *sloping box test*, first described by Robbins et al (1995a) with variants used in other studies (Halasi et al 2005; Kynsburg et al, 2006). These tests involved a series of sloping boxes, ranging from 0° to 25° in increments of 2.5°. They employed a psychophysical testing method known as magnitude estimation in which the participant is presented with a series of sloping boxes and ranks them, using a ratio scale (1-15), according to perceived gradient underfoot. In the ratio scale, 1 corresponds with a slope of 0° and 15 with 37.5°. The 12.5° difference between actual maximum slope (25°) and scale maximum was designed to allow overestimation of surface slope (Robbins et al, 1995). Participants were given reference slopes of 0°, 12.5° and 25° initially and every 11 estimates. Attentional and memory demands were high in this test given that as many as 44 trials could be required, taking 45 minutes to complete (Robbins et al, 1995a; Halasi et al, 2005). Foot position sense testing using this approach was full weight bearing and "quasi-static" in that accommodation by the foot to the support surface slope was required, as was maintenance of a stable posture when weight was transferred to the block. Physical demands were likely to be high given the frequency of single limb weight bearing and weight transference required onto the tested limb. Test-retest procedure was reported as 0.89- 0.91 using Pearson product moment correlation coefficient. The slope box test was able to discriminate between different age groups (Robbins et al, 1995) and has been used to investigate the impact of

proprioception rehabilitation on ankle JPS in conservatively and surgically managed ankle instability patients, albeit with inconclusive outcomes (Kynsberg et al, 2006; Halasi et al, 2005). Furthermore, it is apparent that the rotation of axis of the slope box does not correspond with that of the ankle joint, so changes in "slope" may also represent changes in vertical height under foot, not ankle position *per se*, questioning the construct validity of a sloping box. The clinical utility of this method, potentially requiring the placement and removal of up to 11 boxes is also questionable.

Sun et al (2015) developed a device that evaluated detection of passive motion in two planes of ankle movement (dorsiflexion-plantarflexion and inversion- eversion). It was tested in 21 healthy, young participants (mean age =26) who were seated, blindfolded with hearing occluded. The lower extremity was suspended at the thigh by a cuff attached to a steel frame, with 50% of the weight of the lower limb loaded through the foot. The foot rested on a movable platform, which rotated around two perpendicular axes and was driven by two electronic motors (for the two planes of movement). Speed of movement was reported as an angular velocity with each rotation set to  $0.007 \text{ rad} \cdot \text{s}^{-1}$ . As with other measures assessing DPM, the point at which participants' detected movement was indicated through pressing the button on a hand held device with the extent of movement recorded in degrees of rotation before detection was reported. The authors reported that the device and method showed moderate to excellent test-retest reliability across all planes of movement (ICC 0.73 – 0.93) although the dorsiflexion condition demonstrated wide 95% confidence intervals (ICC 0.73; 95% Cl 0.37 to 0.89). Validity in any form was not evaluated. Such a device represents a highly controlled assessment of ankle movement detection in which many potentially confounding factors are controlled. Critics of such approaches argue that whilst they

may represent "pure" movement detection proprioception (Elangovan et al, 2015), they do not reflect real life function and may therefore contribute little to understanding the role of proprioception in everyday activities (Han et al, 2016).

In an attempt to address ecological validity, Fournier-Belley et al (2016) explored the feasibility and robustness of measuring DPM during walking. Recognising that sensory modulation or sensory gating is proposed to occur during walking (Saradjian et al, 2015), the authors developed a robotised ankle foot orthosis (rAFO), which administered torque perturbations to the ankle, in both PF and DF, whilst participants walked on a treadmill. Thirty young participants (mean age=25; SD=3.4), during walking, had to indicate via a hand held switch, when they detected a perturbation. The authors reported good reliability (ICC =0.70, 95% CI 0.45-0.85) albeit with a wide 95%CI and lower mean ICC than other measures of ankle proprioception (Sun et al, 2015; You et al, 2005; Deshpande et al, 2003). There was a strong correlation between movement error detection threshold and the star excursion balance test (r=0.76, p = < 0.001). The nature of this test further highlights a shift away from traditional, seated DPM measures, in which as many extraneous variables are controlled for, with more emphasis on function. Whilst an interesting development, set up, associated equipment cost and practical considerations mean this method is likely to be limited to research and laboratory settings.

Neuro rehabilitation has in the last few years witnessed advances in technology with the increasing application of robotics in intervention-based protocols. Such protocols have also been applied to assess the degree of JPS impairment in the upper limbs in stroke (Dukelow et al, 2010; Leibowitz et al 2008), and lower limbs in spinal cord injury

(SCI) (Domingo & Lam, 2014). More recently, guantification of lower extremity movement sense deficits in the lower extremity have used robotic exoskeletons (Chisholm et al, 2016). These methods involved the use of computer-controlled motorized gait rehabilitation system (Lokomat, Hocoma AG, Volketswil, Switzerland). They consisted of robotic legs (exoskeleton) to which the thighs and shank were strapped. A gantry hoist system suspended the participant in the air, and foam padding was used to minimise cutaneous input from the thigh and shank strapping whilst a curtain obscured the lower extremities. The system administers passive movement through the sagittal plane only, augmented by linear motors housed within the exoskeletal structure. Encoders within the exoskeleton measure hip and knee joint angles. Their use has reportedly enabled the precise control of movement to either assess JPS (Domingo & Lam, 2014) and DPM/MDD (Chisholm et al, 2016) via customised software. Both approaches are entirely passive using a participantcontrolled joystick so the test subject "actively" repositions the limb or DPM/MDD indicated as appropriate. Assessment time has been reported to be 1.5 hours and only single joint proprioception (either hip or knee) have been evaluated. Moderate to excellent test-retest reliability in SCI participants (ICC= 0.55 for the hip, and ICC = 0.88 for the knee), and in healthy controls (ICC = 0.49 for the hip and ICC = 0.66 at the knee) was reported (Domingo & lam, 2014). The method was sufficiently sensitive to discriminate lower extremity JPS between healthy and SCI participants ( $p \le 0.008$ ) and in SCI participants, moderate to strong statistically significant correlations were demonstrated with the existing manual clinical assessment of JPS (as described by Gilman, 2002) at the hip (r= 0.507, P = 0.013) and knee (r = 0.790, p < 0.0001) (Domingo & Lam, 2014). This approach, whilst an interesting adaptation of the

robotised system has practical drawbacks: the extent and associated expense of the exoskeleton; the gantry hoist and/or treadmill; the associated software; and set up and administration time of the assessment. All are considerable and question the clinical utility of the system. In addition, despite controlling for as many variables as possible, reliability was only moderate at the hip in both control and SCI participants and the potential cutaneous input of the various straps required to both suspend the participant and move the limb may confound results.

Waddington et al (1999, 2000) designed a test to discriminate between five different knee flexion movements using a purpose-built device: the Active Movement Extinction Discrimination Apparatus (AMEDA). Tests required participants, in full weight bearing, to flex the knee, without using vision, until it contacted a horizontally adjustable knee plate. Using a similar approach to the ankle JPS test described earlier (Han et al, 2014) participants were familiarised with predetermined knee plate positions which reflected knee flexion of 37°, 38°, 39°, 40° and 41° relative to vertical. As with the ankle JPS AMEDA, participants were familiarized with series of five test angles over a series of 50 repetitions. Following familiarisation, the task was to indicate verbally which of the predetermined test positions they had just actively positioned their knee into (i.e. 1, 2, 3, 4 or 5). Between active movements, participants returned the shank to relative vertical whilst the next random test position was set (Waddington et al, 1999, 2000; Han et al, 2013). Test-retest reliability was reported as excellent (ICC 0.82) amongst a cohort of young, healthy participants (mean age 21.4 years; SD  $\pm 1.4$ ). The measure was sufficiently sensitive to discriminate between preferred and non-preferred limbs (Han et al, 2013), but was not correlated with sporting ability (r = -0.02, p = 0.866) (Han et al, 2015). Forward knee flexion in standing involves changes in muscle length at both

the ankle and hip in addition to the knee, so the extent to which this measure evaluates knee JPS is questionable. The extent to which this test is dependent on cognitive factors such as working memory and attention would also appear to be substantial.

Efforts to measure lower extremity proprioception, largely led by the sports science literature, have increasingly strived to develop measures that more closely reflect function and assess multi-joint or whole limb proprioception. For example, in a cohort of 62 elite, amateur and novice tennis players, Lin et al (2006) developed the Shuttle Miniclinic constant resistance device, a closed chain method in which hip and knee JPS was simultaneously assessed. In this method, seated, blindfolded participants actively flexed or extended the lower limb to match a passively predetermined target. Socks and an air splint around the foot and ankle minimised plantar cutaneous information, whilst extension/flexion resistance was set to 15% of the participants' bodyweight. The method discriminated lower limb proprioceptive ability between elite and novice tennis players and between dominant/non-dominant lower limbs across all groups (p<0.01). Whilst the device reflected an attempt at measuring whole limb JPS rather than individual joint JPS, further psychometric properties, such as reliability, were not reported.

In an effort to isolate potential multi-joint interactions on single joint proprioception at the knee, Brindle et al (2010) recognised the potential mechanoreceptor input from the two-joint muscle gastrocnemius. They investigated the influence of gastrocnemius state (elongated or shortened) during various knee movement velocities on knee DPM. They used a Biodex dynamometer, fitted with a custom foot/ankle apparatus to

control ankle dorsiflexion/plantarflexion. Whilst an interesting approach to multi joint interaction, their findings suggested that gastrocnemius elongation or shortening did not sufficiently influence knee movement sense at any of the three ankle movement velocities in a healthy, intact CNS. The clinimetric properties of this approach were not reported.

Stillman & McMeeken (2001) looked at three separate tests to examine both knee and whole leg position sense. They compared supine non-weight bearing (NWB) knee JPS, supine NWB whole limb JPS and weight-bearing (WB) whole limb JPS. Using video imaging to capture limb position accuracy in active –active repositioning, they calculated relative error (i.e. the difference between test and response positions) and absolute error from the images. They concluded that the WB approach produced results that were significantly more accurate in terms of absolute and relative error and more reliable in terms of variable error than both the NWB procedures (Stillman & McMeeken, 2001). However, they suggest that movement cues in the WB approach may confound JPS and in fact "mask" position sense deficits. In both NWB conditions, the test limb was *passively* positioned and then *actively* repositioned, whereas in the WB approach, the test limb was *actively* positioned and then *actively* repositioned to and from the test position. As discussed earlier poor correlations have been identified between JPS and DPM/movement sense approaches of the same joint on the same participant, suggesting different aspects of proprioception may be being measured (Gregory et al 1988; Goble, 2010; Proske & Gandevia, 2012). In addition contributions from the plantar cutaneous mechanoreceptors of the weight bearing foot may further enhance lower extremity positions sense (Hsu et al, 2006; Kavounndias, 2001) questioning the construct validity of weight bearing measures. However, the WB
approach has clear face and ecological validity in reflecting everyday function, although the authors did not investigate its association with measures of functional outcome or establish its reliability (Stillman & McMeeken, 2001).

# 4.8. Discussion

This narrative review provides a critical overview of several current approaches to measuring tactile sensation and proprioception in the lower limb. Its purpose was to describe the function, and draw out the relative merits and drawbacks of several methods of somatosensory assessment. In doing so, favourable aspects of each approach were extracted, and considered to help inform the development of novel measures.

Considering the neurophysiology of somatosensation and the complexities surrounding sensory processing, it is not surprising measurement of such a construct is theoretically and practically difficult, especially considering the neural basis of sensory processing is relatively unexplored (Borstad et al, 2012). Despite this, a range of measures have been developed, particularly in the area of proprioception, with many developed within the sports science and orthopaedic literature. Whilst this review is not exhaustive, the applicability and appropriateness of many of these measures to a stroke population is not established and given their physical and cognitive requirements, remain questionable for use in this population. For example, measures that utilise sophisticated equipment are likely beyond the scope of most clinical departments and measures that are very time-consuming and cognitively demanding, pose a serious consideration in a population in which fatigue and cognitive deficits are common. Furthermore, the psychometric evaluation of many of these measures remain limited. For example, with respect to reliability, test-retest reliability has been the area of greatest focus and assumed from correlational analysis, with data on agreement rarely reported, despite recommendations (Kottner et al, 2011). Few studies have assessed inter-rater reliability and validity, to date, has generally been limited to face or discriminant validity. The few studies that have examined the association between somatosensation and function, have found them to be mostly weakly correlated.

Current standardised clinical measures of somatosensation used in neurological populations do not fare much better as most are based, to a greater or lesser extent, on the traditional clinical assessment outlined earlier. The emphasis of these measures is at an impairment level, with the aim of screening for the presence/absence of sensory impairment. From a clinical perspective, the presence of impairment does not automatically require treatment. The juxtaposition is that the goal of rehabilitation, and indeed patients, is to improve function, not reduce impairment. Sensory measures need to reflect this yet many use dichotomous or ordinal classifications that are difficult to interpret in rehabilitation environments and within functional contexts (Connell & Tyson, 2012). Within a clinical context, objective measures should inform and guide the treatment approach and be responsive enough to monitor change. They should provide an indication of the impact and/or relationship an impairment has with functional (dis)ability. Clear and compelling evidence linking somatosensory measures with those of patient function is yet to be established, so the contribution of somatosensory impairment to functional (dis)ability is stagnantly equivocal (Lee et al, 2015; Schmid et al, 2013; Tyson et al, 2013; Connell et al, 2008; Lin et al, 2012; Connell & Tyson 2012). This is nothing new. Gowers in his seminal text (1888) warned his

readers that the practical value of sensory tests might be less than anticipated, as interpretation of findings on the sensory examination was difficult.

Many clinical measures continue to assess separate tactile (and proprioceptive) sensory modalities, which stems from the peripheral neurophysiology of cutaneous mechanoreceptors and the anatomical structure of ascending sensory tracts. Whilst anatomically separate transmission pathways exist for different modalities, there is a high degree of interaction, integration and overlap so that the idea that different modalities act independently is largely redundant (Preusser et al, 2015; Borstad et al, 2012; Borstad et al; 2014). The magnitude of correlations between sensory modalities is variable (Connell et al 2008; Winward et al, 2002), questioning the extent to which different constructs are measured and whether they should be assessed separately. The functional relevance of individual or summated tactile modalities has not been consistently demonstrated and summating ordinal scores from each modality to create a sensory score total should be interpreted with caution (Fawcett, 2007). Critics suggest such multi-modal measures fail to draw on a clear theoretical construct to guide either the choice of sensory modalities to be tested or the manner of testing (Connell & Tyson, 2012) and redundancy has been shown between body areas (Busse & Tyson, 2009). Revisions to original versions are reflective of this position with pressure and pin prick assumed to be normal if light touch is recorded as normal, and proximal sensation assumed to be normal if distal parts are. Systematically completing what can be time consuming assessments with known redundancy, and difficult to interpret individual and total scores may in part explain why most healthcare professionals do not complete a full, multi-modal standardised sensory assessment. Most clinicians opt instead for assessing just light touch and proprioception supported

by subjective reporting of impairments and observation during motor tasks (Pumpa et al, 2015; Winward et al, 1999). Studies and tools in which the limits and capabilities of the tactile system are assessed using textures, materials and objects with quantifiable physical properties provide an interesting adjunct or potential alternative to such traditional multi-modal assessments. The ability to decipher different textures, materials and objects through active or haptic sensation in the hand is not new and has been strongly linked to hand motor function (Meyer et al, 2016; Carey et al, 2011). Further, such approaches in the hand are commonplace in the clinical environment highlighting their clinical feasibility, yet studies of clinician assessment choices suggest the use of quantifiable textures and materials remain restricted to this body part and for the most part unused in clinical practice (Pumpa et al, 2015).

The peripheral and central sensory structural similarities between the glabrous skin of the soles of the feet and palms of the hands has led to an increasing recognition of the foot as a sensory organ (Alfuth & Rosenbaum, 2012; Wright, 2012). Enhancing plantar somatosensation through under-foot texture may have functional benefits. A recent systematic review with meta-analysis (Orth et al, 2013) identified a small to moderate improvement in balance when under-foot textured surfaces were applied to the sole of the foot through textured insoles, textured standing surface or footwear, in mostly young, athletic populations (SMD=0.28, 95%CI =0.46-0.09, Z=2.99, p=0.001). The evidence base for elderly populations included in the review was significantly heterogeneous (Tau2=0.16; X2=29.50, df=5, p<0.001; I2=83.05%) and only two studies involved a neurological population, both with inconclusive findings (SMD -0.14, 95%CI -0.43, 0.15, Jenkins et al, 2009 – Parkinson's; SMD -0.04, 95%CI -0.54, 0.46, Kelleher et al, 2010, Multiple Sclerosis). Similarly, Paton et al (2017) completed a systematic

review of the effects of foot or ankle devices, including but not restricted to, all types of footwear (therapeutic and retail), insoles (customized and prefabricated) and anklefoot orthoses (AFOs) on balance, gait and falls. Their review included studies involving participants with bilateral peripheral sensory loss, most notably people with MS and peripheral neuropathy. Although meta-analyses were not possible due to the heterogeneity of study participants and interventions, the review suggested that insoles and AFO's might improve static balance and gait consistency. With both these reviews, the methodological quality of included studies was poor and the heterogeneity of interventions and participants made cross study comparisons problematic. Recently, Kalron et al (2015) found 4 weeks of wearing in shoe textured insoles improved postural control (centre of pressure excursion) but not spatiotemporal parameters of gait or plantar sensitivity in relapse-remitting MS patients. The evidence investigating plantar textured surfaces, whilst limited, is encouraging. It also highlights a clear need for further research in both elderly and clinical populations.

With regard to measures of proprioception, it appears that two key questions should be asked before choosing an appropriate measure, as no single approach can capture or quantify *proprioception* (Krewer et al, 2016; Hilier et al, 2015; Elangovan et al, 2014). Firstly, which proprioceptive sense is of interest, motion or position? Secondly, which aspect of that sense do I want to measure, detection thresholds (i.e. the intensity of the smallest detectable difference or sensitivity) or discrimination thresholds (the smallest perceived difference between two stimuli or acuity)? However, the above two-question approach may be too simplistic; the concept of measuring either motion or position may be undermined because it is unclear to what extent movement information contributes to position sense and vice versa (Gregory et al, 1988). Furthermore, when the velocity of passive movement detection is manipulated, there is little correlation between tests suggesting there may be confounding factors other than detection or discrimination of movement (de Jong et al, 2005). Finally, when comparing passive movement threshold detection to movement discrimination at the same ankles, the two measures are not significantly correlated, suggesting different aspects of proprioception motion are being measured (de Jong et al, 2005).

The DPM and MDD methods mainly reflect the processing of external feedback (i.e. the peripheral transmission of proprioceptive signals) and the central processing in the contralateral somatosensory cortex with minimal "noise" from motor activity (Radovanovic et al, 2002), auditory, visual or tactile inputs. Thus, they have been suggested as the "purest" measure of proprioceptive function (Elangovan et al, 2014) as they attempt to minimise extraneous variables and reduce factors thought to be confounders in order to explore proprioceptive sense in isolation. Proprioception, however, is not just an accumulation of neural inputs to the CNS from the distal mechanoreceptors, and it is suggested that it is inappropriate to interpret either passive movement detection without muscle activation as overall proprioceptive ability. Gibson (1966) for example classifies the proprioception arising when an external device passively moves a body part (as occurs in DPM and MDD) as "imposed proprioception", which he contrasts with the "obtained proprioception" that arises from active, voluntary movements. Critics thus argue that such methods do not reflect real life function and may therefore contribute little to understanding the role of proprioception in everyday activities (Suetterlin & Sayer, 2014; Han et al, 2016). In

order to assess detection of movement thresholds, the literature overwhelmingly highlights the use of motorised equipment in which movement velocity and detection thresholds can be very accurately controlled and detected. There are potentially many expensive and sophisticated tools that do this, but most do not draw a link with function. Recently developed methods recognise the impact of sensory gating with movement and the complexity of somatosensory integration during walking tasks. Rather than attempt to control for as many variables as possible, they attempt to establish detection of movement thresholds during functional activities. Whilst these represent an interesting trend toward linking somatosensation with function, their use is likely focused on the laboratory environment.

The literature also highlights a seemingly similar need for equipment when assessing JPS reproduction, with many controlling movement velocity to the same degree and measuring errors between test position and matched position requiring some form of potentiometer or electrogoniometer. Further, JPS is heavily reliant on attention and working memory; cognitive abilities that are known to be impaired in chronic stroke (Barker-Collo, 2010). JPS often require additional constraint of the foot, usually over the dorsum, providing additional cutaneous input, a potential contributor to ankle position sense (Lowrey et al, 2010). In addition, ipsilesional somatosensory impairment post stroke has been reported in substantial proportions of stroke survivors (Connell et al, 2008; Carey & Matyas, 2011; Borstad et al, 2012) questioning the validity of JPS in which one ankle/foot is matched to the other. Furthermore, in healthy subjects, bilateral proprioceptive asymmetries exist in the ankles (Han et al, 2013), a phenomenon possibly due to interhemispheric asymmetries and the functional differences between preferred and non-preferred limbs during bilateral tasks (Goble,

2009). Finally, the extent to which the abnormal foot and ankle biomechanics, range of movement and motor impairment evident in stroke populations (Forghany et al, 2014; Kunkel et al, 2017) impede both active and passive movement exploration may also restrict the utility of such methods.

Most standardised and clinically feasible methods that assess "proprioceptive ability" involve non-weight bearing conditions and are manually administered to a passive limb by an assessor. Efforts to standardise assessor handling and provide detailed instructions have improved historically poor inter-rater reliability, yet the accuracy and validity of this approach remains questionable. Such measures may be seen to be screening tools that can detect the more profound impairments but lack the finesse and accuracy to detect subtle changes. Some studies have tantalisingly demonstrated associations between "crude" clinical measures of proprioception and function or "activity", but those associations are mostly weak and unconvincing. Conversely, the compelling link between proprioception and motor output demonstrated by laboratory and neurophysiological studies suggest that somatosensation provides feedback and feedforward mechanisms involved in movement execution. The missing link between findings of laboratory studies and the more real-life oriented observational/correlational studies is perhaps due to a lack of sensory measures that reflect the functioning of the somatosensory system and are clinically usable in a stroke population. Sophisticated methods and equipment have been introduced that reportedly can detect subtle proprioceptive deficits yet they lack clinical utility. Further, the detection of subtle impairments prompts one to question whether they show clinically meaningful differences, particularly if they do not demonstrate compelling associations with functional ability. It would appear that with most

methods claiming to measure "proprioception" there is a trade-off between ecological validity versus construct validity, and accuracy versus clinical utility. Measures that have ecological validity and reflect functional activity may not be measuring "proprioception" but a collection of integrated afferents. Measures that are clinically feasible are not very "accurate" and vice versa. The question of "accuracy" remains.

#### 4.9. Conclusion.

Themes and conclusions emerging from this narrative review and other reviews suggest that if we are to have a greater understanding of the role of somatosensation in function, measures need to begin to reflect how the system operates within a functional context. Suetterlin & Sayer (2014) in their clinical narrative highlight a need for functional weight bearing measures of proprioception, as they may be more accurate and clinically relevant. Similarly, Connell & Tyson (2012), in response to a Cochrane Review of sensory interventions in the upper limb following stroke (Doyle et al, 2010), made a plea for "interventional studies to include psychometrically robust measurement tools which are relevant and important to function" (Connell & Tyson, 2012, p.78). The need to establish somatosensory ability within the context of function is widely discussed by multiple authors, across various populations (Sullivan & Hedman, 2008; Tyson et al 2013; Suetterlin & Sayer, 2014; Elangovan et al, 2014; Han et al, 2016; Donaghy et al, 2016). As discussed earlier, measures administered in weight-bearing may lack construct validity, as they do not necessarily measure a sense in its stripped back, raw form, as other variables potentially confound the outcome. This of course is true. Weight bearing generates both tactile and proprioceptive cues. These cues in turn combine to provide a perceptual representation of our lower limb and posture sense. Attempting to distinguish and isolate individual sensory inputs and

expecting to demonstrate any meaningful association with function may be inherently flawed. The somatosensory system does not operate in isolation, either within itself or in relation to other systems and the idea that individual senses act in isolation is outdated; and so it would seem, are the somatosensory measures that continue to reflect this position. The development, feasibility, reliability and validity of functionally oriented measures of lower limb somatosensation in a stroke population requires further investigation.

In carrying out this review, the relative merits and drawbacks of existing measures, led to a list of desirable attributes that any novel measure should aim to possess. This list informed the design brief which was developed in conjunction with a Plymouth University technician (AC) in which the key requirements of any novel measure should (in no particular order):

1) Administered in full weight bearing;

2) Require "active" exploration;

3) Reflect "real" ground-foot interaction;

4) Portability;

5) Inexpensive to produce;

6) Clinically utility;

7) Easily understood by both patients and clinicians;

8) Administered by a single (trained) person;

9) Use a continuous/interval measurement scale.

The measures aimed to assess three components of lower limb somatosensation. These were: 1) Tactile sensory ability of the sole of the whole foot, thereby reflecting foot/ground interactions; 2) Foot and ankle position sense acuity thereby reflecting slope/gradient under foot; 3) Hip and knee joint position sense acuity thereby reflecting step height awareness. 5.0. Study 3. The development and psychometric evaluation of three novel measures of lower limb somatosensory discrimination

#### 5.1. Chapter Overview

This chapter describes the development and psychometric evaluation of three novel measures of lower limb somatosensory discrimination. The measures were developed in response to the lack of feasible, functionally oriented and psychometrically robust measures available for use in a chronic stroke population. They aim to assess higher level cortical processing of somatosensation by quantifying somatosensory ability through tactile and proprioceptive discrimination thresholds. The measures were developed having reflected on findings from: the qualitative study (Chapter 2) in which foot and ankle sensory changes and the functional difficulties experienced by community-dwelling stroke survivors were explored; issues arising with current clinical tests in an observational trial (chapter 3); and the synthesis review of existing somatosensory measures (chapter 4). Subsequent collaboration with patient, carer and public involvement (PCPI) groups facilitated further development of these measures, with the aim of ensuring they reflected as much as possible real life function. In response, four measures aimed to assess three components of lower limb somatosensation: 1) tactile sensory ability of the sole of the whole foot, thereby reflecting foot/ground interactions; 2) foot and ankle position sense acuity thereby reflecting slope/gradient under foot; 3) hip and knee joint position sense acuity thereby reflecting step height awareness.

### 5.2. Introduction

One of the key challenges to understanding how lower limb somatosensation interacts with functional, weight bearing activities such as walking and balance, is to quantify how tactile and proprioceptive inputs enable individuals to recognise and thus respond to variable foot-ground interactions such as surface type, slope or compliance. Understanding such complexity involves aspects of both neuroscience (O'Doherty et al 2011) and psychophysics (the branch of psychology that attempts to quantify the relationship between physical stimuli and the sensations and perceptions they produce) (Kingdom & Prins, 2009; Johnson et al, 2002).

It is widely recognized that sensation refers predominantly to the first stages in the functioning of the senses, from the effect of a physical stimulus on mechanoreceptors in skin and muscle, to their transduction and transmittal from the peripheral nervous system along pathways to the sensory areas of the brain. Sensory perception, however, involves the supraspinal and cortical structures where the "raw" sensation is processed, organized and interpreted so that it may be encoded, for example, to guide movement (Gold and Ding, 2013; Gardner & Johnson, 2013). It is thus one's perception of a stimulus that ultimately guides and informs contextual, goal oriented movement and behaviour.

Since it is the CNS rather than the peripheral sensory transducer that is affected after stroke, there is a clear rationale that any measure designed to evaluate somatosensory ability in stroke populations should attempt to assess higher level cortical processing of somatosensation and thus perception. Borstad and Nichols-Larsen (2014) suggest a model of somatosensory hierarchy may be useful in organising somatosensory

measurement from simple, to higher level, more complex tasks. In this model, sensory testing is hierarchical in nature in which stimulus *detection* lowest, followed by stimulus *discrimination*, stimulus *grading* and finally, stimulus or object *recognition*. Quantifying conscious sensory perception to an objective physical stimulus however has clear difficulties in stroke populations. For example, the relevance of impaired cognitive functions such as selective and divided attention, working memory, concentration, understanding and fatigue need to be seriously considered, especially where conscious perception of the somatosensory experience is the critical dependent measure (Winward et al, 2007).

In an attempt to understand and quantify human responses and perception to various sensory stimuli, the estimation of discrimination thresholds using alternative forced choice (AFC) design procedures is a widely used and valid approach in sensory performance and psychophysical testing (Bi, 2006; Leek et al, 2001; Gold & Ding, 2013). The AFC approach involves the exposure and subsequent mental comparison of two or more sensory stimuli, which differ along a certain physical dimension. In this approach, the participant is required to indicate which stimuli most closely reflects a particular, usually more extreme, physical property. Presenting stimuli of similar, but easily confusable physical properties thus allows the quantification of the minimal physical difference in stimulus intensity that produces a reportable difference in perceived sensation (Romo & Lafuente, 2013). In other words, the point at which two (different) sensory stimuli cannot be reliably and consistently distinguished, can be considered a discrimination threshold. Using quantifiable and graded tactile and proprioceptive stimuli may allow the quantification of these abilities along a

continuous or interval scale. Discriminative analysis, including discrimination tests and measurements, is a fundamental type of methodology in sensory science (Bi, 2006).

Current clinical approaches to evaluating somatosensory discrimination vary, as the term is used in many contexts: localisation of touch (localisation discrimination); the ability to detect whether being touched by one or two points (two-point discrimination); the ability to discriminate different textures; the appreciation of object size, shape, form and weight; and the ability to discriminate limb movement, and direction (Carey & Matyas, 2011). When unpacking these characteristics, they do not necessarily represent *discrimination per se*, or if they do, have not been applied to the lower limb. Firstly, touch localisation for example, is not a discriminative test. It is a passive test of touch detection, not a test in which two confusable stimuli are presented and discriminated between. Touch detection and touch localisation have unsurprisingly been shown to be almost identical (Tyson et al, 2008). Two-point discrimination is a discriminatory test, but has almost exclusively been used in the hand, is entirely passive and has questionable reliability in both upper and lower limbs (Stolk-Hornsveld et al, 2006). Texture discrimination tests have been established as reliable and valid active tactile tests in the hand (Carey, 1997; Miller et al, 2009), but have not been evaluated for use in the lower limb. Tests involving the appreciation of size, shape, form or weight of objects have been established but are exclusively related to the hand (Eckstrand et al, 2016; Williams et al, 2006), with questionable applicability in the lower limbs due to dextrous function requirements. Whilst measures of proprioceptive (movement) discrimination are more commonly applied to the lower limb, they are often insensitive, crude and lacking ecological validity, asking the subject to discriminate, in a single joint only, whether that joint has been moved up or down

following an imposed, passive movement by an assessor (Han et al, 2016; Gilman 2002).

Satisfaction with current approaches to somatosensory assessment, discussed earlier, is low (Lincoln et al, 1998; Sullivan et al, 2008; Connell & Tyson, 2012; Pumpa et al, 2015; Hilier et al, 2015; Han et al, 2016). More robust and sophisticated measures designed for research studies address some of these limitations yet tend to lack clinical utility in neurological populations and are often poorly evaluated (Connell & Tyson, 2012; Hilier et al, 2015). Furthermore, most clinical sensory measures are geared toward stimulus detection and identifying the presence or absence of impairment, not the severity of that impairment. In rehabilitation, measures of sensory impairment should establish their severity with a view to planning, or evaluating the effects of treatment (Connell & Tyson, 2012). Optimising function and well-being is the ultimate goal of rehabilitation. The presence of somatosensory (or any other) impairment does not automatically require treatment. Clinicians and patients need to know whether it affects function.

Clear and compelling evidence linking lower limb measures of somatosensation with measures of patient function in chronic stroke, however, is yet to be established. The contribution of somatosensory input to ongoing functional (dis)ability remains equivocal (Lee et al, 2015; Schmid et al, 2013; Tyson et al, 2013; Robinson et al, 2011; Lin et al, 2012; Connell & Tyson, 2012). In part, the shortcomings of somatosensory assessment methods may have contributed to this position (Lincoln et al, 1991; Connell & Tyson, 2012; Suetterlin & Sayer, 2014). Psychometrically robust, functionally oriented and clinically feasible measures of lower limb tactile and proprioceptive

ability which use a graded and quantifiable discrimination approach have yet to be explored.

# 5.3. Study aims and objectives

The overall aim of this study was to design, develop and evaluate functionally oriented measures of lower limb somatosensory discrimination. The measures, carried out in weight bearing evaluate: 1) active tactile discriminative ability of the foot's plantar surface, 2) foot and ankle dynamic position sense or proprioception, and 3) whole leg joint position sense. Each measure quantifies higher-level somatosensory ability by employing a two alternative forced choice (2AFC) approach to establish a discrimination threshold.

The primary study aim was to evaluate the psychometric properties of these novel lower limb somatosensory measures in chronic stroke and age-matched healthy participants. For each measure, the objectives were to:

Evaluate intra- and inter-rater reliability;

2) Determine discriminant and convergent validity;

Determine sensitivity and specificity;

4) Explore the relationship with measures of gait speed, balance, and selfreported falls.

It is anticipated that these functionally orientated measures of lower limb somatosensory discrimination will have several advantages over existing measures in terms of their sensitivity to detect somatosensory impairment, ability to quantify impairment severity, and their relationship to functional measures of gait speed, balance and falls in chronic, ambulatory stroke survivors. In comparison to sensory measures that evaluate individual sensory modalities, these composite measures potentially provide more meaningful sensory data. For example, they target higherlevel cortical processes involved in somatosensory discrimination. They also target key parts of the foot and lower limb involved in functional foot-ground interactions, such as on slopes, different surface types and steps. They evaluate active sensation, in which stimuli are manually explored for the express purpose of obtaining their sensory qualities, so combine both tactile and proprioceptive inputs. It is anticipated these measures will primarily appeal to researchers although given the simplicity of equipment, may be appropriate to clinical settings.

It is hoped these novel measures will open a dialogue regarding somatosensory assessment and inform targeted tactile and proprioceptive retraining of lower limb somatosensory impairments following stroke.

### 5.4. Methods

## 5.4.1. Patient, carer and public involvement and stakeholder Input

A key catalyst to developing these measures was patient report. In order to explore how findings from the broader foot and ankle qualitative work highlighted in Chapter 2 could inform the development of functionally oriented measures of lower extremity somatosensation, stroke survivors, their carers and stakeholders working in stroke rehabilitation were informally consulted through face-to-face meetings. A patient, carer and public involvement group (PCPI) comprising four chronic stroke survivors and three carers was set up in line with INVOLVE guidelines (NIHR, 2012). Three of the four PCPI stroke survivors were involved in the original qualitative study (Gorst et al,

2016). The brief given to the PCPI was to: 1) help enhance/clarify the qualitative findings; 2) help develop a design brief for measure idea generation; 3) ensure any proposed measures were relevant; and 4) ensure the study design and protocol was acceptable.

The PCPI group met on two occasions during the test development stage. The purpose behind setting up the group and the role of the members was explained covering the four points previously mentioned. The rationale behind the study was explained, as were key findings from the initial qualitative study with members encouraged to discuss their thoughts freely. The group agreed with the rationale that any test should be relevant and reflect the "real life" challenges encountered during standing and walking indoors and outdoors. Further meetings with the PCPI group highlighted three key areas that posed particular challenges and echoed the findings of the qualitative study (Gorst et al, 2016). These included difficulties with slopes, especially going down, misjudging the height of steps and kerbs, and not feeling fully aware or confident in knowing the surface under foot, whether that be barefoot or in shoes (which was even more challenging).

In addition to service users, other stakeholders were engaged from Northern Devon Healthcare Trust (NDHT) research team, stroke clinicians, and rehabilitation professionals working in stroke inpatient and community based early supported discharge teams. Suggestions from stakeholders were made around measure development; awareness of fatigue and attentional demands of higher level sensory testing; the involvement of speech and language therapists to ensure the inclusion of aphasic patients; clinical utility; and thoughts on optimising recruitment. Points made

through these informal stakeholder discussions were incorporated into both measure and study design.

### 5.4.2. Test development

# **Roughness discrimination test**

It is reasonable to suppose that the discrimination of surface roughness through the plantar aspect of the foot may be used to assess tactile sensory ability, as it has in the hand (Carey et al, 1997; Eckstrand et al, 2016; Miller et al, 2009). A review of existing approaches of texture discrimination and their theoretical underpinnings was discussed in chapter 4. Such methods, in which the textural qualities of a surface are actively explored for the purposes of discrimination, are suggested to challenge higher level cortical processing of somatosensation, provide more sensitive and meaningful sensory data and may more closely reflect the functioning of the somatosensory system. No study to date has established the reliability or validity of using under foot textures to assess plantar sensory ability although interventional studies investigating the effect of textured materials underfoot on perceptual-motor performance have been reviewed (Orth et al, 2013; Paton et al, 2016).

Grated footplates were produced using acrylic plates measuring 5mm x 150mm x 340mm to provide the quantifiable and graded stimulus of roughness. The gratings were machine laser cut along the direction of the shortest edge (150mm) so that the gratings ran 90° to the long axis of the foot (Fig 5.1 b). Gratings were machined using an Epilog Legend EX32 (Epilog, Colarado) with a 60 watt laser tube with a reported precision of +/- 0.3mm. Eleven sheets (including x 2 at a spatial interval (SI) of 1500µm) were produced (table 5.1) using the below ratio measurements (Fig. 5.1 a). Unit cost

was £25/sheet. The resulting spatial intervals (SI), ridge width (R), groove depth (GD) and grove width (GW) were all measured in micrometres ( $\mu$ m) with  $1\mu$ m = 1/1000 millimetre (mm).

**Fig 5.1 (a & b).** Diagrammatic representation (not drawn to scale) showing (a) cross section of grating and (b) overall dimensions of grated footplates.



	SI (µm)	R (μm)	GW (μm)	GD (μm)
Base Stimulus	1500	150	1350	900
CS1	1550	155	1395	930
CS2	1600	160	1440	960
CS3	1700	170	1530	1020
CS4	1800	180	1620	1080
CS5	2000	200	1800	1200
CS6	2200	220	1980	1320
CS7	2400	240	2160	1440
CS8	2700	270	2430	1620
CS9	3000	300	2700	1800
CS10	3250	325	2925	1950
CS11	3500	350	3150	2100

#### Table 5.1 Measurement characteristics of textured plates

Abbreviations: CS, Comparator Stimulus; SI, Spatial interval; R, Ridge Width, GW, Groove Width; GD, Groove Depth; μm, Micrometres

The SI of the base stimulus was therefore 1.5mm (1500µm) increasing to 3.5mm for the largest plate (3500µm). Comparator stimulus gratings were produced which differed from the base stimulus plate gratings by spatial intervals ranging from 50µm (i.e. 1550µm) up to a maximum of 2000µm (i.e. 3500µm) representing a spatial interval change or just noticeable difference (JND) from the standard of between 3.3% and 133% respectively. A spatial interval change of between 5-19% is considered the discrimination threshold in the fingertips of unimpaired older adults (Morley, 1983; Carey et al, 1997) and can be up to 100% in stroke patients (Carey et al, 1997). No normative data exists for the foot. The greater the spatial intervals, the rougher the

surface texture is perceived to be up to a point of between 3000 -3500µm (Morley et al, 1983; Hollins et al 2007). After that, the increasingly large width of the SI means that tactile contact with the bottom of the groove (GD) during active tactile exploration begins to diminish the perception of roughness, so that the surface is perceived as smoother (Hollins et al, 2000, 2007).

Previous studies have suggested that lateral movement, perpendicular to the gratings, is an essential requirement to discriminate roughness. These studies have thus actively assisted stroke participants to explore the stimulus where significant hemiplegia is present (Carey et al 1997; Miller et al, 2009). However, Hollins et al (2000, 2001, 2007) have developed the "duplex theory" suggesting that at least two neural codes exist for the coding of roughness. According to their theory, textures with spatial intervals greater than 100µm are encoded spatially through the firing of slow adapting (SA1) mechanoreceptors, so roughness perception is largely independent of movement, speed of movement or direction of movement (Hollins & Bensmaia, 2007).

Conversely, the roughness perception of fine surfaces less than 100µm, is based on temporal factors such as the vibrations elicited on the skin during exploration and mediated by the rapidly adapting receptors (Bensmaia and Hollins, 2003). Hollins et al (2000, 2001, 2007) further suggest that whilst intuitively "rubbing" a surface is the best way to examine its texture, movement is only necessary to the perception of much finer textures, with spatial intervals less than 100µm. It was therefore decided that those with no active toe movement would not be assisted to explore the textured surfaces and were encouraged to use whatever strategy they could to actively explore the surface (excluding visual feedback). This was felt to reflect their "real life" foot-

ground sensorimotor interaction. The purpose of this measure is to assess, in accordance with the International Classification of Functioning, Disability and Health (ICF) (WHO, 2001), the body function of touch function (b265) of sensing surfaces and their texture or quality.

## Hardness-softness test development

A second measure, designed to explore the tactile ability of the plantar surface of the foot during weight bearing, utilised the sensory perceptual (texture) dimension of hardness-softness. Perceiving the compliance of an object is crucial to the ability to grasp and manipulate an object in the hand (Carey et al, 2011) and may also be an important component of postural control in the feet (Lynch et al, 2007). Cutaneous and pressure sensation on the soles of the feet are critical for maintenance of standing (Kavounoudias et al, 2001) and stepping (Perry et al, 2000) with standing and walking on surfaces of varying compliance naturally eliciting unique postural responses (Thies et al 2005; MacLellan 2006). Intuitively, the compliance of surfaces underfoot during everyday weight-bearing activities and community ambulation (e.g. carpet, gravel, grass, soil, sand) and the difference in shoe sole compliance also varies, so potentially the ability to perceive and respond to surfaces of varying compliance is key.

To the author's knowledge, only one study to date has used quantifiably distinct foam plates under the plantar foot (Morioka et al, 2003) although these were used as part of a retraining intervention, rather than to establish sensory acuity.

Eleven foam foot plates (measuring 210mm x 400mm x 10mm) spanning a range of compliance from Shore A10 (softest) up to Shore A 60 (hardest), in increments of Shore A5 were sourced via Algeos). Shore A values were calibrated in house by the

manufacturer. Due to the mechanical limits of test instruments and the available material range, elastomers, polymers, rubber and foam are rarely expressed more precisely than Shore A5 points (<u>www.algeos.co.uk</u>). The purpose of this measure is to assess, in accordance with the International Classification of Functioning, Disability and Health (ICF) (WHO, 2001), the body function of touch function (b265), i.e. sensing surfaces and their texture or quality.

### Gradient discrimination test development

Considering the complexity involved in objectively quantifying and measuring proprioception, no one approach or measure has been established as superior in the lower limb. Multiple methods were reviewed earlier (chapter 4) which purport to measure foot-ankle position sense and/or movement sense, each with clear merits and limitations. Insight gained from the review of these approaches and methods was applied to the development of the gradient discrimination test (GDT). The key consideration in developing this test was administration in weight bearing to reflect functional foot-slope interactions. A further consideration was deciding which aspect of proprioception to assess; movement or position sense. Both are functionally important as highlighted in the literature, but accurate movement detection tools largely require sophisticated motorised equipment. Procedural considerations were to apply the 2AFC testing procedure described earlier targeting higher- level somatosensory discrimination of underfoot gradient.

In conjunction with the University laboratory technician, an adjustable platform was developed in which the support surface could be manipulated under the tested foot to produce a bi-directional slope in the sagittal plane (Fig. 5.2). The axis of the platform

was aligned with the lateral malleolus (within 3mm) as in other methods (Deshpande et al, 2003; You et al, 2005) which is broadly speaking, the biomechanical axis of rotation when the foot is dorsiflexed and plantarflexed (Palastanga & Soames, 2012). To ensure symmetrical weight bearing, the non-tested foot was positioned on an adjustable horizontal platform, which mirrored the height of the rotating platform when positioned at 0° relative to horizontal.

The measure was also evaluating quasi-static foot position sense; quasi in that the foot-ankle complex was required to accommodate to the gradient of a surface without visual input and to maintain a stable posture when weight was transferred onto that foot. Without motorisation, the platform angle was adjusted manually, requiring the participant to raise the tested foot off the test platform during each trial, and actively reposition it back onto the (adjusted) sloping platform. Hence the need for the foot-ankle complex to accommodate the surface gradient.

A laser cut acrylic "staircase" template was produced to allow for quick, quiet, nonmotorised adjustments of the surface slope. When placed into the opening between the standing platform and the base, a precise angle of the platform could be created and changed quickly, easily and quietly. The template was designed and calibrated so that each "step" corresponds to a change in platform angle of 0.5°. The template was cut and calibrated to the platform using a Wixey 365 Digital angle gauge (Barry Wixey Development, USA) and a fixed Digipas inclinometer (Digipas Technologies Inc., Dundee, UK) both of which have a reported accuracy of 0.1° and repeatability error of 0.1° (www.wixey.com; www.digipas.co.uk).

Fig. 5.2 Experimental set up of the gradient discrimination test



Participants were tested in ankle plantarflexion and ankle dorsiflexion conditions. The maximum slope into both conditions was 10° relative to horizontal and established through: the pilot study findings; reported joint position sense matching errors in previous studies (Halasi et al, 2005; Deshpande et al, 2003; Ko et al, 2015; Yalcin et al, 2012); the likely maximum available range in stroke (Forghany, et al 2014); and the functional consideration that a 5-7 ° slope is typically the angle of pavement slopes. The purpose of this measure is to assess, in accordance with the International Classification of Functioning, Disability and Health (ICF) (WHO, 2001), the body function of proprioception function (b260). I.e. sensing the relative position of body parts.

# Step height test development

The precise and skilled locomotor control of the foot over an obstacle, such as a step or kerb requires effective sensorimotor integration of visual and lower extremity proprioceptive inputs (Marigold et al, 2011; Lajoie et al, 2012; Qaiser et al, 2016). Given the complexity underlying the neurophysiological processes of gait adjustments, such as obstacle clearance, it is unsurprising that reported "misjudgements" of step height and trips over steps/kerbs are common post stroke (Hyndham, 2002) and are associated with an increased incidence of falls (Said et al, 2013). Scientific evidence demonstrates that obstacle-crossing time is increased after a stroke and, although people post stroke show a higher toe clearance (Said et al, 2008), the success of obstacle avoidance is reduced (Den Otter, 2005). Although tripping post stroke is commonly attributed to motor deficits, such as foot drop (Said, 2008; Weerdesteyn et al 2008; Van Swigchem et al, 2013), impaired lower limb proprioception is implicated in clearance errors when stepping over an obstacle (Qaiser et al, 2016). Even if live, online visual clues are obscured, healthy individuals can reduce errors and precisely step over an obstacle with minimal clearance height provided they be given performance feedback (Lam & Dietz, 2004).

In light of this, and the comments by the PCPI group in this study, a simple measure was designed to assess and reflect lower limb position sense awareness during such tasks. A key consideration in this test was to ensure it was as simple as possible, maximising clinical utility. Further, the aim was for it to challenge higher level somatosensory processing of simultaneous hip and knee static joint position sense, in a functionally oriented manner, and closely reflect hip and knee position during lead leg step/obstacle clearance.

In conjunction with the University laboratory technician, a prototype step in which the height could be easily, quickly and quietly adjusted in minimal increments was produced to provide the stimulus for whole limb joint position sense testing (fig 5.3).



Fig 5.3. Experimental set up of the step-height discrimination test

The height adjustable step was produced from a series of easily removable, interlocking and stackable, 6mm thick multiple density fibreboard (MDF) sheets. The step heights ranged from 100mm, which sits within the range of a standard kerb height, up to a maximum of 154mm. The procedure involved the passive placement of the hemi/stroke leg onto the step by the assessor use of vision discouraged and monitored by the assessor. The purpose of this measure is to assess, in accordance with the International Classification of Functioning, Disability and Health (ICF) (WHO, 2001), the body function of proprioception function (b260), i.e. sensing the relative position of body parts. In summary, the four tests were designed to measure, in weight bearing: 1) active (haptic) tactile acuity of the plantar aspect of the foot through texture/roughness discrimination; 2) active (haptic) discrimination of surface hardness; 3) discrimination of surface gradient and 4) discrimination of step height awareness.

# 5.4.3. Discrimination Testing

# Two-Alternative forced choice design

To establish the discrimination threshold in each test, a discriminative testing approach using a two-alternative forced choice design was used. Discriminative analysis, which includes discrimination tests and measurements, is a fundamental type of methodology used in sensory science (Bi, 2006). In discrimination experiments, the aim is to determine at what point two (different) stimuli, such as for example, two weights, two sounds, two textures, cannot be accurately and consistently distinguished.

The 2AFC task is a psychophysical method, developed by Gustav Theodor Fechner (1889) for eliciting responses from a person about his or her experiences of a stimulus. Specifically, the 2AFC experimental design is commonly used to test the accuracy of choices between two sensory alternatives given in a timed interval. The task is an established controlled measure of choice and is widely used to test a range of choice behaviours in animals and in humans (Macmillan & Creelman, 2005). The standard procedure of the 2AFC task involves: 1) the presentation of two alternative sensory choices in quick succession (e.g. two tactile stimuli), 2) a delay interval to allow a response/choice, 3) a response indicating choice of one of the stimuli (Gold & Ding

2013; Leek, 2001). The standard 2AFC method is widely used for measuring detection or discrimination thresholds (Bi, 2006; Leek, 2001).

The basic premise behind the 2AFC design involves the participant making a decision about the perceived difference between two stimuli with regard to a particular stimulus parameter of interest. The participants' task in in 2AFC trials is to actively explore a base stimulus and a comparator stimulus, mentally compare the two stimuli and then decide which one of the two most closely reflects the property or parameter of interest. Trials are repeated, progressively manipulating the comparator stimulus to more closely reflect the physical qualities of the base stimulus. The point, at which the two (different) stimuli can no longer be discriminated, is the discrimination threshold. Gold and Ding (2013) suggest a theoretical schematic (fig 5.4), supported by signal detection theory (Green & Swets, 1974) illustrates the complex sensory-perceptual decision processes that occur during a two alternative forced choice task. When discriminating between two stimuli, for example, which standing platform is sloping upwards the most, A or B, the process can be broken down into three processes: (1) the encoding or representation of relevant sensory information by populations of neurons (i.e. tactile/proprioceptive); (2) readout or decoding of that information to form a decision variable; and (3) application of a rule to the decision variable to generate a choice. The scheme illustrated in fig 5.4 uses a weighted sum of the outputs of sensory neurons (indicated by line thickness) to generate a decision variable so the participant is able to (or not) distinguish between the two choices.





"Sensory processing" in Signal Detection Theory

It is hypothesised that positive weights are assigned to neurons that encode one alternative, negative weights to the others. The resulting decision variable represents a difference in activity between pools of neurons whose activity represents the two alternatives (Gold & Ting, 2013). Readout reflects how information in the sensory representation is interpreted to form the decision variable that guides behaviour (response). Applying the model for example to an underfoot gradient discrimination task in which the task is to discriminate whether platform A or B is sloping up the most (i.e. placing the foot in greater dorsiflexion). In this instance, a greater level of neuron activity in heel tactile pressure mechanoreceptors and posterior lower limb proprioceptive mechanoreceptors would be assigned a positive weight. Conversely, reduced neuron activity in the pressure mechanoreceptors of the toes and fore foot and anterior proprioceptive receptors would be assigned a negative weight. Combining this overall weighting of neuronal activity, decoding it and combining it with other sensory information would then (hopefully) lead the participant to conclude that one platform is sloping more upwards than the other is. To maximize discriminability using this scheme, each weight is proportional to the relative sensitivity of the associated tactile and proprioceptive sensory neurons (Gold & Ding, 2013).

The use of the 2AFC design specific to these measures was developed in conjunction with a research psychologist with experience in psychophysical testing (Dr. K Yarrow, City University). Advantages for use in a neurological stroke population is that it requires subjects to perform a simple decision task, discriminating between just two stimuli. By restricting participants' response to a binary decision (A or B), it minimises cognitive overload, fatigue, attention and working memory requirements thereby reducing potential contamination of the measured perceptual thresholds from such factors. It also provides a threshold measure in the units of measurement. Furthermore, psychophysicists suggest the 2AFC procedure discourages response biases and produces an especially high level of performance (Macmillan & Creelman, 2005). With 2AFC there also exists a well-accepted and simple observer framework in signal detection theory (SDT) (Green & Sweets, 1974; Macmillan & Creelman, 2005).

As discussed earlier Borstad & Nichols-Larsen (2014) propose that, a model of *somatosensory hierarchy* is useful in organising somatosensory measurement from simple, to higher level, more complex tasks. They propose a hierarchical four-tier model with levels representing the range of somatosensory processing from: 1) simple stimulus detection through to the higher level requirements of; 2) stimulus discrimination, the ability to distinguish between different stimuli; 3) stimulus scaling, the ability to arrange stimuli in a graduated series and finally; 4) object recognition, recognising objects through touch. The use of the third tier, the grading of stimuli, has

been incorporated into texture and position sense discrimination in the hand and wrist in stroke (Carey et al, 1996, 1997), surface hardness discrimination under foot in stroke and elderly (Morioka et al, 2003, 2009), and slope discrimination under foot in young and elderly (Robbins et al, 1995; Waddington & Adams, 1999; Witchalls et al 2012). Despite this, it was felt that for the purposes of this study, the grading of multiple stimuli would be too time consuming when applied to multiple tests and potentially confounded by attention, working memory and fatigue levels. The 2AFC approach that is discriminating between two stimuli and targeting the second tier of "higher" level processing was felt the most appropriate in the context of assessment, measure development and the stroke population. The cognitive demands of discriminating between more than two stimuli (i.e. in 3AFC, or 4AFC approaches) were felt to be too great and would increase testing time.

#### **Discrimination testing procedure**

The 2AFC design was used to estimate the tactile and proprioceptive discrimination thresholds of the lower limb. With this method, the subject mentally compared two movement or tactile stimuli, then reported which of the two most closely reflected a given property. In these tests, the predefined property for each test was the roughest (Foot Texture Discrimination Test - FTDT), the most sloping (Gradient Discrimination Test), the softest (Hardness Discrimination Test), and the highest (Step Height Discrimination Test).

In each of these tests a 2AFC in combination with a "one-up, three-down" staircase procedure (Leek, 2001) was employed. The participant's task in each of the four tests was to discriminate between two stimuli: a base stimulus (A) and a comparator

stimulus (B). These stimuli were presented randomly (i.e. AB or BA) over the course of up to 11 trials with participants blinded as to whether the base stimulus was presented first or second in each trial. A staircase approach to the 2AFC approach involved changing the comparator stimulus dependent on whether the participants' response was correct (fig 5.5). If the participant correctly discriminated between the two stimuli, they were, for a further two trials, presented with the same base and comparator stimuli (order randomised). If they answered correctly three times in a row, they were presented in the next trial with a comparator stimulus which was marginally but quantifiably less extreme (e.g. smoother) and more similar in its properties to the base stimulus and so went down a level (the three-down part). If the participant was unable to discriminate between the two stimuli i.e. answered incorrectly just once, they went up a level and were presented in the next trial with the base stimulus and a new comparator stimulus which was quantifiably, but marginally, more extreme in its properties (e.g. rougher) than the previous comparator stimulus (i.e. the one-up part). The procedure involved increasingly challenging trials meaning the 1st trial was theoretically the easiest and involved base and comparator stimuli that differed most in their physical properties. However, given the staircase procedure, the first comparator stimulus presented does not necessarily need to be the most different. The testing procedure can begin at any point (i.e. presenting any comparator stimulus alongside the base stimulus). The procedure is designed to converge on a discrimination threshold with participant response (i.e. correct/incorrect) determining whether they go up the staircase or down the staircase.

If participants continued "down the staircase" recording correct responses through the progressively more difficult trials, the first incorrect response counted as the first

"reversal". After four reversal points (e.g. incorrect-correct-incorrect-correct) the test was stopped. The final discrimination threshold or just noticebale difference was then calculated from the mean of those four reversal points. The discrimination threshold was thus expressed in the original measurement unit and was the point at which participants could not consistently differentiate between base and comparator stimulus. It was calculated by subtracting the mean value of the four reversal points from the base stimulus value. It was also expressed as the just noticeable difference (JND) which reflected the percentage difference between (mean) comparator and base stimulus.




Whilst the one-up, three-down staircase method is a relatively quick and accurate way of reaching a discrimination threshold, as with any method involving a forced choice design the probability of guessing the correct stimulus by chance can be calculated. For example, the probability of getting a correct response in one single trial equates to a performance level of 50% (0.5) i.e. no greater than chance. To target a higher level of performance, the number of consecutive correct responses can be increased before a downward reversal is considered; thereby increasing the probability the response is not due to chance (guess). In this study, three consecutive correct responses are required in a row so the performance level or probability of three correct responses in a row occurring not by chance is 87.5% i.e.  $(0.5 \times 0.5 \times 0.5 = 0.125)$ . Reducing the probability that a reversal (i.e. three correct responses) is due to chance alone could be achieved by increasing the number of correct responses required before a step down (i.e. a one-up, four down staircase). Doing so would increase performance level but would also increase overall testing time and the cognitive and physical demands placed on the participant. The one-up, three down procedure at 87% performance levels is considered sufficient in this population in which factors such as fatigue and attention are considerations.

Each test involved placing the stimulus (gradient, texture, foam, step) under the single hemi/stroke side bare foot of the participant in standing (Description of Standard Operating Procedure for each test is included in Appendix 12). In the case of healthy controls, the stimulus was either placed under the right or left foot to reflect the proportions of stroke tested on right or left. For example, to reflect the 56%/44% split between right and left hemisphere strokes, 56% of controls (n=18) were tested on their left foot and 44% (n=14) on their right foot. The non-tested foot was placed on a

platform to ensure equal weight bearing and symmetry where required. Upper limb support, via a wall frame, was available to all participants to provide reassurance so that they were able to concentrate on the task in hand, and minimise falls risk during testing. Testing in standing was important as a) it is a functional position and b) discriminatory ability varies with the strength of the underlying stimulus and the amount of additional background "noise" (Romo & Lafuente, 2013). Stimuli were presented in a way that participants were unable to rely on any visual or auditory clues and base-comparator stimuli were presented as a pair in a random order. Simple randomisation software used in Microsoft Excel (Microsoft, USA) was applied to randomise the order of test administration and reduce random error.

#### 5.4.4. Final test development and participant, carer and public involvement

Outlines of these test ideas and the proposed 2AFC testing procedure were presented to the PCPI and stake holders who felt the preliminary ideas were innovative and appeared to reflect "real-life" functioning of the lower extremity. Stakeholders felt the proposed measures, compared to most current clinically used tests, were more reflective of lower extremity somatosensory functioning and potentially reflected the central processing of somatosensation. Concerns were expressed by stakeholders regarding the likely time it would take to administer the tests and their clinical utility given the need for equipment.

The proposed testing procedure was also discussed with the PCPI who suggested the following: background distraction should be kept to a minimum i.e. administered in an enclosed room rather than open gym/cubicle; sufficient time should be allowed for rests between each test given the attentional demands this approach requires; "warm

up" trials might be needed to ensure participants' understanding. These thoughts reflect the recommendations made by other studies in which 2AFC approaches have been used (Leek, 2001; Garcia-Perez, 1998). A general recommendation by the PCPI regarding the overall study protocol, were to ensure at least two assessment centres were available to minimise participant travel time given the geographical spread of the Devon population. Community hospitals were reported as being preferable to home testing or alternative venues. Further, the testing battery should last a maximum of 1.5 hours and include a rest period to minimise fatigue. All of these suggestions were incorporated within the final study protocol.

## 5.4.5. Pilot Study

A small pilot study was conducted in a stroke (n=8) and age-matched control population (n=6) with the aim of establishing the clinical feasibility of the tests and protocol, (which included ease of tester administration and ease of understanding the 2AFC approach) and highlighting potential ceiling effects. Recruitment of participants into the pilot study was undertaken following the same procedure as recruitment into the main study (section 5.3.6.1).

The pilot study established that the 2AFC approach was feasible and easily understood by participants provided the procedure and participants' task was clearly explained and reinforced through demonstration. The pilot highlighted the circumstances when participants had misunderstood the discrimination task. For example, two out of 14 participants initially discriminated between left foot platform and right foot platform during the gradient discrimination task, rather than discriminating between platforms

presented to the same limb. Clarity of participants' task was reinforced during verbal explanation given prior to testing.

The pilot also highlighted that participants required a period of adjustment to the stimuli being presented, especially in the roughness texture test with the optimal number of "warm up" trials established as two to three. Some of the pilot participants reported "desensitisation" to the texture tests with the grated plates beginning to feel the same (when they were not). This tended to occur if plates were changed too quickly between trials or the test was prolonged. In response, short (15- second) delays after three to four trials of the texture-roughness discrimination tests were introduced into the procedure. No ceiling or floor effects were found with the roughness texture tests in the pilot sample for either the stroke group of healthy controls.

In the gradient discrimination tests, only one participant (healthy) could consistently discriminate between two platforms that differed by the minimum difference (i.e. 0.5°) suggesting ceiling effects were unlikely. Varying base stimulus slopes were tested (0°, 3° or 5°) with no apparent difference appearing between them i.e. threshold discrimination scores were similar regardless of standard stimulus slope, in line with Weber's law (Engen, 1971). The maximum discrimination threshold identified in the pilot was 8° so it was determined that the standard stimulus should be set at 0° to allow for a greater range of thresholds.

Concentration and attention were key requirements of the tests so the testing environment could potentially confound results. Both an enclosed, quiet room and a busy, physiotherapy outpatient cubicle was used during the pilot study. All participants

indicated that a quiet room was preferential as distractions affected ability to concentrate on the task. In addition, preliminary analysis of test performance between the two environments suggested testing environment did influence test performance with almost all participants tested recording higher discrimination thresholds in the cubicle environment. Reports from some participants also indicated that as well as mental effort, the physical effort of repeatedly transferring weight on and off the stance (non-tested) leg to allow placement of the stimulus under the tested foot was considerable, so rest periods were incorporated into testing time.

A ceiling effect occurred in the hardness discrimination test with c. 40% of stroke and 100% controls able to score maximally and discriminate between the two "softest" samples (A10 and A15). Materials in which the properties were closer in physical magnitude could not be sourced so the hardness test was removed from this study. However, studies in which underfoot materials of differing densities/hardness have been used as perceptual learning exercises have demonstrated positive outcomes on postural sway (Morioka et al, 2003, 2009). The use of hardness-softness as a measure of plantar tactile ability merits further investigation, particularly given its potential reflection of real-life foot ground interactions.

#### 5.4.6. Participants

## 5.4.6.1 Participant identification and recruitment

Potential stroke and control participants were identified from the previous study (Chapter 3) in which the prevalence, distribution and functional importance of lower limb sensori-motor function was investigated. All participants recruited to that study, regardless of sensory status, were asked if they would be happy to be contacted in the

future about further studies, namely the development of novel tests of somatosensory discrimination. A consent to contact letter and form was completed (appendix 10) and a copy given to the participant. It was explained to all those providing consent to contact that their details would be kept on a secure, password-protected folder, on a secure, password protected computer. Their details would not be shared with any third party and they had simply consented to being contacted about this study. Potential participants were informed that they would be contacted within six months and that their details would be deleted after that time.

Consenting stroke and control participants were contacted by the PhD researcher using their preferred method (phone/email/post), between one to six months after participating in the previous study. In line with local guidelines and Trust ethics recommendations, the status of each participant was established through online medical records prior to making contact to ensure they were not deceased or hospitalised at the time. In accordance with their preferred contact method a participant information sheet (PIS) was either emailed or posted where requested (Appendix 11) which provided written information about the study and the contact details of the researcher should they have further questions and/or wish to participate. Participants could then choose to contact the researcher on receipt of the PIS.

Potential participants, who preferred to be contacted directly by telephone, were called by the PhD researcher who explained the nature of the study, their potential involvement and posted a PIS when requested. If participants were happy to be considered for inclusion, following verbal explanation, and did not require additional information when prompted, they were then screened for potential inclusion. All

potential participants were screened via telephone and if selection criteria were met, an appointment was arranged at their local hospital for consenting/assessment. Once recruitment targets had been reached, anyone who had completed the consent to contact form and had not been contacted/recruited, were thanked for their interest and advised that recruitment targets had been met and the study had now closed. They were also advised that their contact details would be deleted.

# 5.4.6.2. Stroke Participant inclusion/exclusion criteria

The inclusion/exclusion criteria was the same as that used in study 2 (Chapter 3, section 3.4.2.2)

# 5.4.6.3. Control Participant inclusion/exclusion criteria

The inclusion/exclusion criteria was the same as that used in study 2 (Chapter 3, section 3.4.2.3).

#### 5.4.7. Sample Size

The number of participants required to estimate intra-rater reliability was based on the work of Shoukri et al (2004); this provided guidance on sample size calculation based on the planned intra-class correlation coefficient (ICC) and their 95% confidence intervals (Cl). For a 95% Cl of 0.25 and a planned ICC of 0.8 ( $\alpha$ =0.05), 32 participants were required. Estimating a 10% drop out rate between test sessions, a target of 36 participants was set. For inter-rater reliability, a study sample of 20 with two raters and a planned ICC of 0.8 ( $\alpha$ =0.05) provides sufficient power for establishing a 95% Cl of ~0.4 (Doros and Lew, 2010). A sample size of 36 was sufficient for the test of convergent validity to detect a correlation coefficient of 0.3 (power=0.85,  $\alpha$ =0.013), to account for the multiple comparisons used (n=4). To test discriminant validity, 36 healthy controls were compared to 36 stroke survivors; this is sufficient to detect an effect size of 0.86 (power=0.85,  $\alpha$ =0.013, to account for the multiple comparisons used (n=4)).

# 5.4.8. Plan of investigation

#### 5.4.8.1 Assessment procedures

Participants (n=32) were tested with the three novel discriminatory tests on two occasions, between one week and up to two weeks apart. The researcher (TG) was the rater on test session 1 and test session 2, to establish intra rater-reliability. A third testing session, involving 20 participants, was completed by a physiotherapy assistant practitioner (PAP) with eight years clinical experience between three days and one week after session 2, so data on inter-rater reliability could be established. The time-frame for the three testing sessions thus spanned at most 14 days. The PAP was given ½ day training to familiarise them with the research protocol and ½ day training in the administration of each test. The PAP also completed Good Clinical practice (GCP) training as part of NHS Research Ethics requirements.

In testing session 1, in addition to the three discriminatory tests, participant characteristics and the Erasmus MC version of the Nottingham Sensory Assessment was administered to allow an assessment of convergent validity. In session 2, the measures of gait speed (10 meter timed walk) and balance (FRT, Postural sway) were taken following the discriminatory tests, to allow for hypothesis testing. Performance on the novel tests was expected to moderately correlate with participants' functional ability. Healthy, age and gender matched controls (n=32) were tested using the same procedure, although on only one occasion. In testing session 3, the PAP completed the

discriminatory tests independently. Up to 20 minutes of rest was made available during each session should it be required. In order to minimise effects of fatigue and systematic error, the administration order of the three sensory tests was randomly generated for each of the three sessions using simple randomisation software in Microsoft Excel (Microsoft Corp, USA)

# 5.4.8.2 Assessment measures

The following characteristics were collected: (a) Demographics – age, height, and gender; (b) Time since stroke, type of stroke (sub-cortical or cortical); (c) Modified Rankin Scale (Bonita & Beaglehole, 1988); (d) Visuospatial function as defined by the Star Cancellation test (Friedman, 1992); (d) Subjective reporting of lower extremity sensory changes; (e) reported use of walking aids indoors/outdoors; (f) Reported incidence and nature of falls within the previous three months

#### Somatosensory assessment

The Erasmus MC modified Nottingham Sensory Assessment (EmNSA) (Stolk-Hornsveld, 2006) (Appendix 6) was administered to stroke participants to investigate the convergent validity of the novel measures. Whilst there is no single gold-standard measure of somatosensation, the EmNSA is considered one of the most robust and clinically feasible measures available (Connell & Tyson, 2012). See section 3.4.4.2 for further detail.

#### Subjectively reported sensation

The subjective reporting of lower limb sensation was obtained during the first session. Participants were asked whether since their stroke, they have experienced any changes in how their foot or leg feels. If participants failed to understand the question,

they were given minimal prompting, using such phrases as "reduced or increased sensitivity to your skin being touched" or "not quite knowing where your foot is" or "not quite feeling the same as the other side".

## Gait Speed

10 m timed walk (Bohannon, 1997). The 10m timed walk is a performance measure used to assess walking speed in metres per second over a short distance. See section 3.4.4.2 for further detail.

#### Dynamic balance

*The Standing Forward Functional Reach T*est (Weiner et al, 1992) (Appendix 8) is a standardised, validated measure of dynamic balance that mirrors the everyday activity of reaching for objects beyond arm's length. See section 3.4.4.2 for further detail.

### Static standing balance

Postural control requires the ability to both orient to the environment and to maintain the centre of gravity within the weight-bearing base of support. Whilst this is referred to as "static" standing balance, it is a dynamic sensorimotor function that incorporates aspects of both anticipatory and reactive control (Shumway-Cook & Woolacott, 2012). Postural sway during quiet standing was measured by recording quiet standing using a Tekscan pressure mat (Matscan, Biosense Medical, Essex UK), a low-profile pressure sensing mat that captures static and dynamic pressure measurement data for foot function, balance and sway. See section 3.4.4.2 for further detail.

## **Falls incidence**

Falls incidence was quantified through participant retrospective recall in the first session. Further detail can be found in section 3.4.4.2.

# 5.4.9. Ethical considerations

# **Ethical review**

Ethical review was undertaken and approved by the NHS Health Research Authority NRES - Committee South Central – Berkshire B (15/SC/0191).

# Study funding

A Chartered Society of Physiotherapy (CSP) Charitable Trust Physiotherapy Research Foundation Grant (PRFB06) funded this study.

# Informed consent

Written informed consent was obtained from all participants using procedures detailed by the Council of Research Ethics Committees (UK) and in accordance with the International Declaration of Helsinki (Goodyear et al, 2007). Due to the effects of stroke, it was anticipated that some participants would be unable to write with their dominant hand so were asked to make a written indication of consent using their nondominant hand. Where participants had difficulty reading the form, it was read to them. Consent forms were completed before any study- specific procedures were performed.

Judgement on the potential participant's capacity to give informed consent was made by the PhD student who has several years' clinical experience of working with people with neurological conditions, including stroke and had completed General Good Practice (GCP) training prior to commencement of the study.

### **Potential Harm**

Participants were fully informed of the nature of the research, risks and burdens, possible benefits, amount of involvement, the voluntary nature of participating, and the right to withdraw at any time, as set out in the study PIS. As impairments in balance and mobility are common in both stroke and elderly populations (Tyson et al, 2006), during any activities that could constitute a risk, precautions were taken. Stand by assistance, use of walking aids, chairs and/or wall bars were available during assessments of walking and balance

# 5.4.10. Data Analysis

Data were summarised using frequencies and percentages, mean and standard deviation (SD) or median and inter-quartile range (IQR) as appropriate. All data was screened for outliers using mean and two standard deviation (2SD) calculations, along with box and stem-and-leaf plots. Normality of raw data was assessed to ensure it was not dependent upon the mean, which would affect statistical power (Bland, 2015). Shapiro-Wilks tests of normality were used and normality was assumed when p>0.05. Data were analysed with the SPSS version 22.0 for Windows statistical program.

Data presented for the novel test performance represents discrimination thresholds, or the just noticeable difference (JND) between base and comparator stimuli for each of the tests. The discrimination threshold is expressed in the original measurement unit, using an interval scale, and is the point at which participants could not consistently tell the difference between the base stimulus and the comparator stimulus. It was calculated by subtracting the mean value of the four reversal points (e.g. incorrect-correct-incorrect-correct) from the base stimulus value. For example, if

in the texture test the 1<sup>st</sup> (incorrect) reversal occurred at plate 1900µm, the 2<sup>nd</sup> (correct) reversal at plate 2000µm, the 3<sup>rd</sup> (incorrect) reversal at plate 1900µm and the 4<sup>th</sup> (correct) reversal at plate 2000µm, the mean value would be 1900 + 2000 + 1900 + 2000/4 = 1950µm. This value, subtracted from the base stimulus value (1500µm) establishes the discrimination threshold as 450µm. This can be expressed as the JND, which is the percent difference between the mean of the reversal (comparator) and the base stimulus and is calculated as below using the example values:

$$JND = \frac{1950\mu m - 1500\mu m}{1500\mu m} x100 = 30\%$$

The JND is calculated in the foot texture discrimination test (FTDT) and step height discrimination test (SHDT) but not the gradient discrimination test (GDT) which reports thresholds discrimination in degrees(°) which is at the interval level of measurement.

#### **Reliability testing**

Necessary assumptions in reliability testing were accounted for, as much as practicably could be. These assumptions, outlined by Bland (2015) assert that firstly, participants' true scores do not change between administrations; and secondly, the time between administrations is long enough to prevent learning, carry-over effects or recall. A minimum of three and maximum of 14 days between the three administrations means natural sensory recovery/degradation or a learning/recall effect was not likely in this chronic stroke cohort.

Statistical methods for assessing the reliability of a measure have varied rationales and limitations and no single approach is universally agreed. Both inter- and intra-rater reliability and agreement were analysed and a combination of statistical methods were used in line with recent and robust recommendations (Kottner et al, 2011). Intra class correlation coefficient (ICC<sub>2,1</sub>) was used in combination with Bland –Altman plots (Bland & Altman, 1986) as values of ICC in isolation show only the linear correlation between two sets of data, and not the agreement between them (Bland & Altman, 1986). The ICC and limits of agreement were both used together since this is recommended in order to provide sufficient information (Kottner et al, 2011). Andresen's (2000) evaluation criteria were used where an ICC >0.75 =excellent, 0.40-.74 =adeguate, and <0.40= poor.

Two-way random effects intra class correlation coefficient (ICC<sub>2,1</sub>), standard error of measurement (SEM), and coefficient of repeatability (CoR) scores were analysed. ICC<sub>(2,1)</sub> provides a reliability index to indicate the measurement error and the ICC<sub>(2,1)</sub> equation was considered the most appropriate as the aim is general application in clinical practice or research trials (Rankin & Stokes, 1998). The SEM is the standard deviation within-subjects and provides an indication of the score likely due to measurement error. It was calculated using the formula:

$$SEM = SDx\sqrt{1} - ICC$$

Coefficient of repeatability (CoR), also referred to as the "smallest real difference (SRD)", is a useful index that quantifies absolute reliability measurement error (Vaz et al 2013). This provides a score change (in the original measurement scale) which includes random and measurement error and is likely reflective of a true/real change (Vaz et al, 2013). The CoR is the value below which the absolute differences between two measurements would lie with 95% probability (Bland, 2015). It was calculated using the formula:

$$CoR = 1.96 \ x \sqrt{2} \ x \ SEM$$

Bland-Altman plots were also reported for each of the tests in which the quantification of agreement was established across both inter- and intra-rater testing. The Bland-Altman plot is a simple way to quantify agreement between two measurements by constructing limits of agreement. These limits were calculated using the mean and standard deviations of the differences between two measurements (Bland & Altman, 1986). They evaluate potential bias between differences of the second method, compared to the first one. Including the mean of the differences and the 95% CI relative to the line of equality (i.e. no difference), thus allowed the identification of any bias (Giavarina, 2015). The extent of agreement was also reported as indicated by levels of agreement (LOA) with 95% confidence intervals (CI) which demonstrate the range of measurement error within the sample (Bland, 2015).

#### **Discriminant validity**

Discriminant validity determines whether each of the novel measures discriminate between two groups expected to differ. Differences between the scores between the paretic and the matched healthy control leg were determined using a Mann Whitney U test as data was not normally distributed (p<0.05). To provide evidence of discriminant validity it was expected that the affected paretic limb would have statistically significantly higher discrimination thresholds on all tests compared to the matched healthy control limb. A comparison with the non-paretic side was not performed as the

pilot study indicated the physical effort associated with repeatedly standing on the non-test leg. It was felt participants would potentially have difficulty in repeatedly standing and balancing on the most affected leg when testing the opposite foot. In addition, it was felt by the PCPI group to prolong the assessment time for stroke participants. Finally, bilateral sensory impairment, especially in higher cortical sensory tasks, has been reported in 17% (Connell et al, 2008), 20% (Carey & Matyas, 2011) and 44% (Kim & Choi-Kwon, 1996) of stroke survivors.

To provide further evidence of discriminant validity, the ability of the novel measures to distinguish between those people with stroke reporting sensory impairment and those reporting no impairment, was investigated. Differences between the two groups were determined using a Mann Whitney U Test, as data was not normally distributed. It was expected that those reporting changes to their lower limb sensation would have significantly higher discrimination thresholds on all tests than those reporting no lower limb sensory changes.

The significance level was set at 0.05 for all analyses. Effect sizes were also reported to give an indication of the size of the differences between the groups. Effect size for normally distributed and parametric tests was calculated using Cohen's d using the formula:  $\frac{mean \, difference}{standard \, deviation}$  The effect size for non-normally distributed data and Mann Whitney U tests was calculated using the formula where effect size  $(r) = \frac{z \, score}{\sqrt{N}}$  as suggested by Grissom & Kim (2012; p. 177). Cohen's (1988) evaluation criteria was used to interpret effect size with <0.5 = small, 0.5-0.8 = medium and >0.8 = large.

### **Convergent validity**

Convergent validity refers to the degree to which two measures of constructs that theoretically should be related, are in fact related. There is no "gold-standard" measure of somatosensation, although the EmNSA is a widely used (Pumpa et al, 2015), robust and clinically usable measure of sensation in neurological populations (Connell & Tyson, 2012). Convergent validity of the novel measures was therefore determined by examining the relationship between the Erasmus MC version of the Nottingham Sensory Assessment (EmNSA) and the novel measures. A Spearman's rank order correlation was employed as data was not normally distributed (p<0.05). To provide evidence of convergent validity it was anticipated that the foot texture discrimination test (FTDT) would have a moderate correlation (r = 0.30-0.49) with the tactile score of the EmNSA. In addition, the gradient discrimination tests (GDT) and step height discrimination tests (SHDT) would moderately correlate with proprioception scores from the EmNSA. Strength of correlations were interpreted using Cohen's (1988) classification where  $\leq$  0.29 = weak, 0.30- 0.49 = moderate and,  $\geq$ 0.50 = strong.

## Sensitivity and specificity

Establishing the sensitivity and specificity of a measure is one approach frequently used to quantify a measures diagnostic ability (Bland, 2015). Measure sensitivity indicates the proportion of true positives that are correctly identified and specificity the proportion of true negatives correctly identified. The sensitivity and specificity of each measure was explored and evaluated by investigating whether those who report foot and leg sensory changes, and those who report no changes, could be identified by their performance in the novel discrimination measures. Thus, the extent to which

performance on the functionally oriented measures of somatosensory discrimination reflects subjectively reported sensory impairment was assessed through analysis of the receiver operating characteristics (ROC) curve. ROC Curve analysis evaluates a test measures' ability or accuracy to classify participants into clinically relevant groups (Zweig & Campbell, 1993); in this instance sensation impaired or sensation not impaired. In light of a lack of gold standard measure in which the presence of sensory impairment can be categorically defined (i.e. yes or no), the classification of impaired/not impaired was determined from participant reporting of sensory impairment. ROC curve plots the sensitivity and 1-specificity values at all possible values for each test with the optimal cut off point (i.e. maximal sensitivity and specificity) determined using least distance analysis and the formula:

*Least Distance* = (1 - sensitivity)2 + (1 - Specificity)2)

Youdens Index (*J*) further confirms the optimal cut off point when equal weight is given to sensitivity and specificity (Youden, 1950). This was calculated using the formula:

#### Hypothesis testing

Hypothesis testing was undertaken to examine whether the results produced on the novel sensory measures have any significant relationship with measures of functional ability. Independent t-tests or non-parametric alternative with  $\alpha$ =0.05 were used to establish whether the results produced were consistent with theoretical explanation as highlighted in the four hypotheses below. Where multiple comparisons were made, a Bonferroni correction was applied. Specifically, the following hypotheses were tested:

1) Stroke participants who report at least two falls in the last three months, will have a significantly larger discrimination threshold score on each of the sensory measures than those who report having no falls or a single fall episode;

2) Stroke participants whose gait speed is  $\leq 0.80$ m/s will have a significantly larger discrimination threshold score on each of the sensory measures, than those whose gait speed is  $\geq 0.81$ m/s;

3) Stroke participants whose postural sway (COPvelocity) is greater than the mean (+2SD) of control participants' COPvelocity will have a significantly larger discrimination threshold score on each of the sensory measures than those whose COPvelocity is less than mean (+2SD) of control COPvelocity;

4) Stroke participants whose dynamic forward reach standing balance is less than 15cm will have a significantly larger discrimination threshold score on each of the sensory measures than those who are able to reach equal to or beyond 15cm.

# 5.5. Results

# 5.5.1. Study population characteristics

Characteristics of both stroke and control participants are detailed in table 5.2. Data for age was normally distributed with no statistically significant differences in age or gender between stroke and control groups. The age profile of the stroke group was similar to that of other studies in which community-dwelling, chronic stroke survivors have been investigated (Durcan et al, 2016; Robinson et al, 2011; Lee et al, 2015).

	Stroke	Control	p value
Characteristics	(n=32)	(n=32)	
Age, years, mean (SD)	70 (9)	70 (7)	0.94ª
Gender n (%)			
Male	22 (69)	19 (59)	0.42.4b
Female	10 (31)	13 (41)	0.434~
Indoor walking ability n (%)			
Uses aid	6 (19)	0 (0)	0.01 <sup>b</sup>
No aid used	26 (81)	32 (100)	0.01°
Outdoor walking ability n (%)			
Not able	1 (3)	0 (0)	
Uses aid	19 (59)	8 (25)	0.009 <sup>b</sup>
No aid used	12 (37)	24 (75)	
No. of Falls Reported n (%)			
0	16 (50)	27 (84)	
1	6 (19)	3 (9)	
2	3 (9)	2 (7)	0.009 <sup>b</sup>
3	5 (16)	0	
>4	2 (9)	0	
			· · · ·

Table 5.2. Stroke and control participant demographics, walking aid use and falls

a: p value from independent samples t-test; b chi squared test for independence

Statistically significant differences were found between stroke and control groups with respect to self-reported indoor and outdoor walking ability, and reported falls using a chi-squared test for independence. Nineteen percent (n=6) of the stroke group reported using a walking aid indoors, whereas no control participants did so. Twenty-five percent (n=8) of the control group reporting using a walking aid when outdoors compared with 19/32 (59%) of the stroke group. Overall, one participant (in the stroke group) reported being unable to walk outdoors.

With respect to falls reporting, 50% (n=16/32) of the stroke group reported no falls over the previous three month period, with 19% (n=6/32) reporting at least one fall and 34% (n=10/32) reporting two or more falls (repeat fallers). Previous falls studies (Hyndman et al, 2002; Macintosh et al, 2005; Blennerhesset et al, 2012; Schmid et al, 2013) report similar levels in chronic ambulatory stroke patients. By comparison, 9% (n=3/32) of the control group reported falling at least once in the last three months, and 7 % (n=2/32) were repeat fallers. This is minimally lower than other studies of elderly fallers, which indicated falls occurring in 18-35% of community dwelling person's aged 65-75, and 40% of those aged >75 years (Lord et al, 1991; Rubenstein et al, 2006).

The clinical characteristics of participants with a stroke are described in table 5.3. The majority of people (78% n=25/32) had an ischaemic stroke within a cortical location (68% (n=22/32). Mean time since stroke was 22 months (SD= 18 months) indicating participants were in the chronic phase of their stroke. The Modified Rankin Score of the participants indicates that they were evenly spread between scores of 1-3. Just over one third (38%, n=21/32) had no significant disability, just under one third (31%,

n=10/32) had slight disability and the remaining 31% (n=10/32) had moderate

disability, as a result of their stroke.

Stroke Type	n (%)		
Ischaemic	25 (78)	Stroke Location	n (%)
Haemorrhagic	7 (22)	Cortical	22 (68)
		Subcortical	11 (32)
Side most affected	n (%)		
Right	18 (56)	Modified Rankin Score	n (%)
Left	14 (44)	1	12 (38)
		2	10 (31)
Time since stroke	Mean (SD)	3	10 (31)
Months mean (SD)	22 (18)		

**Table 5.3.** Stroke Participant Clinical Characteristics

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# 5.5.2. Intra-rater reliability

Individual test performance across testing sessions, expressed as mean discrimination thresholds in the original measurement scale, intraclass correlation coefficients ( $ICC_{2,1}$ ), standard error of measurement (SEM), and coefficient of repeatability (CoR) are presented in table 5.4.

In the Foot Texture Discrimination Test (FTDT), the mean discrimination threshold score, expressed in spatial intervals ( $\mu$ m), was 854 $\mu$ m in testing session 1 and 885 $\mu$ m in testing session 2. Stroke participants' mean discrimination threshold in the FTDT across the two testing sessions was 869µm (SD=517µm) representing a Just Noticeable Difference (JND) of 58% between the base stimulus and the comparator stimulus in the FTDT. SEM for the FTDT was 193µm and CoR 534µm.

In the Gradient Discrimination Test (GDT), mean discrimination thresholds across the two testing sessions were 3.2° and 3.0° for plantarflexion and dorsiflexion conditions respectively. The SEM was calculated as 0.60° in the plantarflexion test and 0.63° in the dorsiflexion test with CoR 1.6° and 1.7°.

In the Step Height Discrimination Test (SHDT), mean discrimination threshold across the two sessions was 2.4cm representing a JND of 24% from the base step height stimulus with a SEM of 0.27cm and CoR of 0.75cm.

Intra-rater reliability for all tests was excellent using Andresen's (2000) classification with mean ICC's ranging from 0.86 (95% CI 0.72-0.92) for the FTDT through to 0.95 (95% CI 0.90 - 0.97) for the SHDT. The GDT had excellent intra-rater reliability with mean ICC's of 0.91 (95% CI 0.82-0.96) for plantarflexion and 0.89 (95% CI 0.79-0.95) for dorsiflexion discrimination.

	Intra-rater Reliability (n=32)						
Measure	Test 1 (T1)	Test 2 (T2)	Mean (T1 &T2)	SEM	ICC <sub>(2,1)</sub> (95% CI)	CoR	
FTDT discrimination threshold, μm mean (SD)	854 (550)	885 (523)	869 (517)	193	0.86 (0.72-0.92)*	534	
GDT (Plantarflexion) discrimination threshold degrees (°) mean (SD)	3.1 (1.9)	3.4 (2.1)	3.2 (2.0)	0.60	0.91 (0.82-0.96)*	1.6	
GDT (Dorsiflexion) discrimination threshold degrees(°) mean (SD)	2.9 (1.9)	3.1 (1.9)	3.0 (1.9)	0.63	0.89 (0.79-0.95)*	1.7	
SHDT discrimination threshold cm mean (SD)	2.5 (1.2)	2.4 (1.2)	2.4 (1.2)	0.27	0.95 (0.90-0.97)*	0.75	

**Table 5.4.** Intra-rater reliability scores for the novel measures (stroke participants)

Abbreviations:; FTDT, Foot Texture Discrimination Test; GDT, Gradient Discrimination Test; SHDT, Step Height Discrimination test;  $\mu$ m, micrometres; cm, centimetres; SD, Standard Deviation; SEM, Standard error of measurement; ICC<sub>(2,1)</sub> Intraclass Correlation Coefficient model 2,1; CI, Confidence Interval; CoR, Coefficient of Repeatability

\*P<0.001

## 5.5.3. Intra-rater Agreement

#### Foot Texture Discrimination test (FTDT)

Bland-Altman plots indicate the mean of the differences (*d*) between test 1 and test 2 was -30µm (SD 290µm) with stroke participants' (n=32) texture discrimination threshold on average 30µm higher in the second testing session (i.e. they performed less well) compared to testing session 1 (fig 5.6). The line of equality/zero is within the 95% CI of the mean of the differences (*d*) (95% CI -131µm to 70 µm) indicating no systematic bias. The 95 % level of agreement (+/-1.96 SD) ranged from -599µm (lower LOA) to 538µm (upper LOA). Two measurement points (participants 9 and 13) fell outside this LOA with respective differences of +700µm and -950 between test 1 and test 2. Of the 32 participants, eight scored the same on test 1 as test 2.





# **Gradient Discrimination Test (Plantarflexion)**

The mean of the differences (*d*) between test 1 and test 2 was -0.3° (SD 0.82°) with stroke participants' plantarflexion gradient discrimination threshold on average 0.3° higher in the second testing session (i.e. they performed less well) compared to testing session 1 (Fig. 5.7). The line of equality/zero is within the 95% CI of *d* (95% CI 0.02°, - 0.57°) indicating no systematic bias.

The 95 % level of agreement (+/-1.96 SD) ranged from -1.9° (lower LOA) to +1.32° (upper LOA). Two measurement points (participant 13 and 21) fell outside the 95% LOA (+/- 1.96 SD) with respective differences of -2.5° and +1.5° between test 1 and test 2. Of the 32 participants, five scored the same on test 1 as test 2.



**Fig 5.7.** Bland Altman plots of the Gradient Discrimination test (plantarflexion) discrimination thresholds showing difference between test 1 and test 2 scores plotted against mean threshold scores for test 1 and test 2

### **Gradient Discrimination Test (Dorsiflexion)**

The mean of the differences (*d*) between test 1 and test 2 was -0.14° (SD 0.9°) with participants' dorsiflexion gradient discrimination threshold on average, 0.14° higher in the second testing session (i.e. they performed less well) compared to testing session 1 (Fig. 5.8). The line of equality/zero is within the 95% CI of *d* (0.18°, -0.45°) indicating no systematic bias. The 95 % level of agreement (+/-1.96 SD) ranged from -1.9° (lower LOA) to +1.62° (upper LOA). One measurement point (participant 13) fell outside the 95% LOA (+/- 1.96 SD) with a respective difference of -3.5° between test 1 and test 2. Of the 32 participants, four scored the same on test 1 as test 2.

**Fig. 5.8.** Bland Altman plots of Gradient Discrimination Test (dorsiflexion) discrimination thresholds showing difference between test 1 and test 2 scores plotted against mean threshold scores for test 1 and test 2



## Step Height Discrimination Test (SHDT)

The mean of the differences (*d*) between test 1 and test 2 was +0.04cm (SD 0.37cm) with participants' step height discrimination threshold 0.04cm lower in the second testing session (i.e. they performed better) compared to testing session 1 (Fig. 5.9). The line of equality/zero is within the 95% CI of *d* (0.17, -0.09cm) indicating no systematic bias or learning effect occurring between testing sessions. The 95% LOA ranged from -0.69cm (lower LOA) to 0.76cm (upper LOA). One measurement point (participant 11) fell outside the 95% LOA (+/- 1.96 SD) with a respective difference of +0.9cm between test 1 and test 2. Of the 32 participants tested, 18 scored the same on Test 1 as Test 2.

**Fig .5.9.** Bland Altman plots of Step Height Discrimination test discrimination threshold scores showing difference between test 1 and test 2 scores plotted against mean threshold scores for test 1 and test 2



#### 5.5.4. Inter-rater reliability

Individual test performance in 20 stroke participants when assessed by two different raters is presented in table 5.5. As with intra-rater reliability testing, scores are expressed as mean discrimination thresholds in the original measurement scale, with reliability scores of intra-class correlation coefficients (ICC<sub>2,1</sub>), standard error of measurement (SEM), and coefficient of repeatability (CoR) included (table 5.5)

In the FTDT, the mean discrimination threshold score, expressed in spatial intervals ( $\mu$ m), was established as 835 $\mu$ m by rater 1 and 847 $\mu$ m by rater 2. Stroke participants' mean discrimination threshold in the FTDT across the two testing sessions was 841 $\mu$ m (SD=512 $\mu$ m) representing a JND of 56% between the base stimulus and the comparator stimulus in the FTDT. The SEM for the FTDT was 161 $\mu$ m and CoR 448 $\mu$ m.

	Inter-rater Reliability (n=20)					
Measure	Rater 1 (R1)	Rater 2 (R2)	Mean (R1 &R2)	SEM	ICC <sub>(2,1)</sub> (95% CI)	CoR
FTDT discrimination threshold, μm mean (SD)	835 (541)	847 (511)	841 (512)	161	0.90 (0.76-0.96)*	448
GDT (Plantarflexion) discrimination threshold degrees (°) mean (SD)	2.8 (1.7)	2.5 (1.8)	2.6 (1.7)	0.45	0.93 (0.82-0.97)*	1.2
GDT (Dorsiflexion) discrimination threshold degrees(°) mean (SD)	2.5 (1.5)	2.6 (1.9)	2.5 (1.7)	0.48	0.92 (0.79-0.97)*	1.3
SHDT discrimination threshold cm mean (SD)	2.0 (1.0)	14 (1.1)	1.7 (1.0)	0.38	0.85 (0.64-0.94)*	1.1

Table 5.5. Inter-rater reliability scores for novel measures of discrimination (stroke participants)

Abbreviations:; FTDT, Foot Texture Discrimination Test; GDT, Gradient Discrimination Test; SHDT, Step Height Discrimination test; μm, micrometres; cm, centimetres; SD, Standard Deviation; SEM, Standard error of measurement; ICC<sub>(2,1)</sub> Intraclass Correlation Coefficient model 2,1; Cl, Confidence Interval; CoR, Coefficient of Repeatability \*P<0.001

In the GDT, mean discrimination thresholds across the two testers were 2.6° and 2.5° for plantarflexion and dorsiflexion conditions respectively. SEM were calculated as

0.45° in the plantarflexion test and 0.48° in the dorsiflexion test with CoR 1.2° and 1.3° respectively. In the SHDT, mean discrimination threshold across the two raters was 1.7cm representing a JND of 17% from the base step height stimulus with a SEM of 0.38cm and CoR of 1.1cm.

Inter-rater reliability for all four tests was excellent with mean ICC's ranging from 0.90 (95% CI 0.76-0.96) for the FTDT through to 0.85 (95% CI 0.64 - 0.94) for the SHDT. Both GDT had excellent inter-rater reliability with mean ICC's of 0.93 (95% CI 0.82-0.97) for plantarflexion and 0.92 (95% CI 0.79-0.97) for dorsiflexion discrimination.

### 5.5.5. Inter-rater agreement

### **Foot Texture Discrimination Test**

The mean of the differences (*d*) between rater 1 and rater 2 was -12.5μm (SD<sub>diff</sub> 242μm) meaning rater 2, on average, scored participants' texture discrimination threshold 12.5μm higher (i.e. they performed less well) compared to rater 1 (Fig 5.10). The line of equality/zero is within the 95% Cl (Cl 94μm, -119μm) suggesting that there is no systematic bias between rater 1 and rater 2. The 95% LOA ranged from -487μm (lower LOA) to 462μm (upper LOA). One measurement point (participant 7) fell outside the 95% LOA (+/- 1.96 SD) with a respective difference of -550μm between rater 1 scores and rater 2 scores. Of the 20 participants tested, six were scored the same by both rater 1 and rater 2.

**Fig. 5.10.** Bland Altman plots of Foot Texture Discrimination Test discrimination threshold scores showing difference between rater 1 and rater 2 scores plotted against mean threshold scores for rater 1 and rater 2



### **Gradient Discrimination Test - plantarflexion**

The mean of the differences between rater 1 and rater 2 was +0.3° (SD<sub>diff</sub> 0.7°) meaning rater 2, on average, scored participants' plantarflexion discrimination threshold 0.3° lower (i.e. participants performed better) than rater 1 (Fig. 5.11). The line of equality/zero falls within the 95% CI of *d* (95% CI 0.58°, -0.03°) suggesting that there is no systematic differences or bias in the scoring of participants between rater 1 and rater 2. The 95% LOA ranged from -1.0° (lower LOA) to 1.6° (upper LOA). One measurement point (participant 7) fell outside the 95% LOA (+/- 1.96 SD) with a respective difference of -1.5° between rater 1 scores and rater 2 scores. Of the 19 participants tested, five scored the same when tested by both rater 1 and rater 2.





# **Gradient Discrimination Test - dorsiflexion**

The mean of the differences between rater 1 and rater 2 was -0.04° (SD<sub>diff</sub> 0.7°) meaning rater 2, on average, scored participants' plantarflexion discrimination threshold 0.04° higher than rater 1 (i.e. participants performed less well when tested by rater 2) (Fig. 5.12). The line of equality/zero falls within the 95% CI of *d* (95% CI 0.29°, -0.38°) suggesting that there is no systematic bias occurring between rater 1 and rater 2. The 95% LOA ranged from -1.4° (lower LOA) to 1.3° (upper LOA). One measurement point (participant 11) fell outside the 95% LOA (+/- 1.96 SD) with a respective difference of -1.7° between rater 1 scores and rater 2 scores. Of the 18 participants tested, two scored the same when tested by both rater 1 and rater 2.

**Fig 5.12.** Bland Altman plots of Gradient Discrimination Test (dorsiflexion) discrimination threshold scores showing difference between rater 1 and rater 2 scores plotted against mean threshold scores for rater 1 and rater 2



#### **Step Height Discrimination test**

The mean of the differences (*d*) between rater 1 and rater 2 was 0.7 cm° (SD 0.6cm) with rater 2, on average, scoring participants' step height discrimination threshold 0.7cm lower than rater 1 (i.e. participants performed better when tested by rater 2) (Fig. 5.13). The line of equality/zero is outside the 95% CI of *d* (95% CI 0.41cm - 0.91cm) indicating a degree of systematic bias in participant performance when assessed by rater 2. As can be seen by fig 5.13 no single participant scored worse on the SHDT when assessed by rater 2. Of the 20 participants tested, six scored the same when assessed by raters 1 and 2 whilst 14 performed better when assessed by rater 2. The 95% level of agreement ranged from -0.48cm (lower LOA) to 1.8cm (upper LOA). No measurement points fell outside the 95% LOA (+/- 1.96 SD).

**Fig. 5.13** Bland Altman plots of Step Height Discrimination Test discrimination threshold scores showing difference between rater 1 and rater 2 scores plotted against mean threshold scores for rater 1 and rater 2



# 5.5.6. Validity Testing

#### **Discriminant Validity; Stroke and control**

Data was not normally distributed as indicated by the Shapiro-Wilks test for normality (p<0.05). A Mann-Whitney U test revealed significant differences in all discrimination test scores between the most affected lower limb in the stroke participants and the matched lower limb of control participants with effect sizes moderate to strong (r=0.51-0.58) (table 5.6.). Texture discrimination threshold scores of the stroke limb (median = 750µm) were significantly higher than matched control limbs (median=300µm, U = 267, z=-3.313, p=.001, r= .58). Plantarflexion gradient discrimination thresholds of stroke participants (median=3.1°) were also significantly higher than controls' gradient thresholds (median = 1.5°, U=213, z=-4.031, p<0.001, r=.71). Similarly, stroke participants' gradient discrimination thresholds in dorsiflexion (median=3.0°) was significantly higher than that of controls (median = 1.2°, U=164, z =-

4.690, p<0.001, r=.83). Finally, the ability to discriminate the height of a step was significantly worse in stroke participants with height thresholds greater (median=1.8cm) than that of control participants (median=1.2cm, U=202, z=-4.252, p<0.001, r=.75).

Measure	Stroke (n=32)	Control (n=32)	p value <sup>a</sup>	Effect size <sup>b</sup>
FTDT discrimination threshold, μm median (IQR, range)	750 (875, 1850)	300 (325, 850)	0.001**	0.58
GDT Plantarflexion discrimination Threshold degrees (°) median (IQR, range)	3.1 (2.8, 8.3)	1.5 (1.1, 2.5)	<0.001**	0.71
GDT Dorsiflexion discrimination threshold degrees (°) median (IQR, Range)	3.0 (2.4, 8.3)	1.2 (1.0, 2.5)	<0.001**	0.83
SHDT discrimination threshold cm median (IQR, Range)	1.8 (2.4, 3.6)	1.2 (0.6, 1.8)	<0.001**	0.75

**Table 5.6.** Stroke and control participants' discrimination test performance.

Abbreviations: FTDT, Foot Texture Discrimination test; GDT, Gradient Discrimination Test; SHDT Step Height Discrimination Test; IQR, Inner Quartile Range; <sup>a</sup>: p value derived from Mann Whitney Test; \*P<0.05; \*\*p<0.01

### Discriminant validity; subjectively reported impairment versus no impairment

Seventy-five percent (n=24) of stroke participants at assessment felt they had altered sensation in their leg and/or foot following their stroke. Conversely, 25% (n=8) felt their sensory ability in their lower limbs was normal. There were no statistically significant differences between the subjectively impaired and not impaired groups in terms of age, time since stroke, type of stroke or side of stroke (p>0.05) (table 5.7).

Data was not normally distributed for sensory test performance scores so Mann

Whitney U tests were carried out to establish whether those stroke participants who

reported altered sensation in their lower limb (n=24) differed in their test performance

on the novel measures and the EmNSA compared to those who subjectively reported no sensory changes (n=8). Statistically significant differences between the impaired and not impaired groups in the discrimination tests and all but the proprioceptive assessment of the EmNSA were demonstrated.

**Table 5.7.** Subjectively impaired and subjectively not impaired stroke participant characteristics and test

 performance

Characteristics		Subjectively altered sensation (n=24)	Subjectively no altered sensation (n=8)	p value	Effect size
Age (mean, years) Time since stroke (mean, months)		69.5 20	70 28	0.87ª 0.30ª	-
Type of stroke Cortical n (%) Sub Cortical n (%)		16 (66) 8 (34)	6 (75) 2 (25)	0.66 <sup>b</sup>	-
Side of stroke	Left n (%) Right n (%)	9 (37) 15 (63)	5 (62) 3 (38)	0.21 <sup>b</sup>	-
EmNSA total score/40		35	37.5	0.04 <sup>c</sup> *	0.36
Proprioc	Tactile total/32 ception total /8	27 7	30 7.5	0.019 <sup>c*</sup> 0.64 <sup>c</sup>	0.41 0.08
FTDT discrimina threshold, medi	tion an μm	1000	300	0.003 <sup>c**</sup>	0.52
GDT (Plantarflexion) discrimination threshold median degrees (°)		3.5	1.5	0.002 <sup>c**</sup>	0.54
GDT (Dorsiflexion) discrimination threshold median degrees (°)		3	1.5	0.005 <sup>c**</sup>	0.50
SHDT Discrimination threshold median.cm		2.5	1.2	0.03 <sup>c</sup> *	0.37

Abbreviations: EmNSA, Erasmus Medical Centre Modified Nottingham Sensory Assessment; FTDT, Foot Texture Discrimination test; GDT, Gradient Discrimination Test; SHDT Step Height

Discrimination Test;

a: Independent samples t-test; b Chi-squared test for independence; c Mann Whitney U test; \*P<0.05; \*\*p<0.01

Effect sizes for the difference between the groups were calculated and revealed small effect sizes for both the tactile component of the EmNSA, overall EmNSA and the SHDT (0.41, 0.36 and 0.37 respectively). Medium effect sizes (≥0.50) and greater significance levels were demonstrated between the groups in performance in the FTDT and GDT.

Further evaluation of how participants' scores on the EmNSA reflected people's reporting of impairment was conducted. Of those reporting no impairment (filled circles, n=8), all scored  $\geq$ 30/40 on the EmNSA (i.e. comprising both tactile and proprioception components) (Fig 5.14). Conversely, those who did report altered sensation in their feet and/or legs (non-filled circles, n=24) scored from 8/40 through 40/40. A maximal score in the EmNSA indicates no impairment.





### **Convergent Validity**

Data was not normally distributed; therefore, Spearman's rank order correlation (rho) analysis was carried out to evaluate convergent validity. Associations between the discrimination tests and the tactile and proprioceptive scores of the EmNSA, were investigated (table 5.8). The FTDT had a strong correlation with the total tactile score of the EmNSA (r=0.70; p<0.01) and a weak and non-significant correlation with
proprioceptive scores of the EmNSA (r=0.29; p>0.05). Both GDT's had moderate correlations (r=0.41; p<0.05; r=0.47; p<0.01) with tactile scores of the EmNSA but weak and non-significant correlations with the proprioceptive scores of the EmNSA (r=0.17; p>0.05; r=0.28; p>0.05). The SHDT did not significantly correlate with the tactile or proprioceptive components of the EmNSA. All novel measures demonstrated significant and moderate –strong correlations with each other.

Measure	EmNSA Sens tot	EmNSA Tact tot	EmNSA Prop tot	FTDT	GDT (PF)	GDT (DF)	SHDT
1. EmNSA sensory total	-						
2. EmNSA tactile total	.979**	-					
3. EmNSA proprioception	.660**	.509**	-				
4. FTDT	673**	699**	292	-			
5. GDT (PF)	399*	406*	173	.602**	-		
6. GDT (DF)	471**	469**	284	.627**	.956**	-	
7. SHDT	140	139	052	.494**	.593**	.570**	-

 Table 5.8. Spearmans (rho) correlations between novel discrimination measures and EmNSA.

Abbreviations: EmNSA, Erasmus Medical Centre Modified Nottingham Sensory Assessment; FTDT, Foot Texture Discrimination test; GDT, Gradient Discrimination Test; SHDT Step Height Discrimination Test; PF, Plantarflexion; DF, Dorsiflexion

\*\* Correlation is significant at the 0.01 level (2 tailed) \* Correlation is significant at the 0.05 level (2 tailed)

# Sensitivity and specificity

### **ROC Curve Analysis**

The sensitivity and specificity of each test to classify participants as impaired or not

impaired based on their individual report was analysed using ROC analysis. The area

under the curve (AUC) c statistic for the texture discrimination test was 0.85 (SE 0.081, 95% CI 0.69-1.00 p = 0.004) indicating an adequate overall predictive ability (Andresen, 2000). Using both least distance ((1-Sn) 2+ (1-Spec)2) and Youden index methods, the optimal cut off point to predict subjectively reported sensory impairment using the FTDT was deemed to be a discrimination threshold of 500 $\mu$ m (Youden index 0.67). At this level, the foot texture discrimination test demonstrated a sensitivity of 79% and a specificity of 87% (table 5.9).

Test	AUC	SE	95% CI	p value	Youden Index	Cut Off Point	Sens (%)	Spec (%)
FTDT	0.85	0.081	0.69-1.0	0.004	0.67	500µm	79	87
GDT								
Dorsiflexion	0.83	0.076	0.68-0.98	0.005	0.67	1.9°	79	87
Plantarflexion	0.87	0.064	0.74-0.99	0.002	0.67	2.1°	79	87
SHDT	0.75	0.12	0.51-0.98	0.037	0.62	1.3cm	87	75

Table 5.9. Sensitivity and specificity analysis of novel measures

Abbreviations: FTDT, Foot Texture Discrimination Test; GDT, Gradient Discrimination Test; SHDT, Step Height Discrimination Test; AUC, area under curve; SE, Standard Error; CI, Confidence Interval; Sens, Sensitivity; Spec, Specificity; µm, micrometres; cm, centimetres.

The AUC c statistic for the gradient discrimination tests were 0.83 (SE 0.076, 95% CI 0.68-0.98, p = 0.005) for dorsiflexion and 0.87 (SE 0.064, 95% CI 0.74-0.99, p = 0.002) for plantar flexion with both tests indicating an excellent overall predictive ability (Andresen, 2000). Using both least distance ((1-Sn) 2+ (1-Spec)2) and Youden index methods, the optimal cut off point to predict subjective sensory impairment was a gradient discrimination threshold of 1.9° of dorsiflexion and 2.1° of plantarflexion (Youden index 0.67). At this level, both gradient discrimination tests demonstrated a sensitivity of 79% and a specificity of 87%.

Finally, the step height test, the AUC c statistic was 0.75 (SE 0.12, 95% CI 0.51-0.98, p = 0.037) indicating an adequate overall predictive ability (Andresen, 2000) although the 95% CI indicates the AUC value could be as low as 0.51 suggesting poor predictive value, or marginally better than chance (i.e. 0.5). Using both least distance ((1-Sn) 2+ (1-Spec)2) and Youden index, the optimal cut off point to predict subjective sensory impairment was deemed to be a step height discrimination threshold of 1.3cm (Youden index 0.63). At this level, the step height test demonstrated a sensitivity of 87% and a specificity of 75%. ROC analysis (Fig 5.15) shows individual curves for each measure. The straight reference line running diagonally indicates a 0.5 probability of being diagnosed impaired/not impaired i.e. no greater than chance.





Curves to the left of the reference line indicate better diagnostic value than chance alone, whereas curves to the right of the line indicate worse diagnostic value. The closer the curve follows the top left corner, the better the diagnostic value.

### 5.5.7. Hypothesis testing

**Hypothesis 1:** Stroke participants who are repeat fallers ( $\geq 2$  falls in previous 3 months) will have a significantly larger discrimination threshold score on each of the sensory measures than those who report having no falls/single fall.

Stroke participants were categorised into falls group based on the number of falls (self-reported) in the three months preceding the assessment, in line with previous studies of falls across neurological populations (Soyeur et al, 2007; Belgen et al, 2005). Participants were categorised as non-fallers if no falls had been reported, single fallers if one fall had been reported, and repeat fallers if  $\geq 2$  falls had been reported. A Kruskal-Wallis tests revealed a statistically significant difference in texture discrimination thresholds across the three falls groups (group 1, n=16; No falls, group 2 n=6; Single fallers, group 3, n=10; >2 falls)  $X^2$  (2, n=32; p=0.021). Repeat fallers recorded a higher median discrimination threshold (median=1200µm) than single faller groups (median =300µm) and no falls group (median=500µm). Step height discrimination thresholds were also statistically significant between the three falls groups (p=0.001). Repeat fallers recorded a higher median step height discrimination threshold (median =4.2cm) than single fallers (median =1.8cm) and non-fallers (median =1.8cm). There were no statistically significant differences between the falls groups on EmNSA or GDT performance (Table 5.10)

Sensory Measure median (IQR, Range)	Group 1 No Falls (n=16)	Group 2 Single faller (n=6)	Group 3 Repeat fallers (n=10)	pª
EmNSA Total /40	36 (11,32)	34 (13, 16)	32 (13,16)	0.74
Tactile total /32	28 (11,28)	27 (11,16)	26 (10,13)	0.79
Prop total /8	7.5 (2,4)	8 (3,4)	6 (2,4)	0.54
FTDT threshold $\mu m$	500 (860, 1550)	300 (975, 1850)	1200 (675,1150)	0.021*
GDT threshold(°)				
Plantarflexion	2.2 (2.6, 8.3)	2.0 (2.5, 4.0)	3.2 (3.0,6.3)	0.33
Dorsiflexion	2.8 (2.2, 8.3)	1.8 (1.4, 2.5)	2.6 (3.4,5.8)	0.24
SHDT threshold cm	1.8 (1.2.2.4)	1.8 (2.9, 3.3)	4.2 (0.9, 1.8)	0.001**

 Table 5.10.
 Sensory test performance of stroke non- fallers, single fallers and repeat fallers

<sup>a</sup> Kruskal-Wallis Test \* P<0.05; \*\*P<0.01. Abbreviations: FTDT, Foot Texture Discrimination Test; GDT, Gradient Discrimination Test; SHDT, Step Height Discrimination Test.

Post hoc Mann Whitney U tests between group 1 (no falls) and group 2 (single falls) and group 1 (no falls) and group 3(repeat fallers) across the FTDT and SHDT were carried out with a Bonferroni adjustment (0.05/2 = 0.025) to account for the two comparisons (i.e. no fall v single fall and no fall v repeat falls). There was no significant difference in texture threshold scores between group 1 (no falls) (Md =500µm, n=16) and group 2 (single fallers) (Md = 300µm, n=6) U = 31500, z=-0.707, p=0.48, r=0.15). There was also no significant difference in step height discrimination threshold scores between group 1(no falls) (Md =1.8cm, n=16) and group 2 (single fallers) (Md = 1.8cm, n=6) U = 34000, z=-0.501, p=0.616, r=0.11.).

Comparing non fallers with repeat fallers a Mann Whitney U test revealed significant differences in step height discrimination thresholds (U = 7000, z = -3.894, p = < 0.0001,

*r*=0.76) but not texture discrimination thresholds with Bonferroni correction (U=45000, Z=-1.860, p=0.05, r=0.36).

**Hypothesis 2**: Stroke participants whose gait speed is  $\leq 0.80$ m/s will have a significantly larger discrimination threshold score on each of the sensory measures, than those whose gait speed is  $\geq 0.81$ m/s.

Fastest gait speed (m/s) was recorded during the 10m timed walk with participants categorised according to whether they walked quicker or slower than 0.8m/s. Such a cut off is suggested to predict functional walking status with non/limited community ambulators <0.8m/s and unrestricted community ambulators >0.80m/s (Bowden et al, 2008; Salbach et al, 2014). Data were not normally distributed so Mann Whitney u tests were employed. Table 5.11 shows statistically significant differences between the two walking speed groups in test performance on the GDT and SHDT (p<0.05). A Bonferroni adjustment (0.05/2=0.025) to take into account the two tests of GDT, indicates performance on the GDT was not significant differences between the two group speeds. There were no statistically significant differences between the two groups and performance on the EmNSA. Effect sizes for all tests were small (<0.5).

Spearman rank order correlation analysis indicated that both GDT (r = .467, p<0.01; r = 0.403, p<0.05) and SHDT (r = 0.60, p<0.01) had moderate-strong and significant correlations with gait speed. Conversely, the FTDT showed a weak and non-significant correlation with gait speed overall (r = 0.26; p>0.05) as did the tactile and proprioceptive components of the EmNSA (r = 0.11 and r=0.12, p>0.05).

Sensory Measure median (IQR, Range)	Gait speed <0.80m/s (n=9)	Gait speed ≥0.81m/s (n=23)	<i>p</i> value <sup>a</sup>	effect size
EmNSA Total Score /40	32 (11,16)	36 (15,32)	0.72	0.14
Tactile total /32	26 (10,16)	28 (11,28)	0.80	0.17
Proprioception total /8	7 (2,2)	8 (2,4)	0.77	0.05
FTDT threshold μm GDT threshold degrees (°)	1200 (650, 1750)	600 (900, 1600)	0.15	0.25
Plantarflexion	3.75 (2.9, 7.5)	2.25 (2.3, 7)	0.03*	0.36
Dorsiflexion	3 (3.3, 7)	2 (2, 7)	0.04*	0.36
SHDT threshold cm	4.2 (1.9, 3.0)	18(1836)	0.01*	0.27

**Table 5.11.** Comparison of stroke participants with a gait speed <0.8m/s with those  $\ge$ 0.80m/s in sensory test performance

a Mann Whitney U test; \* P<0.05; Abbreviations: FTDT, Foot Texture Discrimination Test; GDT, Gradient Discrimination Test; SHDT, Step Height Discrimination Test.

**Hypothesis** 3: Stroke participants whose postural sway (COP<sub>velocity</sub>) is greater than the mean (+2SD) of control participants' COP<sub>velocity</sub> will have a significantly larger discrimination threshold score on each of the sensory measures than stroke participants whose COP<sub>velocity</sub> is less than mean +2SD of control COP<sub>velocity</sub>

There were no statistically significant differences (p>0.05) in any of the sensory tests between stroke patients whose COP<sub>velocity</sub> was 2SD greater than healthy controls and those whose COP<sub>velocity</sub> fell within 2 SD (table 5.12). Correlational analysis (Spearman's rho) indicated moderate and significant correlations between COP<sub>velocity</sub> and the GDT (dorsiflexion) (r=0.44, p=0.018) and plantarflexion (r=0.432; p=0.022) conditions. With a Bonferroni correction to account for the two tests (0.05/2 = 0.025) these correlations remained statistically significant. No other significant correlations were identified. **Table 5.12** Sensory test performance comparison of stroke participants with a COP<sub>velocity</sub> <2SD of control</th>COP<sub>velocity</sub> and stroke participants with a COP<sub>velocity</sub> >2SD of control participants COP<sub>velocity</sub>

Sensory Measure	COP(velocity) < 2SD	COP <sub>(velocity)</sub> >2SD	p value <sup>a</sup>
median (IQR, Range)	(n=17)	(n=13)	
EmNSA Total Score /40	32 (11,32)	30 (12,26)	0.28
Tactile total /32	28 (10,28)	26 (10,24)	0.31
Proprioception total /8	8 (2, 4)	7 (2,4)	0.25
FTDT threshold $\mu m$	600 (800, 1750)	750 (800,1450)	0.25
GDT threshold degrees (°)			
Plantarflexion	2.0 (1.8, 7.5)	3.1 (3.1, 7.0)	0.14
Dorsiflexion	2.0 (1.8, 7.2)	3.7 (2.9, 7.4)	0.07
SHDT threshold cm	1.8 (2.0, 3.3)	2.75 (1.9, 3.6)	0.19

a Mann Whitney U test; \* P<0.05; \*\*P<0.001. Abbreviations: FTDT, Foot Texture Discrimination Test; GDT, Gradient Discrimination Test; SHDT, Step Height Discrimination Test

**Hypothesis** 4: Stroke participants with a dynamic forward reach test score (FRT) less than 15cm will have a significantly larger discrimination threshold score on each of the novel sensory measures than those who are able to reach beyond 15cm.

Those stroke participants unable to forward reach beyond 15cm, a cut off deemed as falls risk (Acar & Karantas, 2010) had significantly higher texture discrimination thresholds as measured by the FTDT (p=0.005), ankle position sense through the GDT in both direction of testing (p<0.001) and knee/hip position sense thresholds, as measured by the SHDT (p=0.02), compared with those participants able to reach beyond 15cm. Medium effect sizes were demonstrated between the two groups (>0.5) with respect to FTDT and GDT performance whilst SHDT thresholds, demonstrated a small effect size (0.39). All three measures also showed strong and

significant correlations with the FRT (FTDT, r=-0.62, p<0.01; SHDT, r=-0.59, p<0.01; GDT, r=-0.57, p<0.01). The total score of the EmNSA and its tactile component did also show significant associations, but the strength of these correlations were weaker (r=0.36, p<0.05). The proprioceptive component showed no significant correlation with FRT scores (r=0.18, p>0.05).

Sensory Measure	FRT<15cm	FRT>15cm	p value	Effect size
median (IQR, Range)	(n=9)	(n=23)		
EmNSA Total Score /40	25 (18,24)	36 (13,32)	0.02*	0.40
Tactile total /32	20 (13,21)	28 (6, 28)	0.04*	0.46
Proprioception total /8	6 (2, 4)	8 (2,4)	0.10	0.29
FTDT threshold μm	1200 (900, 1400)	400 (900, 1600)	0.005**	0.50
GDT threshold degrees (°)				
Plantarflexion	5.0 (2.5,5.0)	2.0 (2.0, 8.3)	0.001**	0.57
Dorsiflexion	4.0 (2.9, 5.0)	1.75 (1.5, 8.3)	0.001**	0.58
SHDT threshold cm	4.2 (2.7, 3.0)	1.8 (1.2, 3.6)	0.02*	0.39

**Table 5.13.** Sensory test performance comparison of stroke participants with a Functional Reach Test(FRT) score of less than 15cm and those with an FRT greater than 15cm

a Mann Whitney U test; \* P<0.05; \*\*P<0.01. Abbreviations: FTDT, Foot Texture Discrimination Test; GDT, Gradient Discrimination Test; SHDT, Step Height Discrimination Test

# 5.6. Discussion

This study investigated the reliability and validity of three novel, functionally oriented measures of lower extremity somatosensory perception in an ambulatory, chronic stroke population. All three measures reported good to excellent inter- and intra- rater reliability and agreement. Similarly, discriminant and convergent validity are supported by the direction, magnitude, and pattern of correlations with relevant measures. Further evidence of validity is provided through hypothesis testing in line with theoretical expectation and ROC analysis. These data support the use of these measures in both clinical and research settings.

The demographic profile and clinical characteristics of the stroke group in this study are similar to that of the previous chapter and in line with other studies in which ambulatory chronic stroke survivors have been investigated (Durcan et al, 2016; Robinson et al, 2011; Lee et al, 2015). This stroke sample had similar levels of walking ability/walking aid use (Blennerhassett, et al 2012; Lee et al, 2015) and number of falls (Hyndman et al, 2002; Macintosh et al, 2005; Blennerhesset et al, 2012) as other studies in this arena. Sixteen percent (n=5/32) of the control group in this study, reported one or more falls in the last three months. By comparison, falls incidence has been reported to be 18-35% in those aged >65 (Rubenstein et al, 2006) so the control participants in this study, were representative of the healthy population in relation to falls.

# Reliability and agreement

The foot texture discrimination test (FTDT) assessed active or haptic plantar tactile ability of the whole foot in weight bearing and demonstrated excellent inter-and intra-

rater reliability. The gradient discrimination test (GDT) assessed foot/ankle position sense and demonstrated excellent intra- and inter-rater reliability in both DF and PF conditions. The step height discrimination test (SHDT) assessed joint position sense at the hip and knee and demonstrated excellent intra- and inter-rater reliability albeit with a marginally broader 95% CI compared to the other measures.

Inter-rater reliability is a crucially important property for outcome measures. People with long-term neurological conditions, and stroke, tend to interact with many different health-care professionals during the course of their rehabilitation, so the inter-rater reliability of a measure, which may be administered by different healthcare professionals, is important. Poor or lower inter-rater reliability is commonly reported in standardised measures of sensory testing, particularly, as many involve the passive testing of a body part/limb by an assessor (Stolk-Hornsveld et al, 2006; Winward et al, 2002; Lincoln et al, 1991; Lin et al, 2004). That the lower limit of the 95% CI of the SHDT was below ICC 0.75, suggests assessor handling may have an impact on SHDT performance. The 2<sup>nd</sup> rater in this study was an experienced physiotherapy assistant practitioner and received approximately ½ day training in the administration of these measures. At face value, additional training and/or similar experience levels of assessors could optimise inter-rater reliability and minimise measurement error. However, even when both assessors are equally trained, highly experienced clinicians, inter-rater reliability has shown to be only moderate in certain sensory assessments (Lincoln et al, 1998). Intensive training and practice however can improve this (Sullivan et al, 2011) although such training programmes are perhaps beyond the scope of many. Variable inter-rater reliability appears to be an inherent problem within sensory testing, particularly with assessor handling and perhaps explains why more reliable and

arguably accurate measures of proprioception tend to use motorised equipment, reducing the impact of assessor handling. The poor reliability of measures of somatosensation is frequently considered one of the key challenges facing measurement (Lincoln et al, 1991; Connell & Tyson, 2012).

The measures developed in this study attempted to combine both clinical usability with research accuracy and the reliability results from this study are extremely encouraging. This is even more so considering the increased attentional and cognitive demands involved in the 2AFC approach. They compare very favourably with the reliability scores of other measures of tactile sensation and proprioception of the lower extremities. For example, the Semmes-Weinsten Monofilament test, commonly used in neurological practice (Pumpa et al, 2015) has shown to have variable reliability. Moderate-excellent intra-rater reliability (ICC 0.78, 95%CI 0.68-0.83) has been reported in young healthy populations (Collins et al, 2010) but poor reliability has been found in elderly populations (ICC= 0.51, 95% CI 0.19-0.74) (Lord et al, 2003). Similarly poor inter-rater reliability is reported in healthy (ICC = 0.43, 95%Cl 0.16 - 0.61) and MS populations (Kw 0.48, 95% Cl 0.18 – 0.7) (Collins et al, 2010; Uszynski et al 2016). The reliability results from this dissertation are also favourable to the commonly used EmNSA; the sensory measure used as part of the validity testing. Intra-rater reliability Kappa weighted values (Kw) of the tactile components of the EmNSA ranged from Kw 0.71-0.87 with inter-rater reliability scores ranging from Kw 0.70-0.88 (Stolk-Hornsveld et al, 2006). Similarly, the results compare favourably to inter-rater reliability of the sensory subtest of the Fugl-Meyer assessment without intensive assessor training ( $K_w$ =0.30-0.55 light touch and 0.71-0.90 proprioception; Lin et al, 2004) and following intensive training (light touch; ICC, 0.87; 95% CI, 0.69–0.95; proprioception sub score

ICC, 0.96; 95% CI, 0.90–0.99)(Sullivan et al, 2011). Further, the tactile discrimination test developed in the hand using textured spatial gratings (Carey et al, 1997) was reported with excellent inter-rater reliability (r=0.92) amongst a stroke cohort.

The GDT and SHDT also compare favourably with other measures of ankle, knee and hip JPS; measures which tend to use sophisticated equipment, often limiting their clinical utility. The reliability of knee JPS tests is hugely variable (Smith et al, 2013) ranging from ICC= 0.08 (Kiefer et al, 1998) through to excellent (ICC 0.99; Ghiasi & Akbari, 2007). Such ICC variability may be influenced by the heterogeneity of the populations studied and the varying methodological approaches (Kottner et al, 2011; Rankin & Stokes, 1998). A further test in which ankle JPS is tested but does not rely on reproduction of test joint position and is conducted in full weight bearing, is the sloping box test, first described by Robbins et al (1995a); with variants used in other studies (Halasi et al, 2005; Kynsburg et al, 2006). Test-retest procedure was not reported although reliability was suggested as 0.89- 0.91 using Pearson product moment correlation coefficient, although this statistical approach in isolation has been reported as insufficient for indicating reliability (Kottner et al, 2011). More recently seated tests of both ankle joint position sense (JPS) and movement direction discrimination (MDD) in multiple planes of ankle movement, report mean ICC reliability values ranging from 0.73 to 0.935 (Sun et al, 2015; Ko et al, 2015). What makes the novel measures developed in this dissertation study potentially appealing is that they are comparable to existing measures, which utilise relatively sophisticated, mechanised/motorised equipment, yet they are potentially more clinically feasible as they require much less sophisticated and expensive equipment. Given the accepted crudeness of simple proprioceptive measures which rely heavily on assessor handling

and do not use equipment (Han et al, 2016; Hilier et al, 2015), it appears essential that in order to gain a psychometrically robust measure of proprioception, some form of equipment may be necessary.

Reliability, whilst referring to the reproducibility of repeated measurements and most commonly estimated using ICC, also refers to the absence of random measurement error in that the smaller the standard error of measurement (SEM), the greater the reliability (Bland, 2015). Combined with the CoR scores calculated from the SEM, these potentially provide clinicians and researchers with quantitative indications of score changes in the original measurement scale (or as a percentage change) which is due to real true change thus allowing for systematic and random error (Vaz et al, 2013). For example, in the GDT a change in discrimination threshold of  $\leq 0.60$  is likely due to measurement error whereas a change above ≥1.6° (the CoR) is considered a real, true change. So any difference, greater than the CoR is unlikely to be due to chance or random error and is likely to indicate a real (significant) difference at the 5% significance level. Adding further support to the reliability data, these measures all demonstrated acceptable levels of intra-rater agreement as indicated through Bland-Altman plots. In any one test, a maximum of 2/32 participants fell outside the 95% LOA for the tests. One single participant (P13) fell outside the 95% LOA in the TDT and both GDT. This participant had a right hemisphere ischaemic stroke, and may have had difficulties of both sustained and selective attention, although this was not formally assessed. Attention is required in these tests of somatosensory discrimination, and attentional ability can confound outcomes in sensory tests if not controlled for (Lincoln et al, 1991; Winward et al, 2007). However, excellent reliability and agreement results indicate the testing procedure has, to an extent, controlled for, and minimised, the

impact of attention deficits. For example, back ground noise was minimised through testing in an enclosed environment. Frequent breaks were given during each test and between tests. Three trial runs of each test were completed before scoring commenced and participant instructions were protocolised to ensure they were consistent, clear and concise. Clinical intuition also played a role in that if it was clear a participant had misunderstood the nature of the testing procedure, the test was stopped, instructions were reiterated in the standardised format and testing recommenced after a short break. Reliability was further established through controlling as many variables as possible: administering the tests in the same environment, at the same time of day; randomising test order to minimise potential fatigue/attention issues; and standardising the procedural protocol and participant instructions. The line of equality/zero sits within the 95% confidence interval of the mean difference (d) for each of the tests, indicating no systematic bias in intra-rater testing, suggesting no learning effect took place. Had a learning effect occurred, it would be anticipated that discrimination thresholds would have been systematically lower in the second session.

Bland Altman analysis revealed excellent intra-rater agreement for all tests and excellent inter-rater agreement for the texture and gradient discrimination tests. Systematic bias however was present in inter-rater reliability testing in the step height discrimination test, the only test to use assessor handling. The 95% Cl of mean difference (*d*) fell outside the line of equality (i.e. no difference) with all participants having a discrimination threshold either equal to or lower when tested by rater 2 compared to rater 1. These data indicate a systematic bias, likely because of assessor handling and possible differing sensory inputs across the test conditions, which

confounded participants' seemingly better proprioceptive performance. Whilst assessor training may improve inter-rater reliability, as discussed earlier, it is potentially an inherent problem in sensory testing in which limbs are handled or stimuli are presented to a passive limb. The SHDT test however may be easily adapted and could potentially be further improved by conducting the test without *any* assessor handling whereby the participant actively places the tested leg onto the step volitionally. Given the standard stimulus for the SHDT was set at 10cm to reflect a typical roadside kerb height, and these tests are aimed at ambulatory communitydwelling stroke participants, this simple adjustment may be feasible in this stroke cohort and a focus for testing in future work. Inevitably, this adjustment may exclude those participants with substantial hemiparesis, but it would eliminate assessor passive handling and thereby more closely reflect the "real" and active sensorimotor mechanisms involved in stepping.

#### Discriminant validity

Discriminant validity was demonstrated in all three tests. Statistically significant differences were found in discrimination threshold scores between the most affected lower limb of stroke participants and the lower limb of healthy matched controls in the FTDT, (p=0.001), the GDT PF (P<0.001), the GDT DF (p<0.001) and the SHDT (p<0.001). Effect sizes indicate these significant differences were in real terms, moderate to large. This is in spite of the decline in plantar tactile ability and lower extremity proprioception with age (You et al, 2005; Goble et al, 2010; Bowden & McNulty, 2013; Wingert et al, 2014).

The median texture discrimination threshold of stroke participants in this study was 750µm representing a JND of 50% from the standard stimulus. In controls, this threshold was 300µm or a JND of 20%. Higher threshold scores, and therefore a greater JND indicate lower sensory acuity. Whilst, there are no other studies in the foot to compare these texture data, Carey et al (1997), used textured gratings and found a mean JND of 17%-19% in the fingertips of control participants, and a modal JND of 100% in the fingertips of stroke participants. Mean and median JND scores for stroke participants were not reported. This comparison in itself raises some interesting points. JND scores for age matched healthy controls in this study and Carey's hand study were almost identical. One would intuitively expect healthy control discrimination thresholds in the hand to be much lower than in the foot (given the increased sensory acuity of the hand compared with the foot), which was not the case. One explanation may be the substantially different surface areas of cutaneous skin being stimulated which may account for the levelling out and similar discrimination thresholds and JND between the fingertips and the whole plantar foot. It has been demonstrated that the greater number of peripheral mechanoreceptors being activated equates to greater central processing of that activity (Hollins & Bensmaia, 2007; Bourgeon et al, 2016) which may explain the comparable texture discrimination thresholds. What this comparison thus suggests is that sensory acuity may be influenced not only by the location, but also crucially by cutaneous-surface contact area in a texture discrimination task. It may also suggest that sensory acuity of the hand and feet is not that different and supports the notion of the foot as a highly complex sensory organ as has been suggested (Kavounoudias et al, 1998; Wright et al, 2012). Further studies in the foot would be required to validate this.

Conversely, the difference in stroke participants' discrimination thresholds (JND) in this study compared to Carey's was substantial. The modal JND in Carey's study was reported as 100% (i.e. 3000 µm - the maximum stimulus used) which is suggestive of floor effects. Unfortunately time since stroke characteristics were not reported in Carey's study to allow direct comparisons, although based on the recruitment strategy employed (hospital admitted patients), it appears the participants in Carey's study were acute/sub-acute stroke patients. Recovery of most tactile sensation whilst hugely variable is suggested to occur in the first six months post stroke (Winward et al, 2007; Connell et al, 2008) which may also explain the difference in findings.

This study also found statistically significant differences in ankle JPS as measured by the GDT between stroke and controls. Whilst there are numerous reported measures of ankle JPS, most are developed in healthy and/or ankle pathology populations (Hilier et al, 2015). Most studies examining ankle JPS involve the passive/active reproduction of a passive test position reporting absolute error (in degrees) or mismatch between the two positions. None to date have examined threshold discrimination scores of ankle JPS in stroke so direct comparisons are not possible. Previous tests also tend to involve motorised equipment, and clinimetric properties are mostly poorly evaluated (Hilier et al, 2015). This study utilised non-mechanical, non-motorised equipment to produce an acceptably robust measure of quasi-static ankle joint position sense. In this study, the mean discrimination threshold is reported which is the point at which participants could not discriminate the sloping properties of two platforms presented in quick succession. In stroke participants, that discrimination threshold was 3.1° in the dorsiflexion condition whereas in controls it was 1.5°. Similarly, in the plantarflexion condition, discrimination threshold was 3.0° and 1.2° for stroke and control

participants respectively. Encouragingly, the error scores between actual and perceived joint position reproduction in existing studies and this study in which a threshold is established are similar. Lin et al (2016) produced a mechanised, multidirectional, multi-axle system in which partial weight-bearing, seated ankle JPS absolute error in a young healthy population into dorsiflexion was reported as 1.2° (SD=0.4°) and plantarflexion 1.1° (SD=0.4°). Similarly, Ko et al (2015) produced a seated mechanical device in which they investigated age associations with ankle JPS. Their healthy study sample (age range 51-95) had a much larger matching error than the elderly controls of this study, with matching errors reported between 2.5° - 3.8°. Similar ankle JPS matching errors in the study by Westlake et al (2007) were reported in their cohort of "healthy" elderly (mean age = 74) with dorsiflexion matching errors ranging from 3.15° - 3.21°. The larger matching errors in these studies may be explained by the different testing approaches used. JPS reproduction relies heavily on both attention and memory function due to the inherent time delay involved between position matching. The discrimination approach used in this test, whilst reliant to a degree on memory, may be less impacted by memory as the confusable stimuli are presented in quick succession. Secondly, the testing position differs in that JPS is typically assessed in partial/non-weight bearing whereas in this study it was in full weight bearing. Weight bearing during ankle JPS tests may enhance JPS acuity due to the additional tactile input the foot receives as has been demonstrated in empirical studies (Lowrey et al, 2010). You et al (2005) using a motorised platform under weight-bearing conditions, found a mean ankle proprioceptive acuity threshold (matching error) across inversion, eversion, dorsiflexion and plantarflexion conditions of 1.37° in young adults (mean 22 years, SD=3.7), 2.61° in older adults (mean age 73,

SD=7.7) and 2.32° in older adults who reported falls (mean age 73, SD =7.8). Similarly, a motorised device developed by Deshpande et al (2003) again in weight bearing, found a mean matching error in DF and PF conditions of 2.34° across three healthy groups categorised according to age (20-39; 40-59; and >60) but did not report matching errors for each group, stating significant differences between young and middle aged only. Finally, Halasi et al (2005) using the slope box test, found a mean absolute error of 2.8° between actual slope and perceived slope in a cohort of young, healthy controls (mean age 23 years; SD=5.8). The results from this study are thus comparable to previous measures.

Few studies have investigated ankle JPS in a stroke population in which absolute matching error is reported. Lin P-Y et al (2006) in a study of 68 chronic, ambulatory stroke patients (mean age 62 years, SD= 14; time post stroke 3.9 years; SD= 5.9), provided some data with which to compare the GDT. They found a mean inter ankle JPS matching error (i.e. between paretic and non- paretic limbs) of 7.24° (+/- 4.62°) with a wide range of values (1.15° - 23.7°). Such a large difference to our results and large variability amongst their stroke sample may be explained by several reasons. By comparing most affected ankle with least/non-affected ankle, natural inter-limb proprioceptive asymmetries (Han et al, 2013) may have contributed to a larger matching error. In addition, the presence of bilateral proprioceptive impairments post stroke (Connell et al, 2008; Yalcin et al, 2012) is also likely to confound inter-limb matching error. Thirdly, the reproduction of JPS, as discussed earlier, is influenced by working memory, due to the procedural delay in limb matching (Goble, 2010). No reliability data is reported for this method. More recently, Yalcin et al (2012) reported ipsilateral (paretic) JPS matching error in the ankles of a cohort of 20 chronic,

ambulatory stroke (mean age 54 years, SD=12.4; time post stroke 27 months, SD=44). Using an isokinetic dynamometer (Biodex corp) mean matching errors of the paretic ankle were reported as 12.45°, 11.15° and 1.1° in 5° plantarflexion, 10° plantarflexion and 15° dorsiflexion conditions respectively. Such large and variable matching errors do not correspond with the discrimination thresholds found in this study, although clinical convention suggests tightness in plantarflexors is more common than tightness in dorsiflexors. It may be that the stretch imposed on tight plantarflexors in the dorsiflexed position, gives rise to a lower threshold. The authors did not discuss this difference other than advising caution in the extrapolation of this finding to the wider stroke population given the small sample size, recommending that further research in the area be warranted. Further, the clinimetric properties of the method were not reported. Given the dearth of studies in this area and the variability of reporting either absolute error or discrimination thresholds, there is little comparable or normative data. Further, the different approaches used and the poor reporting of reliability and validity of measures make inter-study comparisons difficult. And finally, whilst the above studies allow for some broad comparison to the novel measures, a recent study of upper limb proprioception found just noticeable difference (JND) or discrimination thresholds to correlate only weakly with scores of position error (r=-0.13) (Elangovan et al, 2014). This further highlighted the need to develop robust measures where discrimination thresholds are reported so that normative data and relationship to function may be further investigated.

# Convergent validity

In the absence of a gold standard measure, to establish convergent validity, the three novel measures were compared against a widely used, standardised and validated

measure of sensation; the EmNSA. Evidence to support the convergent validity of the FTDT was provided by the strong and significant correlation with tactile scores of the EmNSA (r = 0.673, p<0.01). Conversely, very weak and non-significant correlations were shown between the GDT and SHDT with the proprioceptive component of the EmNSA (r =0.173, p>0.05; r =0.052, p>0.05 respectively). A very strong correlation between the tactile component of the EmNSA and texture discrimination thresholds suggests they may be measuring similar constructs. Whether individual sensory modalities (i.e. light touch, pressure, pinprick, temperature etc.) which comprise the tactile component of the EmNSA need be assessed, is debatable. Some (Connell et al, 2008) have found low agreement between tactile modalities whereas others (Lincoln et al, 1998; Stolk-Hornsveld et al, 2006; Winward et al, 2002) have found strong correlations between tactile items, suggesting they are not discrete measures. Data from this study supports the idea that the discrimination of texture may be an appropriate method of determining the limits and capabilities of the tactile system, as has been suggested and established in the hand (Carey et al, 1997; Eckstrand et al, 2016; Miller et al, 2009). The need to assess individual tactile modalities may not be necessary. Such is the crossover between tactile sensory modalities, if light touch is intact, it is not necessary to assess pressure or pin prick (Lincoln et al, 1998; Stolk-Hornsveld, 2006; Winward et al, 2002). Indeed, some measures include only light touch (Fugl-Meyer Sensory test) and most therapists report assessing only light touch detection and proprioception during routine clinical assessment (Pumpa et al, 2015). Considering the overlap and integration of the ascending tactile pathways (Amaral, 2013), the central processing of tactile modalities is also fully integrated (Gardner & Johnson, 2013).

The mechanism of active sensation in which a textured surface is manually explored through digit motion and/or plantar weight redistribution arguably assesses higher level, multi-modal sensation. Functional imaging studies of healthy controls and stroke participants have identified multiple neural correlates of higher level processing during texture discrimination tasks. Activity within primary (post central gyrus) and secondary somatosensory (parietal operculum) cortices (S1 & S2) have been linked with additional activity within the posterior parietal cortex (Hartman et al, 2008), precuneus (Borstad et al, 2012), insula (Carey et al, 2016), and putamen (Preusser et al, 2015) during texture discrimination tasks. Furthermore, cortical activity within primary somatosensory regions differ when a stimulus is actively touched compared with passively received (Simoes et al, 2011). The discrimination of texture is thus a functionally reflective, higher cortical process in which the synthesis of multiple tactile *and* proprioceptive inputs combine to form a sensory perception.

Whilst correlations of plantar tactile ability are strong, the SHDT and GDT have weak and insignificant correlations with the proprioceptive components of the EmNSA. There are perhaps several explanations for this. Firstly, they are arguably measuring different constructs of proprioception. The EmNSA is measuring movement detection/ direction discrimination, whereas the GDT and SHDT are measuring quasi-static JPS. One of the clear juxtapositions of measuring proprioception outlined earlier in this thesis is that JPS and MDD/DPM represent two distinct aspects of proprioception – movement sense and position sense. Whilst there is general agreement they are conceptually different and may weakly correlate in laboratory tests (Elangovan et al, 2014) sense of joint position and joint movement are indisputably always associated with each other in daily activities (Gilman, 2002).

The very weak correlation between the GDT and the proprioceptive component of the EmNSA may be due to differing levels of measure accuracy and validity. The question of validity of the proprioceptive component of the EmNSA was raised earlier in this thesis. Indeed movement detection/discrimination via handling of a passive limb is suggested to be a crude, insensitive approach, incapable of identifying subtle impairments and has been shown to demonstrate significant ceiling effects; an effect demonstrated in study 2 (chapter 3) with 72% (n= 124/167) of stroke participants scoring maximally in the proprioceptive component of the EmNSA. Ceiling effects are generally considered if greater than 20% of a study population score maximally in any one test (Blum et al, 2008).

Further, in this study, 19/32 participants (59%) scored  $\geq$ 7/8 on the proprioception score of the EmNSA, i.e. had intact proprioception. In comparison, 11/32 participants (34%) had a foot/ankle gradient discrimination threshold below 2.0°, the cut off determined by the ROC analysis, therefore were deemed to have intact proprioception. Conversely, 21/32 (66%) were above that threshold, indicating proprioceptive impairment. Meyer et al (2016) also reported discrepancy between the EmNSA and more functional proprioceptive measures. The EmNSA and thumb-finding test (Prescott et al, 1982), were administered to the same sub-acute stroke sample (n=122). The authors reported 76% of their participants scored  $\geq$ 7/8 on the proprioceptive component of the EmNSA, i.e. proprioceptively intact, whilst in the same sample, only 46% were considered proprioceptively intact when assessed with the thumb-finding test. It may of course be that that there is no ceiling effect and that impairment of proprioception is low, although its incidence has been variably reported (Tyson et al, 2008; Tyson et al, 2013; Connell et al, 2008). There are multiple ascending conscious and subconscious sensory pathways, which provide proprioceptive input so proprioception for the large part may be spared in the majority of people post stroke, which may explain the lower incidence of impairment in the EmNSA. However, given the clear discrepancies between measures, administered to the same sample, it would suggest that the consistently high number of participants scoring maximally/sub maximally on the EmNSA is not because their proprioception is spared, but rather that the measure may not be sensitive enough to detect impairment.

### Sensitivity and specificity

This study also investigated the extent to which these tests reflect *participant reported* sensory impairment. To my knowledge, this is the first study in which the sensitivity and specificity of measures of lower extremity somatosensation (tactile or proprioception) have been evaluated against subjective reporting of sensory impairment in chronic stroke. One of the catalysts behind this study was to develop reliable and valid objective measures that reflect patient experience. One observer reported that a key shortcoming of sensory measures is that too often they fail to objectively measure what is subjectively reported (Yekutiel, 2000). This proposition is supported in this study and brings into question the validity of the EmNSA with high proportions of participants reporting impairment yet still scoring highly or maximally on the EmNSA. Whilst there is no universally agreed "cut off" point for the EmNSA and summating ordinal scores does not necessarily provide an indication of impairment in a

recent study of the upper limb (Meyers et al, 2016). Using this criteria, only 31% (n=10) of this sample would be considered "impaired", whilst 75% (n=24) subjectively reported sensory impairments in their legs and feet. The EmNSA as an assessment of sensation thus identified 14 participants (43%) as "normal" or unimpaired despite what those participants reported. It, of course, very much depends on where the cut-off line is drawn to create a dichotomous classification of impaired/not impaired and that is a major shortcoming of using ordinal scales to measure sensation.

Conversely, the developed tests, although testing different aspects of somatosensation, appear to have good sensitivity and specificity to classify subjective reports of somatosensory impairments, in the lower limb. The criteria developed by Andresen (2000) was used to interpret these results. AUC values of 0.75, 0.83, 0.87 and 0.85 for SHDT, GDT and FTDT respectively suggest the tests have good-excellent sensitivity and specificity in predicting the presence/absence of subjectively reported sensory impairment. An AUC of 0.5 indicates a predictive value no greater than chance alone and an AUC of less than 0.7 is considered poor (Andresen, 2000). Furthermore, the ROC analysis allows the classification of impaired/not impaired using the original measurement scale. For example, a gradient discrimination threshold greater than 2.0° indicates impaired foot/ankle JPS, whereas a step height discrimination threshold greater than 1.3cm (13% JND) indicates impaired hip and knee JPS.

In light of the age related decline in somatosensory function, (Goble et al, 2009, 2010), and the fact that sensory impairment does not affect all stroke survivors, these measures appear to be sufficiently sensitive to distinguish sensory function between

and within both "impaired" healthy controls and stroke. The ROC analysis on people with stroke determined the cut off value for impaired/not impaired. In the FTDT, 25% of controls (n=8/32) had a texture discrimination threshold greater than or equal to 500µm (33% JND) suggesting impaired plantar texture discriminative ability. By comparison, however, 69% of the stroke participants (n=22/32) had a texture discrimination greater than or equal to 500µm (33% JND). That both groups showed variability in performance across the three measures supports their sensitivity/specificity. Utilising an interval scale of measurement, each measure was able to provide an indication of impairment severity, with higher threshold scores indicative of greater impairment.

Care in interpretation must be exercised, as these results cannot be generalised beyond the chronic ambulatory stroke population studied. Furthermore, the accuracy of self –reporting of sensory impairment in the lower extremity has yet to be corroborated although in the hand, sensory problems are suggested to be underestimated (Williams et al, 2006; Yekutiel, 2000). The suggestion that stroke survivors find it difficult to articulate and describe sensory impairments (Connell et al, 2014) may also confound the accuracy of self-report. The use of Visual Analogue Scales (VAS) to quantify the severity of sensory loss may provide further insight into selfreported sensory impairment. Nonetheless, the data obtained from these tests is encouraging.

# Hypothesis Testing

The validity of these measures is further supported through testing four hypotheses. The 1<sup>st</sup> hypothesis that *"Stroke participants who are repeat fallers (2 or more falls in* 

previous 3 months) will have a significantly larger discrimination threshold score on each of the sensory measures than those who report having no falls/single falls" is partially supported. Step height discriminative ability and texture discrimination thresholds were significantly different between those stroke survivors who do not fall/single fallers and repeat fallers (p<0.01) implicating the role of knee and hip proprioception ability and plantar cutaneous acuity. The finding that tactile ability and FTDT scores were much higher in fallers and associated with repeat falls was not altogether surprising and in line with empirical evidence which indicates that enhancing plantar somatosensation reduces postural sway and improves balance (Qui et al, 2012; Orth et al, 2012). This study also supports that the ability to discriminate step height using hip and knee position sense, is significantly different, between falls groups. Similarly, Soyuer & Ozturk (2007) found in 100 chronic stroke participants significantly larger knee JPS errors between (p=0.001) between non-faller/single faller and repeat fallers, further suggesting knee and hip proprioception is a factor in falls. Interestingly, and somewhat contrary to theoretical expectation, and the findings from the qualitative study (study 1), gradient discrimination thresholds at the foot/ankle using the GDT were not significantly different across the falls groups. These data suggest foot/ankle position sense is not linked with falls. One possible explanation behind this finding may be due to the aspect of proprioception assessed by the GDT: joint position sense (JPS). As discussed earlier, JPS and movement detection represent distinct aspects of proprioception and have been shown to be poorly correlated (Elangovan et al, 2015). Movement detection, and the speed with which movement is detected, is potentially more pertinent to informing a corrective (potentially fall preventing) motor response. It is thus plausible to suggest, based on proprioceptive

neurophysiology (Grey et al, 2004; Proske & Gandevia, 2012), assessment of sense of movement, and the speed and direction of that movement, may be more relevant than assessing sense of position in the context of falls. That is, the GDT may fail to assess the aspect of proprioception that is most pertinent in the physiology of perturbation correction and therefore falls.

Overall, these findings are promising. Lower limb somatosensation is often demonstrated not to be a key factor in falls studies of chronic stroke. Indeed, physical impairments per se resulting from stroke are not always associated with falls risk at all (Schmid et al, 2013; Robinson et al, 2011; Hyndman et al, 2002). Falls are complex in terms of how they are measured/reported and in terms of the factors which contribute to them (Batchelor et al, 2012). A lack of association could be, at least partially explained by the accuracy/sensitivity of measures used to assess both falls and sensory function as discussed earlier in study 2. That there was no significant difference between fallers and non-fallers in their tactile or proprioception scoring of the EmNSA supports this and suggests the SHDT and FTDT are better able to discriminate between those who fall and those who do not. However, the shortcoming frequently highlighted in the proprioceptive literature is the use of the ipsilateral or least affected limb to match or reproduce JPS of the contralateral (most affected) limb, so their results should be interpreted with caution. Natural proprioceptive inter limb asymmetries exist in the absence of pathology (Han et al, 2013; Goble et al, 2010) and bilateral proprioceptive ability is frequently impaired post stroke (Connell et al, 2008; Yalcin et al, 2012). Such insights inevitably restrict the differentiation between different groups.

The classification of fallers into both single and repeat fallers, in line with other studies (Soyuer & Ozturk, 2007; Belgen et al, 2005) suggests that single fallers are similar in their lower limb sensory ability to non-fallers with no real significant differences between them in terms of test performance. Conversely, repeat fallers appear to be different from single fallers in that their threshold discrimination levels in the FTDT and SHDT were much higher (i.e. poorer). Whilst interesting, an element of caution must be used when interpreting these findings due to the relatively small number of participants within each falls category and the potential underpowered sample size. Further studies with a larger sample size and prospective falls monitoring may enable sample stratification in relation to falls.

Hypothesis 2: Stroke participants whose gait speed is  $\leq 0.80$ m/s will have a significantly larger discrimination threshold score on each of the sensory measures, than those whose is  $\geq 0.81$ m/s.

This study also indicated that lower limb, multi joint position sense is related to gait speed. Increased threshold scores in the SHDT indicated that those with slower gait speed (<0.8m/s) had significantly poorer hip/knee JPS as measured by the SHDT (p=0.01) than those with gait speeds >0.80 m/s. Further the correlation between gait speed and the SHDT was strong (r = 0.60, p<0.01). Conversely, performance on the GDT when the significance level was adjusted by Bonferroni correction to account for the two gradient tests (0.05/2=0.025) was not significantly different between those stroke participants considered limited community ambulators (<0.8m/s) and those unrestricted community ambulators (>0.8m/s). Nonetheless, GDT performance in both PF and DF conditions had a moderate and significant correlation with gait speed

(r = 0.467, p<0.01; r = 0.403, p<0.05). Active plantar sensation however, as measured by the FTDT did not differ significantly between those who had functional community ambulation and those who did not (p>0.05) and showed a weak and non-significant correlation with gait speed overall (r = 0.26; p>0.05).

Similarly, both the tactile and proprioceptive component of the EmNSA were only very weakly correlated with gait speed (r = 0.11 and r=0.12, p>0.05) suggesting the GDT and particularly the SHDT may better measure those functional aspects of lower limb somatosensation used during gait. These results suggest that these measures are associated with lower limb proprioception and gait speed, particularly at the knee and hip, less so at the ankle but not at all with plantar tactile ability.

Associations with gait speed and lower limb somatosensation are limited or certainly tenuous in the literature. Lin P-Y et al, (2006) found a weak but significant correlation (*r*=0.27, P<0.05) between ankle JPS and gait velocity in chronic ambulatory stroke participants. Lin S-I et al (2005), however, found no direct relationship between ankle or knee JPS and gait performance, but did find that ankle JPS contributed significantly to the variance in gait velocity and stride length. Possible explanations as to why lower limb proprioception and somatosensation, is not related to gait speed/balance, may be due to the ability of the CNS to reorganise the sensory system depending on the reliability of that information and the demands made upon it by the environment. Lin S-I et al (2012) found that proprioceptive interference in the form of vibrations administered to the tendo-achilles of the hemi paretic ankle, did not affect gait parameters in their chronic (53 months post onset) stroke sample. They cited sensory reweighting and reliance on central pattern generators as explanations behind the lack

of affect. Interestingly, Mullie & Duclos (2014) also found interference of ankle proprioceptors (triceps surae) did not significantly influence balance during gait or posture in stroke participants but *did* significantly affect static and dynamic balance ability in healthy subjects. Their study suggests that ankle proprioception is *normally* important in functional balance and gait, but given the difference between groups, proprioceptive information is not *used* or integrated by stroke participants in the same way that it is by healthy participants. The reorganisation of the sensory integration process following stroke is well studied and an increased reliance on visual compared to proprioceptive information is well established (Chien et al, 2014; Bonan et al, 2013). There is thus a different emphasis in that stroke may affect the ability to *use* proprioceptive information during balance and gait.

The 3<sup>rd</sup> hypothesis proposed that stroke participants whose postural sway (COP<sub>velocity</sub>) is greater than the mean (+2SD) of control participants' COP<sub>velocity</sub> will have a significantly larger discrimination threshold score on each of the sensory measures than those stroke participants whose COP<sub>velocity</sub> is less than mean +2SD of control  $COP_{velocity}$ 

This study highlighted that lower limb somatosensation is associated with postural sway velocity. Whilst there were no statistically significant differences (p>0.05) between those stroke patients whose COP<sub>velocity</sub> was 2SD greater than healthy controls and stroke participants who fell within 2 SD, moderate and significant correlations were demonstrated between COP<sub>velocity</sub> and the GDT. Foot/ankle dorsiflexion and plantarflexion discrimination thresholds were moderately correlated with COP<sub>velocity</sub> (r=0.44, p=<0.018 and r=0.43, p=0.022) suggesting postural sway may be associated

with foot/ankle position sense awareness. Similar results were found by Niam et al (1999) in which ankle (dorsiflexion) proprioception JPS was found to have the strongest correlation with postural sway (COP displacement) in a cohort of 30 chronic stroke participants (mean time since stroke=11 months; SD= 10.6) . The notion that we normally sway like and inverted human pendulum with the axis point at the ankle reinforces the findings of this study and the role of ankle JPS in maintenance of posture.

The lack of significance and relationship between COP<sub>velocity</sub> and SHDT is not altogether unsurprising as hip and knee proprioception is more associated with dynamic balance and mobility ability (Han et al, 2016; Wingert et al, 2014; Mullie & Duclos, 2014). A lack of association with plantar tactile ability was partly in contrast to expectation as evidence from some studies demonstrate that reduced tactile acuity of the plantar surface results in increased postural sway (Perry et al, 2001; Zhang & Li, 2013). One potential explanation as to why the texture discrimination test did not demonstrate any relationship with postural sway is that the motor task requirements, and thus sensory stimulation, are fundamentally different. Optimal texture discrimination may involve small movements of the foot and toes relative to the support surface in an antero-posterior direction (i.e. perpendicular to the texture), that is, shear movements may be important. In contrast, balance-related ankle movements when standing tend to involve larger ankle dorsi-plantarflexion and it is these that were measured with the GDT.

Finally, the 4<sup>th</sup> hypothesis that *Stroke participants* with a dynamic forward reach test score (FRT) less than 15cm will have a significantly larger discrimination threshold

score on each of the novel sensory measures than those who are able to reach beyond 15cm was also supported. Those stroke participants unable to forward reach beyond 15cm had significantly higher texture discrimination thresholds as measured by the FTDT (p=0.005), ankle position sense through the GDT (p<0.001) and knee/hip position sense thresholds, SHDT (p=0.02) compared with those able to reach beyond 15cm. All three measures also showed strong and significant correlations with the FRT suggesting they may be associated with falls risk. A FRT less than 15cm is suggested to be predictive of falls (Acar & Karantas, 2010). Interestingly, the total score of the EmNSA and its tactile component did also show significant, but weak correlations with FRT scores (r=0.36, p<0.05). The proprioceptive component of the EmNSA showed no significant correlation with FRT scores (r=0.18, p>0.05). The findings from this study support previous studies in which both tactile and proprioceptive sensation have been shown to have a highly statistically significant predictive relationship (p=0.0001) with dynamic balance (Tyson et al, 2006). Tyson's study included sub-acute stroke survivors (TSS= 21 days, SD=5 days) rather than chronic stroke, and multiple regression analysis indicated that sensation and weakness accounted for 47% of the variance in balance disability in this cohort. The findings in this study of chronic stroke suggest lower limb somatosensory function may continue to influence functional balance many years post stroke.

The above discussion points reflect hypothesis testing in which Bonferroni corrections were applied to the GDT plantarflexion and dorsiflexion tests rather than all tests. It was felt that the three tests were measuring three separate aspects of somatosensory function: plantar tactile acuity, foot/ankle position sense, and knee/hip position sense. In addition, this study also intended to evaluate the validity of the EmNSA alongside

the novel discrimination measures, enabling direct comparisons to be made. One difficulty however in comparing the interval scales of the novel measures and measures of function with that of summated ordinal scores of the EmNSA is that statistically, a summated ordinal scale does not necessarily provide an indication of impairment severity (Fawcett, 2007). Whilst ordinal scores from the NSA have previously been transformed through Rasch analysis (Connell, 2007) doing so is complex and beyond the scope of clinicians. The irony being, that whilst measures such as the EmNSA are clinically usable, analysis, comparison and interpretation of the data, is not. Like for like comparisons of measures using ordinal scales with the interval scales in these novel discrimination measures, must therefore be interpreted with some caution.

### 5.7. Study strengths and limitations

This study was, in part, driven by patient reported experience. In doing so, the measures aimed to reflect, as closely as possible, lower limb function of people who live with their stroke during daily ambulatory activities. It attempts to quantify the relationship between lower limb sensory perception and functional ability. This study thus contributes towards and further probes the area of somatosensory assessment in which there has been very little change, for the best part of a century. It questions the ecological validity of current approaches to assessing lower limb sensory function in a stroke population by presenting evidence from three novel measures that assess whole foot tactile ability; ankle/foot position sense and hip/knee position sense in weight bearing. These measures further assess the integrity of higher level cortical processing; targeting the systems, which reportedly form somatosensory perceptions and then guide and inform contextual, goal oriented movement and behaviour. A
further strength of this study is that it provides robust and comprehensive reliability and validity data – which is acknowledged as being essential (albeit not always undertaken) when new measures are developed and introduced to clinical and scientific communities. These measures have been demonstrated to be feasible for use within both clinical and research settings to monitor impairment severity and recovery. They may allow better prediction of lower limb sensory impairment and recovery after stroke and thereby aid in decisions regarding use of health care resources.

This study is not without limitations. The sample recruited was a convenience sample of ambulatory people in the chronic phase of stroke who had participated in a previous study within this thesis hence caution should be undertaken in extrapolating conclusions to those in the acute phase, or who are non-ambulatory. Given the time and effort requirements of this study, those participants with time, practical or physical limitations were likely unable to participate. As with all convenience samples, an element of sampling bias is a possibility. Further, given the nature of this study it may be that those with sensory impairments were more likely to volunteer than those without. The high proportion of the study sample who reported sensory impairment (75%, n=24/32) indicates that there is a possibility that the sample may be biased. It is suggested, however, that this is not likely to be the case based on the EmNSA assessment findings, which indicate an impairment prevalence of 31%, no higher than that of the general stroke population.

The use of an assistant physiotherapy practitioner as 2<sup>nd</sup> rater for determining interrater reliability may draw criticism in that they were not a registered healthcare

professional and unqualified to carry out sensory assessments. The author views this as a strength of the study as it demonstrates the clinical utility of these measures, regardless of clinical standing. It is recognised that determining the responsiveness of a measure is also an important psychometric quality to evaluate in measures such as these, which may be used to evaluate the effectiveness of rehabilitation interventions such as sensory retraining programmes. Whilst this was beyond the scope of this study, it is an important consideration for the future. Finally, assessment of somatosensory discrimination, through its very nature places a relatively high demand on higher cortical functions. Cognitive processes such as attention, working memory, and visuospatial abilities can confound discriminatory ability. This will be explored in more detail in the final chapter.

#### 5.8. Conclusion

These three novel tests were developed in response to a lack of functionally oriented, clinically usable and sensitive measures of lower limb somatosensation. Their focus was derived through qualitative research, undertaken as part of this dissertation, which investigated the patient experience of impairments and associated functional difficulties (Gorst et al, 2016). This was further supported by patient, carer and public involvement. The tests assess three functionally separate aspects of lower limb somatosensory function; plantar tactile acuity, foot/ankle position sense, and knee/hip position sense. They do not require lengthy testing of multiple sites and body parts, but target key functional areas related to stance, gait and stepping. They use an established and robust psychophysical testing approach to establish somatosensory discrimination thresholds thereby assessing higher level cortical processing of somatosensation so are potentially relevant in (central) neurologically impaired

populations. They utilise an interval measurement scale rather than an ordinal scale and have demonstrated in this sample to have no floor or ceiling effects; thereby enabling them to detect both subtle and substantial deficits, providing an indication of impairment severity. SEM and CoR data provide the researcher/clinician with scores due to measurement error and scores required to indicate real, true change. Two of the three measures assess *active* sensation, which is regarded as the synthesis of both tactile and proprioceptive receptors acting as a single functional perceptual system. They have demonstrated statistically significant associations with functional measures of gait speed, dynamic balance and falls so may be of use in examining the relationship between functional ability, motor recovery and lower extremity somatosensation.

### 6. Chapter 6. General discussion and conclusions

#### 6.1. Summary of thesis

This thesis used an exploratory, multiphase mixed methods approach to investigate the prevalence and functional importance of lower limb somatosensory dysfunction in community-dwelling chronic stroke survivors. The findings from the qualitative study (study 1, chapter 2) suggested a more detailed examination of foot, ankle and lower limb sensory impairment was needed in this cohort to further inform the impact of sensory changes on mobility and balance. A second study, an observational, cross sectional study, examined the impact of sensory loss, as determined by clinical tests, on mobility and balance in 180 chronic stroke survivors. The findings from this study were equivocal and did not fully corroborate the patient experience reported in study 1. Interpretations and a review of relevant literature, suggested the limitations of existing clinical tests of foot/ankle and lower limb sensation may have influenced these findings. In response, the findings from study 1 (qualitative study) and patient discussion groups, prompted and informed the final study (study 3, chapter 5), the development and evaluation of the psychometric properties of three novel, functionally oriented tests of lower limb somatosensory discrimination.

### 6.2. Discussion

This thesis presented a mixed picture of findings. Study one (qualitative study, chapter 2) provided insight into the patient experience of somatosensory dysfunction. It demonstrated, from the perspective of the person with stroke, that foot and ankle impairments such as pain, somatosensory impairment and weakness were particularly troublesome. Impairment to somatosensory functioning, namely not knowing where

the hemi-foot or leg was, and not feeling fully aware of the ground beneath the hemifoot, was reported to impact on outdoor mobility, particularly when the terrain became uneven or challenging. Reduced foot and ankle sensation was also reported to contribute to concerns about falling and affected confidence to walk outdoors. As a result, respondents said they restricted activities that involved walking outdoors, particularly on unfamiliar terrain. It highlighted the ongoing challenge faced by many in the chronic phase of stroke.

Study 2 (cross sectional, observational study, chapter 3) identified lower limb sensory dysfunction in the majority (59%) of the 180 chronic stroke survivors assessed. Despite the findings of study 1, only weak associations between lower limb sensation and function were found. Statistically significant, but weak, associations were demonstrated between proprioception and reported falls, distal tactile sensation and falls incidence and fear of falling, and distal proprioception and postural sway (section 3.5, Table 3-11). Walking speed and dynamic balance showed no significant associations with lower limb somatosensory function. In contrast, ankle strength showed moderate to strong correlations with measures of mobility and balance but not reported falls. Correlational analysis and logistic regression analysis identified lower limb proprioception and the Walking Impact Scale (WIS) were significant factors in predicting falls incidence when other predictor variables were controlled for. Age, time since stroke, dynamic balance and ankle strength did not contribute significantly to the logistic regression model for falls (3.5, Table 3-16). Despite the significance, lower limb proprioception and WIS accounted for just 14%-19% of the variance suggesting other variables impact falls incidence. The results of study 2 did not convincingly corroborate the patient reported experiences from the first study, and did

not provide compelling evidence of the functional importance of lower limb sensory dysfunction. Lessons from study 2 highlighted that quantifying sensory status and the prevalence of sensory impairment using a traditional, clinical ordinal scale of sensation, has flaws. The quantification of impairment and the appropriateness of using a measure such as the EmNSA in correlational studies is not recommended.

The incongruence arising from the findings of these first two studies is broadly echoed in the wider literature. On the one hand, data from scientific and neurophysiological studies indicate that lower limb tactile and proprioceptive inputs provide feedback and feedforward to help facilitate motor output, produce corrective stepping, impact gait kinetics and postural sway (see section 1.6.3. and 1.7). On the other hand, data from observational, correlational and interventional studies involving chronic stroke participants do not provide compelling evidence to support a link between lower limb somatosensation and function (see section 1.7.2.)

Several interpretations potentially explain this incongruence, which in part, prompted the final study of this thesis, and will be discussed in more detail below.

Firstly, weak associations between lower limb somatosensation and function following stroke may be explained, in part by the ability of the CNS to reweight the relative reliance between multiple sensory inputs. In the presence of sensory conflict, such as impaired somatosensation, the relative weighting on visual and vestibular inputs increases. The resultant effect is that vision becomes the dominant sense to facilitate walking and standing for many stroke survivors (Chien et al, 2014; Bonan et al, 2013) so lower limb somatosensation becomes functionally less important. A greater postural sway (centre of pressure, COP) measurement from eyes open to eyes closed

condition in the stroke participants compared to control, supported by weak correlations with lower limb somatosensation and COP (section 3.5, table 3-11) suggested visual dominance in standing. Such sensory reorganisation however, does not necessarily enhance function. The qualitative work in this thesis highlighted how stroke participants often described being restricted and felt concerned where they could walk because of the need to visually attend to foot-ground interactions and not, for example, the traffic. The precise mechanisms which cause this altered sensory reweighting are not clear and little is known about the extent to which time dependent factors such as impairment recovery and functional recovery influence sensory integration, nor how sensory reweighting strategies respond during more dynamic, complex situations of postural control such as walking. Understanding the mechanisms which trigger and perpetuate altered sensory reweighting following stroke through investigating chronological changes in sensory reweighting strategies used, may enhance our understanding.

Secondly, the extent to which conscious, higher level cortical input is required during certain walking tasks is unclear. The involvement of spinal networks, or CPG's was highlighted in section 1.6.3. To recap, a CPG for locomotion has been identified as a group of interneurons localised, for the most part, in the lumbar part of the spinal cord in humans. Most work to date demonstrated in decerebrate animals that the generation of reciprocal lower limb movements, could be produced at spinal cord level, without cortical input. Such movement is dependent in part, on afferent feedback from Golgi tendon organs indicating the degree of lower limb loading (Pearson & Gordon, 2013; Dietz et al, 2002).

A further point is that a large proportion of somatosensory afferents, particularly proprioception, do not project to somatosensory cortices, having direct projections with the cerebellum, so are beyond conscious awareness. Several studies have demonstrated that damage to the cerebellum compromises adaptive learning during gait, suggesting it is critical in certain walking tasks (Morton & Bastian, 2006; Jayaram et al, 2012). Weak correlations between impairment to conscious somatosensation and the ability to adapt gait during split belt-treadmill walking tasks, was suggested to reflect the role of sub-cortical structures such as the cerebellum (Reisman et al, 2006, 2010). Certainly, the CNS mechanisms involved in multi-joint movements, compared with single joint movements, are mediated by the cerebellum and its afferent/efferent connections (Lisberger & Thach, 2013). Bosco & Poppele (2001), for example, demonstrated in the cat hind limb that single joint dorsal spinal cerebellar tract (DSCT) neuronal activity showed no clear or consistent neural pattern whereas multi-joint behavioural patterned movements did. They suggested that patterned multi-joint activity comes in part from spinal cord interneuron integration, with the DSCT conveying integrated proprioceptive feedback during movements such as walking. In essence, there is compelling evidence to suggest that the neural control and adaptation of simple walking may be beyond conscious awareness, and therefore cortical structures. Weak correlations between crude measures of sensation and measures of straight-line gait speed may therefore reflect that cortically processed somatosensory input is not important.

However, there seems to be greater activity and demand on cortical structures with greater task requirements and movement accuracy. Section 1.6.3. highlighted the EEG studies in which increased cortical activity levels in supra-spinal areas occur during

more challenging locomotor tasks such as narrow beam walking (Sipp et al, 2013) and incline walking, compared with flat walking (Bradford et al, 2016). The implication is that the somatosensory cortex is involved in both modulating the CPG for locomotion, and is in a "heightened state" to monitor somatosensory feedback during more complex locomotion (Guertin, 2013; Bradford et al, 2016). This evidence suggests that commonly used mobility measures, such as the 10 metre walk, often used for its clinical utility, and conducted in well lit, flat clinical environments with minimal distraction, may not capture the multi-faceted and sensory- dependent function involved in more challenging, "real life" walking. Gait speed may be appropriate as a clinical end-point, but may not be sufficiently sensitive to detect the complex, multidimensional task of real life walking. People with chronic stroke may produce gait speeds within normative limits because of functional adaptation or compensation, within certain environments. Anecdotal evidence and that from the qualitative study suggests that the environment plays a key role in walking ability. People with stroke describe how walking feels much easier in familiar, flat environments, compared to outside. Whilst there are undoubtedly other confounding and interacting factors which contribute, such as motor output, or cognitive requirements (discussed later), mobility when measured using the 10-metre walk and somatosensory function when measured using the EmNSA, may not be sufficiently sensitive to delineate this. Future studies wishing to enhance understanding should involve the use of walking measures in which the complex, multi-dimensional task of community ambulation may be more closely reflected. Tools such as the Community Balance and Mobility Measure (Howe et al, 2006) or measures involving dual task interference (see Plummer et al, 2013)

may address some of these issues, which are discussed later in the context of attention and cognition.

A third interpretation as to why weak associations between lower limb somatosensation and function were demonstrated in the cross sectional study of this thesis, concern the measurement of somatosensation. This interpretation was the impetus behind the final study. This thesis and other papers (Meyer et al, 2016; Uzynski et al, 2016; Lin et al, 2005; Carey et al, 2011; Suertterlin & Sayer, 2014; Sullivan & Hedman, 2008) have questioned the validity, reliability and appropriateness of traditional, clinical measures of somatosensory detection, particularly within the context of function. This thesis questioned the validity of passive tests of tactile and proprioceptive sensation and in particular sharp-blunt discrimination as a measure of somatosensory discrimination. Study 2 also highlighted the difficulties and statistical accuracy of producing prevalence figures from ordinal level data. Multi-modal measures such as the EmNSA arguably lack the sensitivity to capture the complex sensory changes, which may occur follow stroke, identifying only the more profound deficits and missing the majority of impairments. It is geared toward identifying the presence or absence of impairment, not the severity or, crucially, the functional impact of that impairment. In rehabilitation, measures of sensation should provide an indication of impairment severity so that appropriate treatments can be planned and their effect evaluated. Furthermore, optimising function and well-being is the ultimate goal of clinicians and patients alike, so the presence of an impairment does not automatically necessitate treatment. We need to know whether it affects function.

One or a combination of interpretations may explain the inconsistent findings that arise from study 1 and study 2 and that of the wider literature regarding the importance of lower limb sensation. To enhance understanding, the final study of this thesis could have investigated several different directions, all of which would have provided potentially compelling results. However, it was felt that the most pressing clinical need was to open a dialogue and investigate novel methods to assess somatosensory function. Satisfaction with current approaches to somatosensory assessment is low and may be hindering research and clinical developments in this area. Evaluating somatosensory ability is notoriously difficult and the approach has changed little for the best part of a century. Many measures are derived from traditional tests, which are based on examining the properties of the peripheral mechanoreceptors and the transmitting spinal pathways. Since it is mostly the CNS rather than the peripheral sensory transducer that is affected after stroke, there is a clear rationale that any measure designed to measure somatosensory ability in stroke populations should attempt to assess higher-level cortical processing of somatosensation. Borstad & Nichols-Larsen (2014) suggest sensory testing should be considered hierarchical in nature in which stimulus detection represents simple processing, with stimulus discrimination, grading and recognition representing higherlevel somatosensory processing. Tests of sensory detection, administered passively to a supine participant, do not involve to the same extent, the involvement of higherlevel somatosensory processes. For example, neurophysiological studies have demonstrated extensive neural correlates spanning multiple cortical and sub-cortical structures, during simple texture discrimination tasks in the hand. Primary (post central gyrus) and secondary (parietal operculum) somatosensory cortices (S1 & S2)

have been linked with additional activity within the posterior parietal cortex (PPC) (Hartman et al, 2008) precuneus (Borstad et al, 2012), insula (Carey et al, 2016) and putamen (Preusser et al, 2015) during texture discrimination tasks. Furthermore, cortical activity within primary somatosensory regions differ when a stimulus is actively explored compared with passively received (Simoes et al, 2011) as active sensation involves the integration of both tactile and proprioceptive information (Blanchard et al, 2011). Such studies suggest active somatosensory discrimination involves both cortical and sub cortical structures, so assessing the integrity of these structures and the processes they sustain, may be better targeted by measures, which attempt to assess discrimination perception compared with measures of sensory detection.

In response, this thesis developed and evaluated three novel, functionally oriented, measures of lower limb somatosensory discrimination (Study 3, Chapter 5). The measures were informed by patient, carer and public involvement (PCPI), and the findings from study one (qualitative study). A review of the function, merits and limitations of existing sensory measures was carried out to inform their development (Chapter 4). The novel measures assessed three functionally separate aspects of lower limb somatosensory function; plantar tactile acuity, foot/ankle position sense, and knee/hip position sense. Two of the three measures assessed active sensation, that is, involving movement for the purpose of somatosensory perception. They targeted key functional areas related to stance, gait and step clearance with the aim of providing more meaningful somatosensory data. They utilised an established and robust psychophysical testing approach to establish somatosensory discrimination thresholds. In doing so, the integrity of higher-level somatosensory processes active

during functional, weight bearing activities were examined. The measures utilised an interval measurement scale rather than a coarse ordinal scale and had no floor or ceiling effects so provided an indication of impairment severity which may show greater responsiveness to change following intervention (with further investigation). They were feasible to administer, showed excellent reliability and performance on the measures were more strongly correlated with measures of gait speed, dynamic balance and falls than the EmNSA. The findings indicate discrimination thresholds of tactile ability, foot and lower limb position sense, may more closely reflect lower limb sensorimotor function.

However, key components and therefore potential confounders of somatosensory ability also need consideration as higher order cognitive abilities such as attention and working memory may influence somatosensory ability. Control of attention, for example, allows relevant, task specific information to be selected for processing and irrelevant information filtered out (Styles, 2006). Experimental studies have shown that increasing attentional demands can have a detrimental impact on proprioceptive performance in both young athletes (Yasuda et al, 2014) and in obstacle avoidance in the elderly (Hegeman et al, 2012). However, when attention is diverted from the proprioceptive task, this appears to have a more significant effect on older adults than younger (Boisgontier et al, 2011). In older adults, for example, complex bimanual upper limb tasks involve "over activation" in brain regions more typically associated with cognitive functions (Goble et al, 2010). The implication is that movement, and in particular awareness of movement, requires a greater proportion of attentional resources as we age. High proportions of falls in ambulatory people with chronic stroke have been ascribed to impaired mental states, such as poor attention, or whilst

attending to a distraction (Schmid et al, 2013). Reduced dual task performance, cognitively attending to one task, whilst physically doing another (i.e. walking and talking, stepping over something whilst counting backwards), is associated with increased falls risk in community dwelling elderly (Muir-Hunter & Wittwer, 2016). Cognitive-motor interactions are an inevitable and essential part of everyday functional mobility (Plummer et al, 2013). The ability to attend to multiple tasks may be diminished in people with stroke, with ambulatory chronic stroke survivors using greater attentional resources during walking and obstacle negotiation than agematched controls (Smulders et al, 2012). The normal mechanisms of postural control and walking may thus be temporarily, or permanently lost following stroke, with greater reliance on attentional resources to facilitate many movements (as reported in the qualitative study). The findings in both study 2 and study 3 also link proprioceptive performance more strongly with falls than gait speed or balance for example. The need to focus attention on limb position or foot placement may result in an increased falls risk when attention is diverted to other environmental stimuli.

Attention also plays a key role in sensorimotor tasks, because in the first instance, it is required to encode information to be used in working memory (Zanto 2009). Working memory, representing the ability to hold and manipulate information during a short delay, facilitates a response based on that internal representation (Cowan, 1995). That information could be encoded visually i.e. in the approach to a step or gradient change, so working memory and attention are closely related and key cognitive components to complex walking tasks. For example, the representation of an obstacle is thought to be encoded primarily in visual working memory. In series of experiments, Lajoie et al (2012) investigated the sensory source the trail leg derives its information

from when clearing an obstacle. They investigated the relative role of visual memory, lower limb proprioception and efference copy (from lead leg) in providing pertinent information about obstacle characteristics. The authors found that the representation of an obstacle's height was encoded primarily from visual memory, with minimal contributions from lead leg proprioception or efference copy. A neural representation (working memory) of an obstacle lasts up to 2 minutes. The ability to create and access a neural representation or working memory of environmental conditions, such as a step or terrain, is a key component of many functional tasks. Such tasks require cognitive flexibility and higher attentional resources to address the voluntary motor requirements often seen post stroke, while attending to a range of environmental stimuli or concurrent tasks (Patla, 2001; Lord et al, 2006). Greater demands may be placed on executive attention functions such as selective, switching, divided, sustained and spatial attention in tasks that involve deciphering the physical qualities of a surface. The ability to attend to a single stimulus, relevant to a task or goal, filter out and "gate" sensory information represents a key component of efficient sensory reweighting and integration and the production of an efference copy for movement (Saradjian, 2015). Successful, safe and fulfilling community ambulation requires, in part, the ability to attend, and equally ignore, multiple sensory inputs both consciously and subconsciously. The ability to store and access working memory is also integral to tasks of sensory discrimination, when the physical property of one stimulus is compared with a second after a short delay. The findings from study 3 suggest measures must recognise the role of cognitive functions in both movement and somatosensory function. It may be that functionally oriented measures of somatosensory discrimination place greater demands on both attentional and working memory capabilities, than detection tests, and in doing so, have stronger associations with function overall.

Working memory and attention are inextricably linked to higher level somatosensory processing, so sensory discriminative ability may be affected independent of sensory status. Higher order deficits are common in acute stroke and the role of spatial inattention has been implicated in poorer performance in tests of sharp-blunt discrimination (Meyer et al, 2016). Furthermore, lesions to the PPC have resulted in deficits to sustained attention (Malhotra et al (2009), stimulus-driven attention (i.e. bottom-up), self-directed switches in attention (i.e. top-down) (Behrmann et al, 2004) and working memory retrieval (Berryhill & Olson, 2008). In the future therefore, it may be useful to assess the association between performance on the tests of sensory discrimination to standardised tests of visual attention and working memory. It may be that the larger attentional and working memory demands in the discrimination tests compared to tests of sensory detection may explain the greater correlation seen with walking and falls incidence. Investigations of populations with known attentional or working memory disorders and normal sensory function may provide further insight into the extent to which attention, working memory and lower limb discrimination thresholds are inter-related. Comparing test performance in such populations across both sensory detection and discrimination tasks may also enhance understanding of these confounding factors and provide additional validity data for the novel measures. Further, the targeting of attentional and memory processes post stroke through restorative treatments that focus on attention and dual task interference (e.g. Plummer et al, 2013) alongside medications (e.g. methylphenidate) on sensory discrimination test performance would be interesting.

The disabling impact and clinical relevance of stroke on factors such as walking ability, balance and falls have been most strongly associated with deficits in lower limb motor output and motor control. Several studies further demonstrate that people with stroke who have both sensory and motor impairment, achieve lower functional outcomes than those with motor impairment alone (Lee et al, 2015; Patel et al, 2000). Sensory impairment tends to be considered a cofactor in functional decline along with motor impairment rather than an independent or causal factor.

This thesis supports this position in part but also raises some important points. Firstly, the findings of study 2 (chapter 3) indicated that ankle strength, in particular the dorsiflexors and plantarflexors, are significantly associated with most measures of function with falls reporting and postural sway the exception with weak correlations. In contrast, lower limb proprioception did significantly contribute to predicting falls along with the Walking Impact Scale, despite the reported shortcomings of proprioceptive measurement. Study 3 also demonstrated that performance on step height discrimination, i.e. whole limb joint position sense, was significantly poorer in those reporting multiple falls than those reporting no falls. Hip and knee JPS allows for accurate positioning of the lead foot relative to an obstacle and is correlated with obstacle avoidance performance error (Qaiser et al, 2016). Misjudgements of step height resulting in trips over steps/curbs are common post stroke (Hyndham, 2002), and have been implicated in falls (Batchelor et al, 2012; Said, 2013). This was reported in the qualitative study. Although tripping post stroke is commonly attributed to motor deficits, such as foot drop (Weerdesteyn et al 2008; Van Swigchem et al, 2013) this thesis demonstrates lower limb sensory impairments may have greater predictive value than motor impairment in certain functional contexts, with falls reporting one of

those. More detailed investigations with falls as the primary outcome and the use of detailed prospective falls diaries, alongside more sensitive measures of sensation, may provide greater insight.

Secondly, the ease with which motor output and sensory input can be observed and quantified, is contrasting, and has possibly resulted in research efforts and stroke rehabilitation strategies more inclined to focus on motor output. Although poor motor recovery is related with greater spatial and temporal gait asymmetry (Alexander et al, 2009; Balasubramanian et al, 2007; Patterson et al, 2008), some with good motor recovery still walk asymmetrically, which suggests other factors besides motor recovery may play a role (Patterson et al, 2008). The extent to which somatosensory dysfunction contributes to these asymmetries or inefficiencies in gait cannot be quite so easily observed or quantified. Perhaps therefore, somatosensory dysfunction does not quite so readily lend itself to research studies. The knock on effect that the mechanisms underlying somatosensation are less well understood. It subsequently is less likely to be demonstrated as important to function and therefore, it receives comparatively less attention in both rehabilitation environments and clinical guidelines (RCP, 2016). Only one other qualitative study to my knowledge has investigated sensory impairments following stroke (Connell et al, 2014) with participants tending to describe many of their sensory impairments in the context of movement dysfunction. Given the intrinsic links between sensation and movement, further investigations in which motor only deficits, sensory only deficits or sensory-motor deficits may be compartmentalised, using sensitive and robust measures, may provide further insight into their relative contributions and co-dependence. This may require an investigation

of people with selective lesions as confirmed with MRI, as usually stroke does not respect anatomical / physiological boundaries.

Understanding how sensation is processed in the CNS for the control of balance and walking is a compelling and complex area of study. How stroke affects the integration and appropriate reweighting of multiple sensory inputs is yet to be established. For example, people with stroke can show increased whole body responses to selective visual (optokinetic), proprioceptive and vestibular stimulation (Bonan et al, 2013, 2015; Yelnik et al, 2006; Marsden et al, 2005). As eluded to earlier, visual dominance is more commonly demonstrated after stroke (Bonan et al, 2015) which may reflect a preferential re-weighting of sensory information in favour of vision. It is postulated that vision may be preferential over other sensations as less multi-sensory integration is required to interpret visual as opposed to vestibular and somatosensory information, at least within constrained laboratory based conditions (Bonan et al, 2015; Mullie & Duclos, 2014; Lin et al, 2012). Postural responses to altered sensory stimuli may also vary between participants and can be influenced by lesion side. For example, the postural response to proprioceptive stimulation can be similar to healthy age matched controls especially in those with left sided lesions (Bonan et al, 2015; Duclos et al, 2015).

A greater understanding of how the relative weighting and integration of sensory inputs are affected by stroke could potentially inform rehabilitation approaches. In the acute stages, for example, it could be that visual control of balance and walking is encouraged (e.g. by training in well-lit rooms, using visual feedback and cues such as doors that indicate vertical). As mobility and balance improves then the dominance of

vision may need to be discouraged as vision alone cannot distinguish between self- and environmental motion and balance and gait in real world settings relies on multisensory information. Therefore, strategies to reduce visual cues (e.g. training with eyes closed or with moving visual stimuli) and encourage the use and interpretation of somatosensory and vestibular cues (e.g. training on firm surfaces progressing to more compliant / varying textured surfaces as balance and gait improves) may be useful. These strategies have been used in other conditions most notably following peripheral and central vestibular loss where visual dominance is common and in the long term can exacerbate balance dysfunction (Pavlou et al, 2013; McDonnell & Hilier, 2015).

Somatosensation may also be improved through targeted interventions designed to improve impairment and function. Compelling evidence exists in musculoskeletal rehabilitation in which peripheral proprioceptive deficits due to pain, effusion, trauma and fatigue may be improved through manual techniques and exercise (Clark et al, 2015; Roijezon et al, 2015). Proprioceptive performance for example, is determined both by the quality of the available proprioceptive information and an individual's proprioceptive ability. Thus, the hardware (peripheral mechanoreceptors and ascending pathways) provide somatosensory information for the software (processing nuclei within thalamus, S1, S2, PPC) to integrate and use. Physical activity and Tai Chi have also been shown to improve proprioceptive acuity in the elderly (Riberio & Oilveira, 2007; Li et al 2008; Xu et al, 2005) supporting the belief that active movement itself informs proprioceptive processing (Proske & Gandevia, 2012; Goble et al, 2009). Well-designed and robust sensorimotor interventional studies in neurological populations are limited. Such studies may provide the evidence needed to

demonstrate the clinical relevance of, and extent to which changes in sensory function correspond with changes in function for people with stroke.

Sensory interventions in people with stroke have for the large part focussed on the upper limb (Carey et al, 2011; Doyle, 2010; Schabrun & Hilier, 2009; Pumpa et al, 2015) with a dearth of good quality, robust interventional studies in the lower limb (Walker et al, 2014; Morioka et al, 2003; Lynch et al, 2007; Hilier & Dunsford, 2006; Tyson et al, 2013b). Recent systematic reviews (Schabrun & Hilier, 2009; Doyle et al, 2010) found multiple upper limb programmes have been developed, but involved variable treatment methods (passive, active, task-specific, different sensory modalities), variable inclusion criteria, and variable outcome measures. Both reviews indicated there was limited evidence that either passive or active sensory retraining in the upper or lower limb was effective or superior. In the lower limb, no single intervention has demonstrated superiority and systematic reviews for textured insoles (Orth et al, 2013; Paton et al, 2016) and electrical stimulation (Laufer et al, 2011; Robbins et al, 2006) do not conclusively support or refute their use. What passive sensory interventions, through Transcutaneous Electrical Nerve Stimulation (TENS) or textured insoles assert, is enhanced or augmented sensory input may promote improvements in gait or functional parameters. Passive sensory stimulation from TENS may result in an increase in cortical excitability after the period of stimulation (Meesen et al, 2011), but such interventions have yet to convincingly promote functional carry-over effects or learning once the stimulation has stopped (Tyson et al, 2013b; Shamay et al, 2007; Yan & Hui-Chan, 2009), or the insoles are no longer worn (Kalron et al, 2015). It has been suggested that practice and exposure to sensory stimuli alone may not be sufficient to

achieve changes characteristic of perceptual learning (Carey & Matyas, 2005; Morioka et al, 2003).

Task-dependent active lower limb sensorimotor interventions may facilitate longerterm changes in functional ability. For example, interventions in which body weight supported and split-belt treadmill training amplify and retrain gait asymmetries by manipulating hemi- limb load, resistance, stepping and speed, show promise. Splitbelt treadmill approaches in particular have resulted in longer term adaptive changes to gait symmetry (Kahn et al, 2009; Reisman et al, 2007, 2010) but translation of these effects to over ground walking in people with chronic stroke has yet to be established (Wutzke et al, 2013). Despite clearly reaching conscious awareness, gait adaptations because of enhanced lower limb somatosensory inputs, might not be due to conscious processing of somatosensory afferents as discussed earlier. Instead, the somatosensory inputs contributing to locomotor adaptations may be subconscious involving cerebellar afferents (Morton and Batsain, 2006).

More recently, an RCT compared passive and active sensory training approaches in the upper limb. Conducted by Carey et al (2011), 25 chronic stroke participants (median time since stroke =48 weeks, IQR 22-130 months) received sensory discrimination training (experimental), based on perceptual learning, underpinned by principles of neuroplasticity so involved attentive, active exploration of stimuli differing in texture, shape, weight, hardness/softness, with a high level of repetition and becoming increasingly challenging. Vision was occluded for most tasks but was also used to provide performance feedback, and the "unaffected" limb was used to provide intramodal calibration, or an internal reference of "normal". Attentive exploration,

anticipation trials, and regular feedback on performance were included. A further 25 (control) participants received a passive intervention which included repeated exposure to stimuli varying in texture, size, shape, weight, and hardness via passive and active grasping of objects and passive movements of the upper limb. Upper limb tactile and proprioceptive improvements were significantly greater in the experimental group and were maintained at 6 months post intervention. Further data from the RCT outlining how improved somatosensory discrimination was translated into functional gains is eagerly awaited. Several studies using learning based sensorimotor rehabilitation have produced results consistent with these findings. Byl et al (2008, 2003) conducted a series of pre-post test experimental studies in chronic stroke. They applied a learning based sensorimotor training intervention underpinned by principles of neuroplasticity and found significant post intervention gains in functional independence, strength, sensory discrimination and fine motor control. Such gains were influenced by dosage (Byl et al, 2008) and maintained at three months (Byl, et al, 2003).

Such interventions approach the rehabilitation of impaired sensation through learningbased, sensorimotor approaches tending to utilise movement for the purpose of somatosensory perception (i.e. active sensation). They focus not on isolated sensory retraining, but sensorimotor relearning suggesting that training, using tasks that require active exploration and sensory discrimination, facilitates both sensory and motor recovery. In doing so, greater demands are placed on the components of higher level somatosensory processing discussed earlier (i.e. attention, working memory, sensorimotor integration and sensory integration) than passive training. Such interventions to the upper limb have produced intriguing and encouraging results, and

provided appropriate dosages are applied, may promote activity-dependent neuroplastic long-term changes, even in people many years after stroke onset.

Such methods have not been robustly applied to the lower limb and there is a need for well- designed interventional/randomised control studies. Such studies, it is hoped, would further understanding into the functional impact of lower limb somatosensory dysfunction in stroke. The use of robust, reliable, valid, responsive and clinically relevant sensory measurement tools is essential in well-designed interventional studies so treatment effectiveness can be monitored. The novel measures developed in this thesis may provide such tools. They may also be of use as part of a learningbased sensorimotor training programme to inform the development of evidence based treatments. This thesis has provided the platform from which further work may be developed.

### 6.3. Contribution to knowledge

This thesis has provided insight into the nature of foot and ankle impairments in chronic stroke. It included the first study to qualitatively explore the perceived impact of foot and ankle impairments on function from the perspective of people with stroke (study 1, chapter 2). It demonstrated that people felt foot and ankle impairments affected their ability to get out, reinforced feelings of disability and standing out, and despite their perceived importance, were rarely addressed in treatments. Somatosensory impairments affected outdoor mobility and contributed to concerns about falling and confidence to walk outdoors. As a result, sensory impairments restricted doing those activities that involve walking outdoors, particularly on

unfamiliar terrain. Study 1 provided depth and meaning to some of the ongoing challenges faced by many chronic stroke survivors.

This thesis also produced a cross sectional observational study detailing the distribution and prevalence of lower limb tactile and proprioceptive deficits in 180 chronic stroke survivors (study 2, chapter 3). It demonstrated that up to 59% of these people experienced some form of lower limb sensory dysfunction long after stroke onset. This study adds insight into a relatively understudied topic (compared to motor) in a relatively understudied body location (compared to the upper limb) in a relatively understudied population, where efforts tend to focus on the acute/sub-acute phase of stroke. Lower limb proprioception was shown to be significantly predictive of reported falls and foot and ankle tactile sensation was significantly associated with falls reporting and fear of falling. Further, foot and ankle proprioception was significantly associated with postural sway although all associations were less than compelling. It highlighted the difficulties with using ordinal scales of measurement, particularly in the summation of scores and the quantification of prevalence. It highlighted that the shortcomings of current measures of somatosensation may in part be responsible for the difficulty in providing compelling evidence of the link between sensation and function.

In response, this thesis developed novel, reliable, valid and feasible measures of lower limb somatosensory discrimination, opening a dialogue to both rethink and utilise measures that assess higher-level somatosensation in weight bearing. It demonstrated these measures to be more sensitive in predicting the presence of subjectively reported impairments, showing stronger associations with function in chronic stroke

participants, than existing measures. They provide a novel and feasible approach to assessing lower limb somatosensory function.

#### 6.4. Strengths and limitations of methods

The strengths and limitations of each study were discussed in detail in individual chapters. An overall strength of this thesis is its exploratory, multiphase mixed methods approach. With the first qualitative study informing the second cross sectional observational study, which further informed the development and evaluation of three novel measures. Using such an approach allowed somatosensory function to be viewed from multiple perspectives, enabling somatosensory dysfunction to be put into context. Such an approach also provided a more complete understanding of the association between lower limb somatosensation and function and why, despite patient and neurophysiological evidence, it is difficult to demonstrate its role in functional decline. The exploratory sequential approach using qualitative then quantitative methods provided insight and context to inform the development of measures designed to quantify an elusive construct. In essence, this thesis captured a macro picture of lower limb somatosensory functioning in chronic stroke.

A further strength of the methods used in this thesis is the integral role patient and service user experience informed its direction. The narrative, which underlies this thesis, was for the large part driven by the views and experiences of stroke survivors. The qualitative study ultimately acted as a springboard, helping define the structure and narrative of this thesis. Further PCPI involvement aided the design and development of the novel measures of somatosensation.

One limitation of this thesis was the duplication of functional outcome measures across studies 2 and 3. Use of measures which more closely reflect community ambulation and thus higher level mobility and balance function, may have more accurately reflected the "real life" multi-sensory situations faced by ambulatory, community dwelling stroke participants. Measures such as the Community Balance and Mobility scale (Howe et al, 2006) have been validated in stroke population (Knorr et al, 2010) and may represent such a tool. A further limitation of this thesis is the generalisability of findings to the wider stroke population. Although the precise mechansims underlying functional recovery following stroke are not fully understood, recovery in the acute/sub-acute and chronic phases of stroke are likely due to different mechanisms (Ward et al, 2003; Grefkes & Ward, 2013). It is reasonable to assume that the relationships between sensorimotor function and gait performance, balance ability and falls in acute/sub-acute versus chronic populations may differ. A further limitation of this thesis is the lack of detail regarding lesion location. The inclusion of such data could have provided further insight into the neural correlates of somatosensory dysfunction and processing.

### 6.5. Recommendations for practice

The findings of this thesis underline the importance of recognising that somatosensory impairments exist long into the chronic phases of stroke in a large proportion of people so appropriate evidence-based treatment strategies, which include selfmanagement approaches, are essential. Clinicians should also recognise the potential contribution of somatosensory dysfunction in the context of lower limb motor output and control. This thesis also identified that lower limb proprioceptive ability and the perceived impact of stroke on walking ability, as measured using the Walking Impact

Scale (WIS), may be predictive of falls. It also highlighted that the mechanisms underlying tactile sensation and proprioception are complex and that current clinical methods, in particular manual tests of proprioception, may only reveal the most severe proprioceptive impairments. Measures assessing active sensation in weight bearing, such as those developed in this thesis, may more closely reflect higher cortical somatosensory processing, are inexpensive, available and appear feasible to administer.

#### 6.6. Implications for research

Important gaps in current knowledge need to be addressed. There is substantial variation in reported prevalence of sensory impairments amongst the limited studies of lower limb in chronic stroke. As highlighted in chapter 3 and 4, current clinical measures and in particular those that sum ordinal data, may not provide accurate prevalence figures. The appropriateness of measures needs consideration, as do cutoff scores, if overall prevalence is to be reported.

There is a lack of agreement amongst the relatively low volume of studies in which the relationship between lower limb somatosensory and functional outcome after chronic stroke has been investigated. Larger, high-quality cohort studies using robust, functionally oriented somatosensory and functional measures are needed to more fully investigate this.

The relationship between the lesion location and extent of the stroke with somatosensory impairments (detection and discrimination) needs to be further explored, as this information will increase our insights into the neural correlates of somatosensory processing.

A greater understanding is required of the impact of sensory loss on multisensory integration and sensory re-weighting, and how these change over time from the acute to chronic stages of stroke. This would allow therapists to potentially target certain sensory channels at certain time points (e.g. encourage the initial use of vision to aid balance but over time facilitate the multi-sensory integration of visual, vestibular and somatosensory information and avoid/reduce over-reliance on visual information).

Insights are lacking regarding the interaction between motor and sensory deficits, at different stages post stroke, and how these interactions may change as the condition enters the chronic phase of stroke. These insights are crucial in guiding and delineating treatment interventions for somatosensory deficits in chronic stroke survivors.

Finally, well-designed, robust interventional studies, for example, comparing both active and passive stimulation techniques, underpinned by a strong theoretical rationale to inform intervention structure and dosage, are required.

#### 6.7. Future developments

The copyright/trademark and production of the novel measures developed in this thesis, accompanied by an operator manual, is currently underway. Measure refinement and optimisation, is being undertaken by the Engineering Dept., University of Plymouth. It is proposed the measures will be made commercially available for wider use in 2018. It is further proposed that the measures will be evaluated for use in other neurological populations, and expanded to broader impairment levels. Two publications derived from chapters 4 and 5 have been completed and sent for publisher review, with the decision yet to be received. A two-year post-doctoral research position has been secured, with the overall objective to develop a body of

work suitable for a NIHR Clinical Lectureship application in 2019. This may include the development of a sensorimotor retraining intervention and further evaluation of measure responsiveness to change.

### 6.8. Overall conclusion

Lower limb somatosensory dysfunction in chronic stroke survivors is problematic and prevalent. Qualitative work outlined the issues reported by people with stroke in that walking ability was influenced by sensory changes in the foot and ankle. It appears that large proportions of chronic stroke survivors may continue to experience lower limb sensory impairments, although efforts to quantify prevalence and functional relevance are hampered by the shortcomings of current clinical measures of sensation. Novel, functionally oriented tests of tactile and proprioceptive discrimination may provide a sensitive, reliable and valid alternative when assessing lower limb sensory function.

## 7.0. Appendices

# **Appendix 1 - Qualitative Study Interview Schedule**

## The Interview Schedule

Area to be talked around: Do foot and ankle impairments affect perceived balance and mobility Range of topic areas: Description of the impairments of the lower limb experienced following the stroke, with a particular emphasis on the foot and ankle. Thoughts and feelings about how these impairments affect balance and mobility. Description of the advice / intervention that has been made available to help them manage their foot and ankle problems since having had the stroke. Their thoughts and feelings about this advice and intervention.

Ask Demographic/Diagnostic Questions.

- 1) Can you tell me when you had your stroke?
- 2) Can you tell me whether you feel your stroke affected your feet and ankles? Can you tell me how it has affected them? Prompt - any difficulties with stiffness, loss of feeling, weakness or pain?
  - are some of these difficulties more troublesome than others?
  - were any present before you had your stroke?
- 3) Do you feel any of these foot and ankle problems limit how steady you feel on your feet and when you're moving? Can you tell me more about how you feel they affect this? Has this changed over time since you had your stroke? Can you tell me more about this? *Prompts – foot and ankle specifically*
- 4) Do you feel your foot and ankle difficulties affect your walking? Can you tell me how it has affected it? Has this changed over time since you had your stroke? Can you tell me more about this?

Prompts - roughly how long can you walk for (approx. minutes)?

- what stops you walking further?
- how effortful it is for you to walk?
- do you walk outdoors?
- do you use walking aids?
- can you describe your walking pattern?
- 5) Do you feel that some of these foot and ankle difficulties affect how steady you are on your feet, more so than others? Has this changed over time since you have had your stroke? Can you tell me more about this?

- 6) Can you tell me whether you have had any falls since you had your stroke? Why do you think this happened? What footwear were you wearing at the time? Did you hurt yourself? How often have you fallen in the past 3 months? Do you think your foot and ankle difficulties or footwear contributed to those falls? Can you tell me more about that? Have you had any treatment for this?
- 7) Are there any other ways that your foot and ankle difficulties may have affected any aspect of your life?
- 8) Do you feel that your foot and ankle difficulties have affected the style of shoes that you can wear? Can you tell me how this has made you feel? *Prompts – what do you wear on your feet now?* 
  - does this footwear differ from what you used to wear before you had your stroke? If so, how does it differ? how does this make you feel?
  - has this footwear changed over time since you have had your stroke? If so, how does this make you feel?
- 9) Have you been given any advice or received any intervention to help manage the difficulties with your feet and ankles? Can you tell me more about this? Did you find this helpful? Did you find any of this input unhelpful? *Prompts: – provision of orthotics / FES*

advice / provision of footwear podiatry input physiotherapy input falls team

10) Is there anything else you want to tell me about how you're your feet or ankles have been affected by your stroke?

# Appendix 2 – Qualitative Study Letter of Invitation



Dear Madam/Sir,

We are interested in talking to individuals who have suffered a stroke about their views on how the foot and ankle problems they experience affect their balance and mobility. The intention is that we will use this information to improve clinical practice, as well as to help us to decide which specific aspects we should measure in future studies which we will be undertaking within the next year. As part of the research project, it would be very helpful if you could tell us about whether and how you feel foot and ankle problems contribute to difficulties with your balance and mobility; and to describe the type of advice and/or interventions that have been made available to you to help you manage these difficulties.

Please find enclosed an information sheet, which contains some important information about the study. If, having read and considered the information, you would be willing to participate in this research, then please phone me (Terry Gorst) on the contact number provided below or return the form attached to this letter, in the postage paid envelope provided. I will then contact you about the arrangements for meeting you.

Should you have any further questions please ask or phone Terry Gorst on the contact number provided below.

Yours sincerely

Terry Gorst (Research Physiotherapist)

Phone: 01752 587599

## For further information surrounding the study please contact

**Terry Gorst** 

phone: 01752 587599

email: terry.gorst@plymouth.ac.uk

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**REPLY SLIP** 

Re: Letter of invitation to be interviewed

How do foot and ankle problems affect balance and mobility?: The views and experiences of people with stroke

I \_\_\_\_\_\_ would like to take part in an interview for the study above I can be contacted; Telephone number:...... Or email.....

Please return in the postage paid and addressed envelope.

# Patient Information Sheet (PIS) – Qualitative Study



# Re: Foot and Ankle Impairments affecting balance and Mobility In Stroke (FAiMiS): The views and experiences of people with stroke

Chief Investigator: Dr Jenny Freeman

We would like to invite you to participate in a new research study. Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. This information sheet explains the background and aims of the study. Please take time to read it carefully and discuss it with others if you wish. If there is anything that is unclear, or if you would like more information, please ask us. Your participation in this study is entirely voluntary.

## Why have I been invited?

Many people who have suffered a stroke experience difficulties with their balance and mobility. This can be caused by many factors, which include foot and ankle dysfunction. Yet, the impact of specific ankle and foot problems following stroke has received little attention.

You have suffered a stroke, and you may also have experienced difficulties with regard to how steady you feel on your feet and when moving about. If you have lived with stroke for longer than three months and feel that foot and ankle difficulties impact on your mobility and balance, it would be very helpful if you could talk to us about this. We would also like to hear about the types of advice and information you may have received to help you manage any of these difficulties, and your thoughts on this.

## What is the aim of the project?

The overall aim of the study is to find out how people with stroke feel that foot and ankle problems contribute to the difficulties they experience with balance and mobility; and to better understand the way that it may have impacted on different aspects of their life.

It is hoped that the information gained during this study will help improve the multidisciplinary rehabilitation care after stroke, in particular with regard to the management of foot and ankle problems.

## What would I have to do?
Take time to read the information sheet and discuss it with your family and friends if you wish. If you have any questions you would like to ask or think you might be interested in taking part in the study you will need to contact me (Terry Gorst) to let me know. Please either;

- 1) Complete and return the postage paid slip at the bottom of your invitation letter so I might contact you by telephone.
- 2) Telephone me on 01752 587599 or email me at terry.gorst@plymouth.ac.uk

# What will happen to me if I take part

If you choose to take part in the study I (Terry Gorst) will arrange to interview you about how you feel foot and ankle problems contribute to any difficulties you may with your balance and mobility. I will come to visit you at home to conduct the interview. If you would prefer, we can arrange to meet in another place such as the local community hospital.

The interview will last no more than one hour but could be shorter. During the interview I will ask you to tell me about how you feel foot and ankle problems contribute to difficulties with your balance and mobility; and to describe the type of advice and/or interventions that have been made available to you to help you manage these difficulties. Because I would like to hear your story I may not talk much during the interview. Our meeting will be recorded using an audiotape so I can capture what you say.

# Will any expenses be paid?

No expense will be incurred by taking part in this study.

# Do I have to take part?

No. It is entirely up to you whether or not to take part. If you decide to take part you may choose to withdraw at any time without giving any reason. If you decide not to take part your usual healthcare will not be affected in any way. If you decide to take part you will be asked to sign a consent form.

# Will my records be confidential?

All information collected about you during the course of this research will be kept strictly anonymised. All published information including any direct quotations from our interview will be anonymised and reference to services and people deleted.

All information will be stored electronically on a computer which is password protected, in a document file that is also password protected. All information will be handled in compliance with the Data Protection Act (1998).

Your name and address (which we need in order to contact you) will be stored separately from the other information you supply during the project so that you cannot be identified from your study records.

# What are the potential risks or benefits of taking part?

# Risks

The risks of taking part in this study are minimal. Sometimes however talking about life experiences can be distressing. Following the interview, if you want to talk through some of the issues that were raised then you might like to contact your GP, who will be informed of your participation in the study if you wish us to do so. If you want to stop the interview you can do so at any time. During the interview should you disclose any information that may indicate a threat to your well-being, with your permission your healthcare provider will be notified.

# Benefits

There is unlikely to be any direct benefit to you taking part in this study. However, some people find the experience of sharing their view point beneficial.

# What if something goes wrong?

In the unlikely event, negligent harm will be covered by the NHS. No special arrangements have been made for non-negligent harm to patients.

# Who is organising the study?

The organiser of the study is Professor Jonathon Marsden from University Plymouth.

# Who has reviewed this study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the Research and Development team at Plymouth NHS Trust and Northern Devon Healthcare NHS Trust, the Newcastle & North Tyneside 2 Research Ethics Committee, and Plymouth University, Faculty of Health, Education and Society Research Ethics Committee.

# What will happen to the results of the research study?

The information gained will be used to improve future clinical practice, and help us to decide which specific aspects we should measure in future research studies in people with Stroke.

We will aim to talk about the work at meetings in this country and abroad, for example the Society of Podiatrist and Chiropodist Annual Professional Conference and we will aim to publish the findings widely in medical journals, for example in *Stroke*, which is available on line. Your data will always remain anonymous and your name will not appear on any of the results.

You are most welcome to request a copy of the results of the project should you wish.

# Your rights

Your participation in this study is entirely voluntary. You may withdraw at any time without giving a reason for withdrawal or without it affecting your current or future health care treatment in any way.

# What if I have any further questions or require further information?

If you have any questions about our project, either now or in the future, please feel free to contact:

Terry Gorst (Research Physiotherapist) <u>Terry.gorst@plymouth.ac.uk</u>; Telephone: 01752 587599

Or

Dr Jenny Freeman (Chief Investigator) Email: <u>jenny.freeman@plymouth.ac.uk</u> ; Telephone: 01752 588835

# What if I have a complaint?

Should you have reason to complain about the way you have been treated at any stage during the study you can access the NHS patient advisory liaison service (PALS) who will be able to advise and help you (<u>plh-tr.PALS@nhs.net</u> or 01752 517683 / 01752 517657).

Alternatively, you can make your complaint directly to Dr Jenny Freeman, the Chief Investigator involved in this study (contact details below).

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

# Chief Investigator:

Dr Jenny Freeman

FF 21 Peninsula Allied Health Centre Plymouth University Derriford Road Plymouth PL6 9BH Email: jenny.freeman@plymouth.ac.uk Telephone: 01752 588835

# Appendix 3 – Qualitative Study Diagnostic and Demographic data collection

Demographic and diagnos	tic deta	ails:		
Participant ID Code:				
Age (years):				
Gender (underline as approp	oriate):	Male	Female	
Time since stroke:				
Are you?(underline as appro	opriate)	Working	Medically Retired	Age Retired
Do you live alone? (unde	rline as	appropriate)	Yes	No
Do you have any other signif	ficant m	nedical conditior	s? (Please list)	
Prompt if diabetes not listed.				
If diabetic, is it				
Controlled	Yes		No	
If controlled, how?	Medic	ation	Diet	
Did you have any loss of fee your stroke?	ling (?o	or movement) in	your feet or ankles	s before you had
Yes No				
Details				

 Do you have any foot or ankle ulcers (underline as appropriate)	Yes	No
Do you use any walking aids (underline as appropriate): Yes	Ν	0
If yes please specify:		
Do you use any orthotics / FES ? (underline as appropriate):	Yes	No
If yes please specify:		

# Appendix 4 - Stroke Participant Information Sheet – FAIMIS Study



Northern Devon Healthcare NHS Trust

**Project title:** The effects of foot and ankle impairments on mobility and balance in community dwelling adults post stroke

Dear Madam/Sir,

We would like to invite you to participate in a research study because you have had a stroke and it may be affecting your walking and balance. The study will be conducted by a researcher who is a trained physiotherapist. The researcher is employed part-time to conduct the research and is studying for a PhD. To help you know more about the study, please read the question and answer section below. It should help you decide if you would like to take part.

# Study Background

Problems with the foot and ankle such as muscle weakness or tightness, sensation changes, or movement restrictions may contribute to difficulties with walking and balance after stroke. These problems and their impact have yet to be fully explored and more research is needed to help us to better understand how foot and ankle problems experienced after a stroke affect walking and balance.

# What is the purpose of the study?

The aim of this study is to investigate whether foot and ankle problems affect walking and balance so that treatment may be improved. We will also be comparing the feet and ankles of people who have had a stroke with those who have not had a stroke to take account of changes that may occur as a result of age. We plan to recruit up to 180 participants who have had a stroke and up to 45 participants who have not had a stroke to take part in the study.

#### What will I be asked to do if I decide to take part?

You will be asked to attend one assessment session so that we may assess your foot and ankle, your walking and your balance. The session will last about 1½ hours. Measurements will be taken of your foot in sitting, standing and walking. Some of these will involve special equipment applied to your foot and ankle and some will record how your foot moves when you walk using a video recorder. You will also be asked to complete some questionnaires about your mobility and balance.

#### Where will this study take place?

The study will take place at your closest hospital in North Devon Healthcare Trust or at the Penninsula Allied Health Centre, University of Plymouth, Derriford Road, Plymouth.

#### How will I travel there and get back home?

We are happy to help to arrange travel to attend for assessment and there are funds available to pay for the cost of your travel. We will pay the cost of car travel at a rate of 45p per mile. If you require alternative travel arrangements, please discuss this with the research team; we will endeavour to accommodate your requirements and meet your travel costs.

#### Do I have to take part?

No. It is entirely up to you whether or not you would like to take part. If you decide to take part but change your mind, you are still free to withdraw at any time.

#### What are the possible advantages of taking part?

There are no direct benefits to you in taking part in this research. By taking part in the research, you may be helping us to improve the way foot and ankle problems are managed after stroke in the future.

#### What are the possible disadvantages or risks of taking part?

There are minimal risks in taking part in this research. It is possible that you may experience brief and temporary discomfort during some of the tests as they will involve stretching certain muscles. You may also feel tired / stiff for after the test and on the next day similar to that felt after undertaking moderate exercise. There is also a risk of you falling during the mobility and balance assessment although you will be supervised by a physiotherapist during the assessment. We will not be asking you to do anything you do not feel able to do safely.

# What happens if something goes wrong or I am unhappy about my participation in the study?

In the unlikely event, negligent harm will be covered by the NHS. No special arrangements have been made for non-negligent harm to patients. If you are unhappy about any aspect of your participation in the study, wish to report a complaint, or something that went wrong please contact:

Professor Richard Stephenson, Room 403, Rolle Building, Faculty of Human Health and Human Sciences, University of Plymouth, Plymouth, PL4 8AA Telephone Number: 01752 586 740.

You may also contact the Patient Advice and Liaison Service for independent advice or in case of complaint on 01271 314090 or 01752 211818.

# Who has reviewed this study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by the NRES Committee South West – Exeter and it has also been considered by the Research Ethics Committees of the Universities of Plymouth, the West of England and East London. If you have any questions about the ethics of the research or about any of the researchers, please contact: <u>researchethics@uel.ac.uk</u>

# What will happen to the information collected?

All information collected about you during the course of this research will be kept strictly anonymous. All information will be stored electronically on a computer which is password protected, in a document file that is also password protected. All information will be handled in compliance with the Data Protection Act (1998).

Your name and address (which we need in order to contact you) will be stored separately from the other information you supply during the project so that you cannot be identified from your study records.

# What will happen to the results of the research study?

The information gained will be used to improve future treatment of foot, ankle, mobility and balance problems following stroke.

We will aim to talk about the work at meetings and conferences in this country and abroad, and we will aim to publish the findings widely in medical journals. Your data will always remain anonymous and your name will not appear on any of the results.

# Your rights

Your participation in this study is entirely voluntary. You may withdraw at any time without giving a reason for withdrawal or without it affecting your current or future health care treatment in any way.

# Who should I contact for further information or if I would like to take part in the

# study?

Please contact:

Terry Gorst Northern Devon Healthcare Trust- Stroke & Neuro-Rehabilitation Physiotherapy Dept Barnstaple EX32 4JB Telephone number: 01271 314123

Email: <a href="mailto:terry.gorst@plymouth.ac.uk">terry.gorst@plymouth.ac.uk</a>

Thank you for your consideration.

Yours sincerely,

Terry Gorst

# Letter of Invitation to participate - FAIMIS Study





Northern Devon Healthcare NHS NHS Trust

Incorporating community services in Exeter, East and Mid Devon

04.10.2013 Version 1.0 REC Ref:

13/SW/0302

#### Letter of Invitation to participate in a stroke research project

**Project Title:** The effects of foot and ankle impairments on mobility and balance in community dwelling adults post stroke

Dear Madam/Sir,

People who have had a stroke are being invited to take part in a research study. The research is being undertaken by staff from (insert local institution).

The research is looking at how foot and ankle problems following stroke affect walking and balance. The aim of this research is to help understand more about how balance and walking can be improved in people who have had a stroke.

You are being given this letter because you may be suitable to take part in the study. If you are interested in finding out more about the research, we can provide your details to the researchers so that they can contact you about the study. The researchers will be able to tell you more about the research and what's involved.

If you are happy for the researcher to contact you about the study, please tick the statement below and either return this letter to the person who gave it to you or return it in the envelope provided. By agreeing to be contacted by the researcher you are not agreeing to take part. You are only agreeing to being contacted by the researchers so they may tell you more. If you do not complete and return this letter, you will not be contacted by the researchers and they will not receive your contact details.

Any decision you make about taking part in this study will not affect any future treatment you may receive.

Yours sincerely
[Direct care worker]

------

I am happy for the research team to contact me to tell me more about the study

My contact Details are:

Participant Code Date		
Patient Demographic	cs:	
Name:	DOB:	
Height:	Weight:	
Foot length:	Foot width:	Foot size:
Date of stroke:		
Type of stroke:	Haemorrhagic / Ischaemic * (use prompts of bleed/clot)	
Site of stroke: Cereb	rum / Brain stem / Cerebellum *	
Side of stroke:	Unilateral RIGHT / unilateral LEFT / Bilater	ral *
Side (most) affected	: RIGHT / LEFT *	
*circle as appropriate	e	
Recruitment centre:		
NORTH DEVC	)N :	
EAST LONDO	N: Barts Health / Newham / Other	
Walking Aids/Mobili	ty:	
Falls?/No. of falls in	last 3 months:	
Cause of fall:		
Any other comments	s (eg. Medication/comorbidities):	

# **Appendix 5 – Case Report Form – Cross sectional Study**

# Appendix 5 – Case Report Form – Sensory Study (cont)

# Sensory Assessment (Emc NSA):

Tactile sensation:	Affecte	Affected (A)			Non Affected (NA)			
	LT	PR	PP	SB	LT	PR	PP	SB
Thigh								
Leg								
Foot								
Toes								
Total								
Proprioception:	A	NA						
Thigh								
Knee								
Ankle								
Toes								
Total								

**NB:** 0= absent, 1=impaired, 2=normal. If LT score 2 then move onto SB test.

# **Balance and Mobility Outcome Measures:**

Trial	FRT stand	TUAG	10MWT FWS
1			
2			
3			
Average			

FRT= Functional Reach Test; TUAG = Timed up and Go; 10MWT FWS= 10metre walk (fastest walking speed)

# Aids utilized:

**Other Comments:** 

# Appendix 6 - Outcome Measure – Sensation

# Erasmus MC Nottingham Sensory Assessment (Stolk-Hornsveld et al, 2006)

Testing protocol

# Equipment:

Cotton wool ball Neuro tip Pen Plinth Pillows x2.

**Tested sensory properties**: *Tactile sensation (light touch, pin prick (pain), pressure), sharp-blunt discrimination, proprioception.* 

# A) Cutaneous Sensation

- 1. Patient positioned in supine.
- 2. Patient suitably undressed (shorts or trousers or skirt rolled up enough to expose test points, ie to top of thigh, use towel to retain modesty if required.)
- Test explained to subject: "The following test uses various types of objects to see what the feeling is like in your leg/s. I will demonstrate the test first on your non affected side and then on your affected side. Say 'yes' when you feel the object touching you."
- 4. For all tests demonstrate each test on unaffected side first on the hand. Ask participant to respond with a "yes" to indicate if they feel it. Test 3 times at the defined points in a random order. Begin testing distally at the toe. Test affected (A) side then non affected side (NA). Test each point once in any order, gap of no longer than 2-5 secs.
- 5. Start with **light touch** (tactile sensation).
- 6. Touch the skin, at the defined points of contact (Fig. 1), lightly with a cotton wool ball.
- 7. Scoring criteria for light touch, pressure and pinprick:
  - 0) Absent: Patient fails to identify the test sensation on all three occasions.
  - 1) Impaired: Patient identifies the test sensation on only one or two occasions.
  - 2) Normal: Patient identifies the test sensation on all three occasions.

With light touch, if a score of 2 is assigned for all of a limb, then automatically assign a score of 2 for all the pressure and pinprick test items and move onto sharp blunt test.

- 8. For **pressure** testing: Apply pressure to the skin, using the index finger, at the defined points of contact, sufficient enough to just deform the skin contour.
- 9. For **Pin Prick** test: Prick the skin using a neuro tip at the defined points of contact, sufficient enough to just deform the skin contour.

- 10. If score 0 or 1 on tactile sensations. Then move onto proprioception. If scores 2, continue to test sharp-blunt.
- 11. **Sharp –blunt** test: Stimulate the skin six times at each location, in a random order, three times with a neuro tip and index finger as sharp or blunt, using the defined points of contact. Patient is asked to respond whether the stimuli feels sharp or blunt.

Score as follows:

- 0) Absent: Patient fails to correctly describe/ indicate the test sensation on all six occasions.
- 1) Impaired: Patient correctly describes/ indicates the test sensation, but on less than six occasions.
- 2) Normal: Patient correctly describes/ indicates the test sensation on all six occasions.

.....

#### Anatomical Landmarks for testing of cutaneous sensation

#### Thigh

- 1) Medial femoral epicondyle, medial aspect
- 2) Centre of line of femur, anterior aspect
- 3) Greater trochanter

#### Leg

- 1) Medial malleolus, medial aspect
- 2) Centre of the anterior border of the tibia
- 3) Fibular head, lateral aspect

#### Foot

- 1) Base of 5th metatarsal bone, dorsal aspect
- 2) Second metatarsal, dorsal aspect
- 3) Centre of midtarsal line, dorsal aspect

#### Toes

- 1) Distal phalanx, 5th digit, plantar aspect
- 2) Distal phalanx, 3rd digit, plantar aspect
- 3) Distal phalanx, 1st digit, plantar aspect



# **B)** Proprioception

- 1. Specified passive movements are tested in only one joint at a time. The starting positions, specific hand grips for the physiotherapist to use, along with the directions of the movement to be tested are described (in the table) below. The large joints (hip and knee) are moved through approximately a quarter of their total range of motion (ROM). The other joints (ankle and toes) are moved throughout the full available range of movement.
- 2. To demonstrate the procedure, three practice movements are allowed (with the patient's eyes open.) Each joint is then moved three times. The patient is asked, using specific questions, to indicate verbally or non-verbally the direction of the movement taking place.
- 3. If the patient is incapable of doing this, he is then asked to identify (verbally or non-verbally) when movement is taking place.
- 4. Score as follows:

0 Absent: Patient does not detect the movement taking place.

- 1 Impaired: Patient detects the movement taking place but the direction is not correct on all three occasions.
- 2 Normal: Patient correctly detects the direction of the movement taking place on all three occasions.

Body part	Movement:	Ask the patient:	Hand grips	
			Distal (moving) hand:	Proximal (fixing) hand:
Toes	flexion and extension of the first metatarso- phalangeal joint.	' Is your toe moving upwards or moving downwards?'	place the thumb lateral and the index finger medial on the distal phalanx of the great toe.	fix the first metatarsal bone, just proximal to the metatarsophalange al joint with the thumb lateral and the index medial.
Ankle	flexion and extension of the ankle joint.	'Is your foot moving upwards or moving downwards?'	grasp the foot with thumb placed on the lateral margin of the foot and fingers on the medial margin of the foot.	fix the distal end of the tibia and fibula.
Knee	flexion and extension of the knee, with the hip and knee joint in 90° flexion.	'Is your knee being bent or straightened?'	grasp the calcaneus with the thumb medially and the fingers cupped inferiorly. The	grasp the distal end of the femur, with the thumb laterally and the fingers medially.

# Table 1: Proprioception testing – movement, instructions and tester handling.

			foot should be supported by the lower forearm.	
Hip	flexion and extension of the hip joint, starting with the hip in 90° flexion.	Is your thigh moving towards you or away from you?'	grasp the calcaneus with the thumb medially and the fingers cupped inferiorly. The foot should be supported by the lower forearm.	grasp the distal end of the femur and with the thumb laterally and the fingers medially. Maintain knee position accurately as you flex the hip.

# Appendix 7 –Outcome measures

# Walking Impact Scale (Walk-12) (Holland et al 2006)

These questions ask about limitations to your walking due to your stroke during the past two weeks. For each statement, please tick the answer that best describes your degree of limitation. Please answer all questions even if some seem rather similar to others, or seem irrelevant to you.

IN THE PAST TWO WEEKS, HOW	Not at all	A little	Moderately	Quite a bit	Extremely
MUCH HAS YOUR STROKE	1	2	3	4	5
limited your ability to walk?					
limited your ability to run?					
limited your ability to climb up and down stairs?					
made standing when doing things more difficult?					
limited your balance when standing or walking?					
limited how far you are able to walk?					
increased the effort needed for you to walk?					
made it necessary for you to use support when walking					
indoors (e.g., holding on to furniture, using a stick, etc.)?					
made it necessary for you to use support when walking					
outdoors (e.g., using a stick, a frame, etc.)?					
slowed down your walking?					
affected how smoothly you walk?					
made you concentrate on your walking?					
Sub Total					
				Total	/60

# Appendix 7 - Outcome Measures - Mobility and Balance

Timed Up and Go (Podsiadlo and Richardson, 1991):

# Equipment

Chair (46cm seat height, 67cm arm height) Stopwatch 3 metre measured walkway

# **General Information**

The patient should sit on a standard armchair, placing his/her back against the chair and resting his/her arms on the chair's arms. Any assistive device used for walking should be nearby. Regular footwear and customary walking aids should be used. The patient should walk to a line that is 3 meters (9.8 feet) away, turn around at the line, walk back to the chair, and sit down. The test ends when the patient's buttocks touch the seat. Patients should be instructed to use a comfortable and safe walking speed but made aware that they are being timed. A stopwatch should be used to time the test (in seconds).

# Set-up:

Measure and mark a 3 meter (9.8 feet) walkway Place a standard height chair (seat height 46cm, arm height 67cm) at the beginning of the walkway

# **Patient Instructions:**

Instruct the patient to sit on the chair and place his/her back against the chair and rest his/her arms on the chair's arms. The upper extremities should not be on the assistive device (if used for walking), but it should be nearby. Demonstrate the test to the patient. When the patient is ready, say "Go". The stopwatch should start when you say go, and should be stopped with the patient's buttocks touch the seat.

# Appendix 7 – Outcome Measures - Mobility and balance Timed 10-Metre Walk Test (Bohannon, 1997)

Equipment: Stopwatch Measured 10m walkway

# **General Information:**

Individual walks without assistance (but can use normal walking aid) 10 meters (32.8 feet) and the time is measured for the intermediate 6 metres (19.7 feet) to allow for acceleration and deceleration

Start timing when the toes of the leading foot crosses the 2-meter mark

- Stop timing when the toes of the leading foot crosses the 8-meter mark
- Assistive devices can be used but should be kept consistent and documented from test to test

If physical assistance is required to walk, this test should not be performed. It will be performed fastest walking speed possible.

# Set-up:

Measure and mark a 10-meter walkway add a mark at 2-meters and add a mark at 8-meters

# Patient Instructions:

Maximum speed trials: "I will say ready, set, go. When I say go, walk as fast as you safely can until I say stop"



# Appendix 8 – Outcome Measures - Mobility and balance

Functional Reach Test (Duncan, & Weiner, et al. (1990)

General Information:

The Functional Reach test can be administered while the patient is standing (Functional Reach) or sitting (Modified Functional Reach).

# Functional Reach (standing instructions):

The patient is instructed to stand next to, but not touching a wall, positioning the arm that is closer to the wall at 90 degrees of shoulder flexion with a closed fist. The assessor records the starting position of the 3rd metacarpal head on a metre rule which can be attached to the wall. Instruct the patient to "Reach as far as you can forward without taking a step." The location of the 3rd metacarpal is recorded. Scores are determined by calculating the difference between the start and end positions. This will be measured in cms. Four trials are done and the average of the last three is noted.

# Appendix 9 –Outcome measures – Falls

# Falls Efficacy Scale-International (Yardley & Todd 2005)

I would like to ask you some questions about how concerned you are about the possibility of falling. For each of the following activities, please tick the opinion closest to your own to show how concerned you are that you might fall if you did this activity. Please reply thinking about how you usually do the activity. If you currently don't do the activity (example: if someone does your shopping for you), please answer to show whether you think you would be concerned about falling **IF** you did the activity.

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		Not at all	Somewhat	Fairly	Very
		concerned	concerned	concerned	concerned
		1	2	3	4
1	Cleaning the house (eg. sweep, vacuum or dust)				
<u> </u>					
2	Getting dressed or undressed				
3	Preparing simple meals				
4	Taking a bath or shower				
5	Going to the shop				
6	Getting in or out of a chair				
7	Going up or down stairs				
8	Walking around in the neighbourhood				
9	Reaching for something above				
	your head or on the ground				
10	Going to answer the telephone				
	before it stops ringing				
11	Walking on a slippery surface (e.g. wet or icy)				
12	Visiting a friend or relative				
13	Walking in a place with crowds				
14	Walking on an uneven surface (eg rocky or uneven				
	ground, poorly maintained pavement)				
15	Walking up or down a slope				
16	Going out to a social event (eg religious service,				
	family gathering or club meeting)				
	Sub total				
				Total	161
				10101	/04

# Appendix 10 – Consent to Contact Letter – Sensory Discrimination Study

Northern Devon Healthcare

RESEARCH WITH PLYMOUTH UNIVERSITY

# Consent to contact - letter of Invitation to participate in a stroke research project

**Project Title:** The development of lower limb sensory discrimination tests following stroke; reliability and validity testing

REC Ref: 15/SC/0191

Dear Madam/Sir,

People who have had a stroke are being invited to take part in a research study. The research is being undertaken by staff from the University of Plymouth and Northern Devon Healthcare NHS Trust.

The aim of this study is to investigate whether four new tests of assessing sensation in the lower limb are accurate and appropriate enough to be used in clinical practice. It is hoped that by developing new tests of sensation that are more realistic of how our feet and legs receive sensory information will help us to improve treatment of these problems.

You are being given this letter because you may be suitable to take part in the study. If you are interested in finding out more about the research, we can provide your details to the researchers so that they can contact you about the study. The researchers will be able to tell you more about the research and what's involved.

If you are happy for the researcher to contact you about the study, please tick the statement below and either return this letter to the person who gave it to you or return it in the envelope provided. By agreeing to be contacted by the researcher you are not agreeing to take part. You are only agreeing to being contacted by the researchers so they may tell you more. If you do not complete and return this letter, you will not be contacted by the researchers and they will not receive your contact details.

Any decision you make about taking part in this study will not affect any current or future treatment you may receive.

Yours sincerely

[Direct care worker]

-------I am happy for the research team to contact me to tell me more about the study
My contact Details are:
Name......Telephone No.(inc.
code):....
or Email (if you
prefer).....

# Appendix 11 – Patient Information Sheet (PIS) – Sensory Discrimination

# Study





# Project title: The development of lower limb sensory discrimination tests following stroke; reliability and validity testing

Dear Madam/Sir,

We would like to invite you to participate in a research study because you have had a stroke and it may be affecting your walking and balance. This study is assessing some new tests that measure the ability to discriminate different sensations and movements in the feet and legs. The study will be conducted by researchers who are trained physiotherapists. The principal researcher is employed part-time to conduct the research and is studying for a PhD, for which this study is a part. To help you know more about the study, please read the question and answer section below. It should help you decide if you would like to take part.

# Study Background

Problems with poor or reduced sensation in the foot, ankle and leg are common as a result of stroke and may contribute to difficulties with walking and balance. Being able to accurately measure sensation changes in the leg following stroke is therefore important. Despite this, some current measures of sensation in the lower limb are not as accurate as they can be and the impact of reduced sensation has yet to be fully explored. More research is needed to help us to better measure the extent of sensory problems in the lower limb after a stroke and how these problems affect walking and balance.

# What is the purpose of the study?

The aim of this study is to investigate whether four new tests of assessing sensation in the leg are accurate and appropriate enough to be used in clinical practice. These tests are designed to realistically reflect how our feet and legs normally process sensory information. It is hoped that developing new tests of sensation will help us to improve the detection and treatment of these problems.

We will be carrying out these tests on people who have had a stroke and on those who have not had a stroke to take into account any changes in sensation that may occur as a result of age. We plan to recruit up to 36 participants who have had a stroke and up to 36 participants who have not had a stroke to take part in the study. We are looking at whether the tests are reliable. That is if we get similar results on two occasions separated by a short break. Having a reliable test is important if we are to detect changes with recovery or with treatment. We also want to look at how the new tests of sensation compare to currently available clinical tests and whether there is any relationship between difficulties discriminating sensations and people's walking, balance and history of falling.

# What will I be asked to do if I decide to take part?

You will be asked to attend two separate assessment sessions one week apart so that we may test your sensation, your walking and your balance. **The first session will last a maximum of 1 hour. The second session will last a maximum of 1 hour 20mins and will involve a second person also testing your sensation.** Both appointments will be arranged at your convenience. Sensation in your foot and leg will be tested in sitting and standing. Some of these tests will involve you standing on various surfaces (rough/smooth/soft hard/sloping) to see how much you are able to feel through the sole of your foot and how much you can detect your ankle and leg moving. You will also be asked to complete some balance and walking tests along with some questionnaires about your mobility and balance.

# Where will this study take place?

The study will take place at your closest hospital in North Devon or at the Human Movement and Function Laboratory at Plymouth University, whichever is the most convenient.

# How will I travel there and get back home?

We are happy to help to arrange travel to attend for each assessment and there are funds available to pay for the cost of your travel. We will pay the cost of car travel at a rate of 45p per mile. If you require alternative travel arrangements, please discuss this with the research team; we will endeavour to accommodate your requirements and meet your travel costs.

# Do I have to take part?

No. It is entirely up to you whether or not you would like to take part. If you decide to take part but change your mind, you are still free to withdraw at any time. Not taking part or withdrawing from the study will not affect you current or future treatment in any way.

# What are the possible advantages of taking part?

There are no direct benefits to you in taking part in this research. By taking part in the research, you may be helping us to improve the way sensory problems in the lower limbs are treated after stroke in the future.

# What are the possible disadvantages or risks of taking part?

There are minimal risks in taking part in this research. There is a small risk of you falling during the mobility and balance tests although you will be supervised by a physiotherapist during the assessment and provided with support while standing if you need it. We will not be asking you to do anything you do not feel able to do safely.

# What happens if something goes wrong or I am unhappy about my participation in the study?

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. The

University of Plymouth have both Public Liability and Professional Negligence insurance. Regardless of this, if you wish to complain, or have any concerns about this study, the normal National Health Service complaints system is available to you. If you are unhappy with this study please approach the researchers or your doctor:

Professor Jon Marsden, School of Health Professions, Plymouth University, PL6 8BH Tel 01752 587 590; email jonathan.marsden@plymouth.ac.uk

You may also contact the Patient Advice and Liaison Service for independent advice or in case of complaint on 01271 314090 or 01752 211818 or by e-mail: ndht.PALS@nhs.net

# Who has reviewed this study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by the National Research Ethics Service (NRES) South Central –Berkshire B and it has also been considered by the Research Ethics Committees at Plymouth University. If you have any questions about the ethics of the research or about any of the researchers, please contact:

Professor Jon Marsden, School of Health Professions, Plymouth University, PL6 8BH Tel 01752 587 590; email jonathan.marsden@plymouth.ac.uk

# What will happen to the information collected?

All information collected about you during the course of this research will be kept strictly anonymous. All information will be stored electronically on a computer which is password protected, in a document file that is also password protected. All information will be handled in compliance with the Data Protection Act (1998).

Your name and address (which we need in order to contact you) will be stored separately from the other information you supply during the project so that you cannot be identified from your study records.

# What will happen to the results of the research study?

The information gained will be used to improve future assessment and treatment of sensory problems in the lower limbs, mobility and balance problems following stroke. We will aim to talk about the work at meetings and conferences in this country and abroad, and we will aim to publish the findings widely in medical journals. Your data will always remain anonymous and your name will not appear on any of the results. You will also receive a summary of the study findings should you wish. Please let the researcher know if you would like to receive this summary.

# Your rights

Your participation in this study is entirely voluntary. You may withdraw at any time without giving a reason for withdrawal or without it affecting your current or future health care treatment in any way.

# Who should I contact for further information or if I would like to take part

# in the study?

Please contact:

Terry Gorst Northern Devon Healthcare NHS Trust Stroke & Neuro-Rehabilitation Service North Devon District Hospital Barnstaple EX31 4JB Telephone number: 01271 322378 Email: terry.gorst@nhs.net

Thank you for your consideration.

Yours sincerely,

# Terry Gorst

1 copy for the participant; 1 copy for the researcher, Original retained on file

Title of Project: The development of lower limb sensory discrimination tests following stroke; reliability and validity testing

Name of Researcher: **Terry Gorst Please initial box** 

- 1. I confirm that I have read and understand the Participant Information Sheet dated 23.12.14 (Version 1.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily
- 2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected
- 3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals, from regulatory bodies or from the NHS Trust where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
- 4. I agree to take part in the above study

# Optional

5. I agree to my GP being informed about my participation in this study.

Name of GP: Contact address

Signatures:

Name of participant	Date	Signature
Name of person taking consent	Date	Signature

When completed: 1 for participant 1 for researcher site file. This consent form will be securely stored in a locked cabinet at the University of Plymouth

# Appendix 12 – Overview of Standard Operating procedure for novel sensory measures

Each test procedure uses a two-alternative forced choice (2AFC) design to quantify the tactile and proprioceptive discrimination thresholds of the lower limb. With this method, the subject mentally compares two stimuli, then reports which stimulus most closely reflects a given property. In these tests, the predefined properties are roughest (Texture Discrimination test), most sloping (Gradient discrimination test), and highest (Step height discrimination test).

The participant's task in each of the tests is to discriminate between two stimuli: a base stimulus (A) and a comparator stimulus (B). These stimuli are presented randomly (i.e. AB or BA) over several trials, with participants blinded as to whether the base stimulus is presented first or second in each trial. The staircase approach to the 2AFC approach involves changing the comparator stimulus dependent on whether the participants' response is correct. If the participant correctly discriminates between the two stimuli, they are, for a further two trials, presented with the same base and comparator stimuli (order randomised). If they answer correctly three times in a row, they are presented in the next trial with a comparator stimulus which is marginally but quantifiably less extreme (i.e. more similar in its properties to the base stimulus). If the participant is unable to discriminate between the two stimuli i.e. answers incorrectly just once, they are presented in the next trial with the base stimulus and a new comparator stimulus which is quantifiably, but marginally, more extreme in its properties than the previous comparator stimulus (i.e. rougher, more sloping or higher). The procedure involves increasingly challenging trials meaning the 1st trial is theoretically the easiest and involves presenting the base and comparator stimuli

which differ most in their physical properties. However, given the staircase procedure, the first comparator stimulus presented does not necessarily need to be the most different. The testing procedure can be shortened by beginning the test at any point (i.e. presenting any comparator stimulus alongside the base stimulus). The procedure is designed to converge on a discrimination threshold so the participant's response (i.e. correct/incorrect) determine whether they go up the staircase or down the staircase.

If participants continue "down the staircase" recording correct responses through the progressively more difficult trials, the first incorrect response recorded counts as the first "reversal". After four reversals, which, after the 1<sup>st</sup> incorrect response, also includes correct responses (i.e. going down a level), the test is stopped (see examples below). The final discrimination threshold is taken as the mean of four reversal points. The discrimination threshold is expressed in the original measurement units and is the point at which participants cannot consistently differentiate between base and comparator stimulus. It can also be expressed as the just noticeable difference (JND) which reflects the percentage difference between comparator and base stimulus.



# Procedural algorithm of two alternative choice design using 3-down 1-up staircase

# **Test procedure**

# 1. Gradient Discrimination tests - Foot/ankle position sense

Participant barefoot. Lateral malleous aligned with axis of rotation of platform. Non-

tested foot positioned on platform level with adjustable (tested) platform when at 0°

(plantargrade). Ensure participant has upper limb support. Test hemi side. Base

stimulus (BS) is 0 degrees, first comparator stimulus (CS) 6 degrees.

Explanation to participant. "I would now like to test your ability to tell the difference between two platforms, platform A and platform B. These platforms are different in how much they slope (up or downwards). I would like you to stand on this adjustable platform. I will be testing the side most affected by your stroke. You will have 5 seconds to sense how much each platform slopes under your foot. After standing on both platforms, I would like you tell me which platform felt like it was sloping (up/down) the most, platform A or platform B. If you do not know, try not to guess, just say 'I don't know'. I would like you to complete this test looking straight ahead, without looking at your feet, so I will help you place your foot onto the platform. You can hold onto the bar to help with your balance."

Base Stmulus (BS) =0 degree slope. First comparator stimulus (CS) = 6 degree slope (DF or PF depending in which is being tested.

Randomise the order in which BS/CS are presented within each trial.

Follow the procedural algorithm, adjusting the comparator stimulus by 0.5 degrees accordingly. Once the 1<sup>st</sup> incorrect response has been made, this counts as the first reversal. The next step up or step down the staircase counts as second reversal, the third step up/down counts as third reversal and fourth step up/down counts as fourth reversal. The discrimination threshold is then calculated as the mean value of the four reversal points.

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Platform Slope	Correct	Incorrect	<b>Reversal Point</b>
6	x x x		
5.5	ххх		
5	ххх		
4.5	ххх		
4	ххх		
3.5	хх	х	1
4	ххх		2
3.5	ххх		3
3	хх	х	4

Example scoring and performance in gradient discrimination test

Threshold = 3.5 (degrees)

#### 2. Texture Discrimination.

Participant barefoot. Base stimulus  $1500\mu m$ . Test hemi-side. Foot actively placed onto textured plate with guidance if necessary. Ensure foot is centrally positioned. Allow active exploration of surface for up to 5 seconds. Reiterate vision not be used.

Base Stmulus (BS) =1500 $\mu$ m plate. First comparator stimulus (CS) = 3500 $\mu$ m plate. The greater the spatial interval ( $\mu$ m) of the textured plate, the rougher the surface.

Randomise the order in which BS/CS are presented within each trial.

Follow the procedural algorithm, working up or down the comparator stimuli as presented in table 5.1. Once the 1<sup>st</sup> incorrect response has been made, this counts as the first reversal. The next step up or step down the staircase counts as second reversal, the third step up/down counts as third reversal and fourth step up/down counts as fourth reversal. The discrimination threshold is then calculated as the mean value of the four reversal points.

Explanation to participant. "I would now like to test your ability to tell the difference between two surfaces; surface A and surface B. These surfaces are different in how rough they are. The surfaces will be placed under the foot most affected by your stroke, one at a time. You will have 5 seconds to feel each surface under your foot. After feeling both, I would like you tell me which surface felt the roughest, A or B. If you do not know, try not to guess, just say 'I don't know'. I would like you to complete this test looking straight ahead, without looking at your feet, so I will help you place your foot onto the plate. Are you happy to continue?

Textured Surface (µm)	Correct	Incorrect	<b>Reversal Point</b>
3500	ххх		
3250	ххх		
3000	ххх		
2700	ххх		
2400		x	1
2700	хх	x	2
3000	ххх		3
2700	ххх		4

Example scoring and performance in texture discrimination task.

Threshold= 2700 (i.e. mean of four reversal points)

# 3. Step Height

Participant barefoot. Ensure upper limb support. Hemi-foot passively placed onto step.

After 3 seconds, foot is passively placed back onto floor.

Base Stmulus (BS) =100mm height step. First comparator stimulus (CS) = 154mm

height step

Randomise the order in which BS/CS are presented within each trial.
Follow the algorithm, working up or down the comparator stimuli, adjusting the step height by 6mm depending on correct/incorrect response. Once the 1<sup>st</sup> incorrect response has been made, this counts as the first reversal. The next step up or step down the staircase counts as second reversal, the third step up/down counts as third reversal and fourth step up/down counts as fourth reversal. The discrimination threshold is then calculated as the mean value of the four reversal points.

Explanation to participant. "I would now like to test your ability to tell the difference between two steps, step A and step B. These steps differ in height. Your foot will be placed on the steps, one at a time. You will have up to 5 seconds to feel each step under your foot. After feeling both steps, I would like you tell me which felt the highest, A or B. If you do not know, try not to guess, just say 'I don't know'. I would like you to complete this test looking straight ahead, without looking at your feet, so I will help you place your foot onto and off the step. Are you happy to continue?"

Step Height (mm)	Correct	Incorrect	<b>Reversal Point</b>
154	ххх		
148	ххх		
142	ххх		
136	ххх		
126	ххх		
122	ххх		
118	х	х	1
122	ххх		2
118	хх	х	3
122	ххх		4

Example scoring and performance in step height discrimination test.

Threshold =120mm

**Appendix 13** – Statistical evaluation criteria for examining assessment tools for disability outcomes research (Andresen, 2000; Blum & Korner-Bitensky, 2008)

Psychometric Property	Level	
Reliability		
Cronbach $\alpha$ or split-half statistics		
Excellent	≥.80	
Adequate	.70–.79	
Poor	<.70	
Test-retest or interrater reliability (intraclass correlation coefficient [ICC] or kappa statistics)		
Excellent	≥.75	
Adequate	.40–.74	
Poor	<.40	
Validity		
Construct/convergent and concurrent correlations		
Excellent	≥.60	
Adequate	.31–.59	
Poor	≤.30	
Receiver operating characteristic analysis—area under the curve		
Excellent	≥0.90	
Adequate	0.70–0.89	
Poor	<0.70	
Responsiveness		
Sensitivity to change (standardized effect sizes)		
Small	<0.5	
Moderate	0.5–0.8	
Large	≥0.8	
Floor/ceiling effects		
Excellent	No floor/ceiling effects	
Adequate	≤20% of patients attain either the minimum or maximum score	
Poor	>20% of patients attain either the minimum or maximum score	

# Appendix 14 – Publication arising from thesis (reproduced with permission Informa

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RESEARCH PAPER

# Foot and ankle impairments affect balance and mobility in stroke (FAiMiS): the views and experiences of people with stroke

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#### Abstract

Purpose: To explore the nature and impact of foot and ankle impairments on mobility and balance in community-dwelling, chronic stroke survivors. Methods: A qualitative research design using face to face semi-structured, audio recorded interviews. Thirteen community-dwelling stroke survivors, all of whom had self-reported foot and ankle impairments, were interviewed (female n=6, mean age = 67 years, SD = 12 years, mean time since stroke = 4 years, SD = 6 years, right stroke n = 7, left stroke n = 6). A framework analysis approach was used to analyse and interpret transcribed interviews. Results: Three themes emerged: (1) Impact. The influence of foot and ankle impairments on mobility and balance. (2) Standing out. How participants felt they "stood out" because of their impairments and wanted to be normal. (3) Help. The specific help and advice participants received in managing their problems. Conclusions: Foot and ankle impairments such as pain, altered somatosensory input and weakness significantly contribute to problems with community ambulation, balance and fear of falling in people with chronic stroke. Specific foot and ankle impairments may also negatively contribute to perceptions of physical appearance and self-esteem. Therapeutic management approaches within clinical practice appear to focus mostly on the gross performance of the lower limb with little emphasis on the specific assessment or treatment of the foot or ankle.

> Implications for Rehabilitation

· Foot pain, sensory impairments and muscle weakness in the foot and ankle can impact on community ambulation, balance and fear of falling following stroke.

- · Foot and ankle function post-stroke should be routinely assessed and monitored.
- · Clinicians should be aware of the potentially distressing negative perceptions associated with altered gait patterns, footwear and orthotic use.

## Introduction

The desire to regain the ability to walk safely and independently both at home and in the community often underpins the focus of stroke rehabilitation [1,2]. Whilst it is reported that 60-80% of stroke survivors are able to walk independently [3], many have reduced balance [4], walk slower [5], cannot walk as far [6], are more likely to fall [7] and feel less integrated into their respective communities [8]. Unsurprisingly, many stroke survivors capable of independent walking indoors are either unable or lack the confidence to walk unsupervised in their respective communities [9].

In an attempt to address these issues, clinical and research efforts have focussed on gait and the performance of the lower limb. Indeed, lower limb impairment following stroke is

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Keywords

Balance, fear of falls, foot and ankle, mobility, stroke

## History

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considered a greater indicator of participation restriction than upper limb impairment by those experiencing it [10]. However, work has concentrated on the gross performance of the lower limb during gait with little attention given to how foot and ankle impairments contribute to functional decline after stroke.

The foot and ankle complex involves multiple segments and joint mechanisms which strongly influence the interaction between the lower limb and the ground during locomotion and balance [11]. In older people specific foot and ankle impairments have been identified as significant determinants of balance and functional ability [12,13]. Following stroke, foot deformity [14], altered plantar sensory inputs [15], reduced ankle proprioception [16], altered motor control [17], toe clawing [18] and hitch-hikers toe [19] have all been observed, yet identifying how these impairments impact on mobility and balance remains unclear. There is some evidence from quantitative studies demonstrating that reduced strength in the ankle plantarf lexors and ankle joint position sense influences gait velocity [20,21], increased spasticity in the ankle plantarflexors and altered sensory inputs

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contribute to gait asymmetry [22,23], and ankle dorsiflexor activity and altered ankle proprioception are linked with walking endurance [15,24] and balance impairment [25].

Whilst these studies provide some objective evidence of the role the foot and ankle has to play in function and mobility poststroke, they do not enhance our understanding from the patient's perspective. There is growing consensus that the experiences of patients provide invaluable insight into the *real* issues and can help develop complex interventions to facilitate recovery and health [26,27]. Qualitative research studies have highlighted a wide range of issues related to the impact of stroke and the organisation and delivery of services [28] yet the stroke survivor's perspective regarding the nature or impact of foot and ankle impairments on mobility and balance has not been explored.

This qualitative study aimed to explore the views of people with stroke and identify (1) the nature of the foot and ankle impairments they experience, (2) whether and how these may contribute to problems with mobility, balance and falls, (3) whether and how these impairments impact on their life and (4) what healthcare advice and interventions they have received in managing these problems.

#### Methods

An outline interview schedule was developed by the research team based on a review of the literature and discussion with experienced clinicians. In accordance with Paterson and Scott-Findlay's [29] guidelines, three pilot interviews were carried out with stroke survivors which confirmed the interview schedule and procedure were appropriate. These pilot interviews did not highlight any issues with the schedule that required revision and so a further ten face-to-face, semi-structured, audio recorded interviews were then conducted by the same single interviewer (T.G.) using the same schedule. All 13 interviews were included in data analysis. This study was approved by the National Research Ethics Service, North East Committee (2/NE/0416).

#### Sampling and recruitment

Purposive sampling was used to recruit a maximum-variation sample in terms of age, gender, time since stroke, side affected by stroke and general level of function. Participants were recruited from stroke groups in the South West of England and through the South West Stroke Research Network database. To be eligible for inclusion, participants needed to be:  $\geq 18$  years old;  $\geq 3$  months post-stroke (not necessarily their first); report perceived foot and ankle problems as a result of their stroke; able to converse in English at a level considered appropriate to conduct an interview; willing and able to give informed consent and report no pre-stroke foot and ankle impairments as a result of other neurological/ musculoskeletal conditions. Interested potential participants were contacted by telephone or email by the researcher (T.G.) to allow for further explanation and questioning regarding the study and establish whether they met the study inclusion criteria.

#### Data collection

Interviews were arranged at a time and place considered preferable to the participant. Twelve participants were interviewed at home and one at their local community hospital. Informal conversation occurred prior to starting the interview to place the participant at ease and offer the participant an opportunity to ask further questions prior to gaining written consent.

In line with the framework approach an interview schedule was used to guide the conversation (Table 1) and encourage disclosure and elaboration of thoughts and feelings relevant to the Disabil Rehabil, Farly Online: 1-8

#### Table 1. Interview guide.

- 1. Could you tell me about how you have been affected by your stroke?
- 2. Could you tell me how your stroke has affected your foot and ankle?
- Do you feel any of these foot and ankle problems affect how steady you feel on your feet?
- 4. Do you feel these problems affect your walking?
- 5. Could you tell me whether you feel your foot and ankle problems have impacted on any other aspects of your life?
- 6. Could you tell me about any advice or interventions you have been given to help manage the problems with your foot and ankle?

study objectives. Interviews lasted on average 50 min (range 40– 65 min) and on one occasion a third party was present during the interview although did not contribute verbally. A total of 13 interviews were carried out, by which time data saturation had been reached.

#### Data analysis

All but one of the interviews was transcribed verbatim. In one case, expressive dysphasia made transcription difficult and hence, in line with recommendations set out by Lloyd et al. [30] the audio recording and field notes were used for analysis. All data were coded, grouped into sub-themes, summarised into main themes, charted and interpreted using a framework approach as outlined by Ritchie and Spencer [31] utilising software package QSR NVivo 9.2 [32]. Participant names were replaced with pseudonyms to ensure confidentiality but also to maintain an element of personality to each participant.

A framework analysis approach enables both description and interpretation of what is happening in a particular setting with the aim of creating actionable outcomes [31]. It is considered an excellent tool to assess procedures from the perspective of the very people that they affect [33] and has been gaining in popularity as a means of analysing qualitative data derived from healthcare research, because it can be used to manage data and undertake analysis systematically [34]. This enables the researcher to explore data in depth whilst simultaneously maintaining an effective and transparent audit trail, which enhances the rigour of the analytical processes and the credibility of the findings [35].

#### **Ensuring rigour**

Trustworthiness and credibility of the interpretation of the data were optimized through several strategies. Each of the pilot interviews were transcribed in turn, after which analysis and discussion was held by two of the research team (T.G. and J.F.) [36]. A coding reliability check was also completed on the three pilot interviews (T.G. and J.F.) and was deemed acceptable [37]. As further interviews were undertaken, regular meetings between these two researchers allowed de-briefing and ensured decisions could be evaluated and defended [38].

#### Results

Thirteen participants were interviewed. Of these, six were females with a mean age of 66 years 6 months (SD = 12 years, 2 months; range 38–78 years). The mean time since stroke was 4 years 4 months (SD = 6 years 2 months, range 4 months to 20 years). Seven participants had experienced a right stroke, and six a left stroke (Table 2). Levels of mobility ranged from being independently mobile without walking aid through to requiring maximum assistance of one person with all transfers. DOI: 10.3109/09638288.2015.1052888

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Participant	Gender	Age	Time since stroke Years (y) and months (m)	Hemi side	Level of walking ability/use of walking aids	History of falls
Larry	Male	78	10 years 8 months	R	Independent with walking stick	Y
Margaret	Female	70	1 year 1 month	L	Transfers only; quad stick	Y
Neil	Male	72	1 year 6 months	L	Independently mobile indoors; supervision outdoors; walking stick	Y
Barry	Male	70	20 years 1 month	R	Independent with walking stick	Y
Mark	Male	56	5 years	L	Independent no aid	Y
Paul	Male	62	1 year 4 months	R	Independent no aid	Y
Jane	Female	76	1 year 5 months	L	Transfers only; guad stick	Y
Marion	Female	69	6 months	L	Independent with walking stick	Y
Jim	Male	78	4 months	R	Independent no aid	N
Rebecca	Female	38	6 years	L	Independent no aid	Y
Nigel	Male	42	11 months	R	Independent no aid	N
Rose	Female	78	1 year 7 months	R	Independent with walking stick	N
Sandra	Female	76	9 months	R	Independently mobile indoors; supervision outdoors; walking stick	Y

Table 2. Participant demographics (names pseudonymised).

Three main themes were derived from the data, reflecting the underlying objectives of the study. These themes were termed (1) *Impact* which described the nature of impairments and how they contributed to mobility and balance; (2) *Standing out* which described feelings of standing out, perceptions of disability and a desire to be "normal" and (3) *Help* which described the nature and extent of help and advice received.

#### Theme 1: Impact; the nature of impairments and contribution to alterations in mobility and balance

All participants provided descriptions of the nature of the foot and ankle impairments they experienced as a direct result of their stroke. Impairments affected the toes, foot and ankle and included weakness, lack of control, altered sensation, altered tone/spasticity, pain, stiffness and swelling.

All participants believed foot and ankle impairments contributed substantially to difficulties with mobility, balance and falls. Pain (n = 4), tone/spasticity (n = 4), weakness (n = 11), lack of control (n = 10) and impaired sensory inputs (n = 11) were the impairments most commonly associated with mobility difficulties. Participants highlighted the marked impact these had on community mobility:

Cos I've got this lack of feeling there, I'm a bit wary. Especially, if it's rough ground because I have to look down continually to see where I'm walking. Crossing the road is a lottery. I can't look at the traffic and look down at the road at the same time. That is a bit of a problem. I've got to be very, very careful. Barry

Difficulties with lack of volitional motor control and the unpredictable nature of this control at the ankle and foot meant foot placement could also be a lottery, which was reported to increase likelihood of falling:

... I struggle because I don't know which way my foot is going to drop. If it drops flat then I can walk Ok but if it drops sideways, then my ankle rolls over on itself and I'm liable to fall over... Mark

The vital role of the toes in maintaining equilibrium was also reported:

...normally you press down with your toes don't you? I don't think my toes will go down. Cos like your toes grip to stop yourself from falling forward... Margaret Some, however, perceived the lack of control in the toes was not due to weakness, but more to do with the toes "having a mind of their own":

... I didn't even know they [the toes] could do that. So they bunch up, they cramp, so they have moments of calm but they've got a mind of their own. I don't know what causes that. That glamorous spasticity word isn't it? Rebecca

Tone and spasticity was reported by a third of participants (n = 4), its presence being predominantly in the toes and foot, impacting on the role the foot and toes play in maintaining balance:

... All the time I've got tension in the foot, it never feels relaxed. There's so much more tension in whatever that foot has to do. It can't do anything naturally. If that foot is in its clamped up position then it's this balance thing again because I think I'm not using my foot as a base that sort of balances... Paul

Altered sensory inputs were described by all but two participants, with wide variations in both the type and extent of sensory impairments. For example, people described altered feelings of temperature (n = 2), reduced feeling/feedback from the foot/ankle (n = 8), the foot and ankle ''just not feeling right'' (n = 4), through to ''the foot doesn't feel it belongs to me'' (n = 3). Most (n = 10) highlighted the difficulty associated with being unable to accurately discriminate or confidently detect the floor surface and foot position with an increased risk of falls especially on rough or uneven ground:

... it is lack of feeling in the foot and that it doesn't tell me if I am on a flat surface or an inclined surface or tipping my ankle over, I haven't got so much feeling coming back to my brain... Larry

Some people clearly attributed altered sensation with impairments in balance highlighting the inextricable link between sensory and motor function:

... I've got no feeling in the foot so I can't feel, I can't get my balance properly, if that makes sense. You know, when your foot is working properly, you can feel the ball of your foot and your toes, and by using your toes and that, you go push yourself to keep your balance... Mark

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Whereas for others sensory impairment had a clear impact on gait pattern, community ambulation and the increased need for concentration:

...When I put my foot down and I don't get any response, that no feeling comes back that I've got it down and therefore I hesitate to move the other foot forward. When I think about it, it's ok, I can walk in a fairly straight line, but when I get distracted by something else, that's when I stagger... so much so that a policeman stopped me once and smelt my breath...Larry

All participants felt some restriction on where they could go or were cautious and thoughtful about where they could go, directly as a result of their foot and ankle problems. The biggest restriction on mobility, which was mentioned by all but one participant (who was not mobile outdoors), was being able to manage rough/ uneven and unfamiliar terrain:

...I have to be careful where I'm walking... because if it's uneven or you know rough or anything like that. I'm conscious that I'm likely to sort of trip on things because this wretched foot doesn't lift up, very often it doesn't lift. It flops and it drags...Jim

Conversely, the same participant had a very different perspective when it came to walking in a different environment:

I do know that I'm very happy where I know that the surface is flat, say walking through the hospital on Wednesday going to the gym, it's alright. Jim

The presence of pain in the foot and ankle was also highlighted as a problem in a third of respondents (n = 4) with descriptors strongly suggestive of neuropathic pain. For all respondents with pain, it was sometimes sufficient to stop them from walking at all:

...I get pain in my foot more than anywhere. It feels like walking on glass or it's burning. It's the oddest thing. I avoid walking. Rebecca

Increased stiffness through the foot and ankle was associated with increased effort with one participant describing his ankle joint as if it was 'rusted up'':

... it's very stiff and very slow. It's hard work basically to do it [move the foot]. I suppose the joints have rusted up with the stroke... Barry

Whilst swelling was reported in four participants, they did it not relate it to any functional impact, and did not appear to be concerned by its presence:

... My ankle actually swells up quite easily after I've done any exercise. It doesn't seem to affect me. But that's something none of the doctors have ever said that's going to be a problem, they've always sort of said that's to be expected so I've never taken any notice of it and I don't' think that impairs my movement... Barry

#### Theme 2: Standing Out; "I felt like I had three heads"

Most participants described how they felt their foot and ankle impairments made them "stand out" from others. They reported

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feeling very conscious of "being disabled", expressing a desire to "be normal". A number of participants described how acutely aware they had become of their physical appearance to others. This was often manifested by their embarrassment about the type of footwear they had to wear, or the abnormal way they walked as a result of their foot and ankle impairments:

... when I was walking towards someone and my foot would be turning inwards and it looks, well it doesn't look very nice... It's having the confidence in people looking at me and not seeing that I am disabled... Mark

For one participant, it was about wanting to make any orthotic as inconspicuous as possible so she did not appear disabled:

...so hence the orthotic. But I didn't want anything more obvious than this. I've been offered something that will keep it so rigid which is fine if you don't mind looking disabled. Which I do, Rebecca

Whereas for others, wearing footwear out of context created feelings of social unacceptability:

Having to wear trainers with everything makes me feel as if, like a duck out of water you know. I don't feel naturally acceptable in different situations. I went into the hairdressers the other day and they knew that I had had a stroke but I went in with these [trainers] on and he said 'cor crikey, you're alright now you're going out for a run aren't you?' Paul

Concerns around feeling conspicuous and a loss of normality were often related to the type of footwear they had to wear as a consequence of their stroke:

...I don't want shoes that look like they've been made for a purpose. You know I want to wear what everybody else is wearing. I want to fit in. I've never ever wanted to fit in but I suppose with this you do want to fit in. You want to be in the realms of normal because you know that there is an element of abnormality. Rebecca

However, there was a tension between the disadvantages felt about the appearance of orthotics and the functional gains that could be made by wearing them, which often promoted reassurance and confidence:

... with the orthotic I've got now, it stops the foot from turning in and stops it from dropping. So every time I lift my foot, I know it's going to go down flat. So it makes my walking a lot stronger and makes me a lot more confident in my walking. I hardly fall over at all these days... Mark

#### Theme 3: Help; specific advice and interventions received

The overriding sentiment by the majority of participants was that advice and/or interventions had been made available to address their gait and mobility problems although there appears to have been little focus on the foot and ankle. Separating "generic" advice/intervention that addressed stroke impairments *per se* from specific foot and ankle focussed advice/intervention was difficult for most participants whose stroke caused widespread impairments. Input from physiotherapy was received by all but three participants with the predominant focus reported to be on gait re-education and gross performance of the lower DOI: 10.3109/09638288.2015.1052888

limb although there was occasionally some specific foot/ankle advice:

... the thing that I remember most about everything was the heel and toe thing that the physio talked about... and the keeping of a regular stride... rather than dragging this foot along after me... Jim

Some recalled that specific concerns about their foot and ankle function were not addressed:

...Nobody's particularly picked up on the toes scuffing I don't think. They were more concerned about stopping my knee flicking back...Marion

Whereas others chose not to report their concerns to their attending clinician:

... I've never really pointed it out. I haven't really said to anyone "oh look, my toes are curling up, why?" Paul

Five of the 13 had either trialled or were regular users of ankle-foot orthoses (AFO) with the physiotherapist being the main referrer into a specialist orthotic service:

She took me to [the orthotist] and showed him what was happening with the foot and he made me the boot. (APO) Margaret

Only one participant reported being seen by a Podiatrist who:

...showed me my options basically. Do you want this or this?. This will do x-y-z. What do you want it to do?....he said you can have something that keeps your foot very static...a rod up the back of your leg basically which I just couldn't bear...but I wanted something that's subtle... Rebecca

Those that had been issued with off the shelf AFO's by the physiotherapist were reported less successful:

It's supposed to keep my leg square to the shoe. But it doesn't seem to make any difference. Neil

Provision of an AFO made a significant difference to some participants with one participant purchasing the AFO via the internet as the "off the shelf" versions were uncomfortable:

...with the orthotic I've got now, which I bought off the internet, erm it stops the foot from turning in and stops it from dropping. So every time I lift my foot, I know it's going to go down flat. So it makes my walking a lot stronger and makes me a lot more confident in my walking. I hardly fall over at all these days... Mark

Although there were some perceived repercussions of frequent use of the AFO:

The only thing I've found is that my foot is weaker than it was. I think that because I wear the orthotic now, it means my muscles don't move so much so they are a lot weaker than they were... Mark

Interestingly, despite all participants reporting altered sensory input, some very significantly so, none specifically reported any sensory re-education based intervention. Foot and ankle impairment in stroke (FAiMiS) 5

FES was only used with one participant specifically at the foot and ankle although it was reported that this was with limited success:

I was given a FES to wear for my foot. Which when I went to lift my foot it fired a pulse which made my foot straighten out instead of inverting. So it was going down more flat which was good for me, but I just didn't like the FES. I didn't like the feeling of the pulse going through my leg... Mark.

## Discussion

The results of this study provide a unique insight into the type of foot and ankle impairments experienced and how they impact on mobility and balance from the perspective of the stroke survivor. They highlight the wide ranging and significant impact of these impairments on stroke survivor's everyday lives and highlight areas for service development and future research.

The type of impairment participants reported as impacting most on their mobility and balance were, in order of impact, those associated with pain, somatosensory impairment, weakness and lack of volitional control in the foot and toes.

Pain in the foot appeared to have the most profound effect on mobility for some, who chose to entirely avoid walking when pain was present or drastically shorten the time spent on their feet. Descriptors of pain suggest symptoms of central or neuropathic origin rather than mechanical. The average time since stroke (of those four people who reported pain) was 2 years 3 months, suggestive of chronic rather than acute pain. Neuropathic pain syndrome, which is a direct consequence of ischaemic damage, is especially challenging to study because it usually observes an unpredictable latent period, which may be up to 18 months between stroke onset and development of pain or discomfort [39]. Our study suggests that pain can still have a significant impact on mobility many months or even years after formal discharge from stroke services, and because of its central nature, the pain may not follow predictable patterns or time frames. Whilst central and neuropathic pain syndromes may be poorly understood, this study further adds to existing qualitative work which highlights the significant effect of pain on quality of life after stroke [40] and functional independence [41]. The need for clinicians, especially those involved with community-dwelling stroke survivors to be aware of the potential latency and impact of foot pain following stroke, is therefore crucial.

Apparent tactile sensory impairment of the foot and proprioceptive deficits at the ankle were reported equally by participants with some experiencing a combination of these two sensory impairments. Loss of sensory feedback from the foot was reported frequently. Particular concerns included not knowing the position of the foot in space, having a lack of awareness of what it was doing or difficulty discriminating the texture and orientation of the supporting surface. These impairments appeared to lead to difficulties with walking patterns, maintaining balance, adapting to different walking surfaces and gradients, misjudging step heights and co-managing the attentional demands of the environment. This study suggests that mobility and balance are affected by foot and ankle sensory impairments in stroke as has been established in MS [42] and peripheral neuropathies [43]. It further adds to recent qualitative work which highlighted that somatosensory impairments are of concern to stroke survivors, particularly when they return home [44]. The need to investigate the extent and nature of somatosensory impairments of the foot and ankle is clear, as evidence after stroke is largely limited to acute patients [45] and the effect of these impairments is not well understood [46].

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Whilst sensory impairment is suggested as a co-factor in disability and recovery, it is not considered an independent factor when strength or motor performance is included [47]. Lack of automatic and volitional motor control of both toes and ankle due to weakness and spasticity highlighted issues with catching toes during swing phase, lateral ankle instability during stance phase of gait, static standing balance, and multi-directional responses to perturbation and distraction. Worries about tripping, negotiating uneven or rough terrain, crossing the road, walking slowly and an increased fear of falling were common. Such worries have been reported to impact community ambulation and integration, affect quality of life and return to independence. Foot and ankle impairments appear to further contribute to these factors which are commonly reported by patients after stroke [48,49].

Participants conveyed the feeling that their deficits in motor control and sensory awareness could be relatively well managed in predictable, flat and quiet environments with most difficulties arising when the environment became unfamiliar, uneven or busy. Rough ground, busy streets and traffic caused challenges that did not necessarily occur indoors or during clinic-based therapy. These findings support previous research highlighting the role and impact of environmental factors on mobility and disability [50,51] and add credence to a shift in therapeutic focus from clinic-based gait retraining to goal-directed and task specific training within variable environments [52]. They may also part explain why large proportions of independently mobile stroke survivors either cannot or are reluctant to mobilise without supervision in the community [9].

Foot and ankle impairments following stroke were associated with perceptions of standing out, feeling disabled and a loss of "normality". The impact of stroke on survivors is repeatedly described as "loss" in the qualitative literature, with the significance of reduced functional ability being explained in terms of loss of activities, abilities, personal characteristics and independence and a desire to be normal again [28,53]. Within the context of this study, these feelings were predominantly driven by footwear choices (or lack of), the nature of participants' walking pattern as a result of their foot/ankle impairment and the need to wear an AFO. Feelings regarding footwear and the use of an AFO tended to be stronger in the female participants who reported feeling self-conscious because of both the appearance of the AFO and the resultant loss of footwear choice because of the need to accommodate an AFO. The impact of footwear or lack of footwear choice has been established in other non-stroke populations [54] yet despite its importance, footwear advice following stroke is minimal [55]. All of these factors contributed to people feeling self-conscious about their physical appearance which has shown to be a strong predictor of general self-esteem [56]. Low self-esteem following stroke is not uncommon and can influence participation restriction [57,58].

Conversely, whilst some participants reported that the presence of an AFO may reinforce "abnormality" or evoke feelings of disability, the *effect* of wearing one was to "normalise" gait patterns and thereby improve perceived physical appearance. This suggests that the aesthetics of orthotics and adaptive footwear, as well as their therapeutic objective, need to be taken into account when prescribed by health professionals. It emphasises the need for healthcare professionals to be aware of how distressing negative perceptions of others can be for people with stroke.

Our study asked participants to highlight what advice and interventions they had received with respect to their foot and ankle problems. Whilst most had received input from a physiotherapist, the participants reported the focus of that input tended to be generic gait re-education, motor retraining and

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strengthening, in the context of the gross performance of the lower limb. All but two participants reported somatosensory impairments, yet none specifically recalled receiving sensory retraining despite prompting. It appears that, contrary to current recommendations [59] and other qualitative work identifying somatosensory impairments as a concern for patients [44], most stroke rehabilitation remains focussed on motor recovery [44,60]. Furthermore, clinical convention suggests that sensory retraining is more fastidiously administered to sensory impairment of the hand and there is a dearth of evidence applying the learnings from the hand to the foot [23].

Only one participant reported being seen by a podiatrist, regarding the prescription and provision of orthotics. Podiatry services or podiatrists are not considered part of the core multidisciplinary team in the current stroke guidelines [59]. This may offer some explanation as to why, despite its potential importance to people with stroke, few receive advice about foot care or footwear [55]. Only one participant had trialled functional electrical stimulation (FES) for foot drop suggesting its use may be undenutilised, despite recommendations [59] and stroke survivors reporting an overall preference for FES over AFO's [61].

This study has several limitations. First, the participants' willingness to provide information that would satisfy the researcher, who was a physiotherapist, may have led to potential exaggerated and/or inaccurate descriptions. Whilst most participants were informed of the clinical background of the interviewer, it was emphasised at the beginning of the interview that responses would be anonymous and would not affect any current or future clinical care. Second, the majority of interviews were conducted with stroke survivors who were, on average just under 4 years post-stroke and were no longer receiving rehabilitation, so recall of treatments received may have been inaccurate. Third, this study purposively recruited community-dwelling adults with self-reported and stroke-related foot and ankle impairments and therefore reflects the experiences of those with these specific impairments rather than the wider stroke population.

In summary, foot and ankle impairments such as pain, altered somatosensory input and weakness may substantially contribute to problems with community ambulation, balance and fear of falling in people with chronic stroke. Specific foot and ankle impairments may also negatively contribute to perceptions of physical appearance and self-esteem. Therapeutic management approaches within clinical practice appear to focus mostly on the gross performance of the lower limb with little emphasis on the specific assessment or treatment of the foot or ankle.

This first phase of a three-phased research programme has given some insight into the impact and nature of foot and ankle impairments post-stroke, thereby helping to inform assessment and management within the clinical setting. This study will further guide future phases of research which aim to investigate the prevalence of foot and ankle impairments in the wider, community-dwelling stroke population and the relationship between these impairments, mobility and balance.

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#### References

- Bohannon R, Andrews A, Smith M. Rehabilitation goals of patients with hemiplegia. Int J Rehabit Res 1988;11:181–3.
- Lord S, McPherson K, McNaughton H, et al. Community ambulation after stroke: how important and obtainable is it and what measures appear predictive? Arch Phys Med Rehabil 2004:85; 234–9.
- Kelly-Hayes M, Beiser A, Kase C, et al. The influence of gender and age on disability following ischaemic stroke: the Framingham study. J Stroke Cerebrovasc Dis 2003;12:119–26.
   Said C, Goldie P, Patla A. Balance during obstacle crossing
- Said C, Goldie P, Patla A. Balance during obstacle crossing following stroke. Gait Posture 2008;27:23–30.
- Schmid A, Duncan P, Studenski S. Improvements in speed-based gait classifications are meaningful. Stroke 2007;38:2096–100.
   Pohl P, Duncan P, Perera S, et al. Influence of stroke-related
- Pohl P, Duncan P, Perera S, et al. Influence of stroke-related impairments on performance in a 6-minute walk test. J Rehabil Res Dev 2002;39:1–6.
- Mackintosh S, Goldie P, Hill K. Falls incidence and factors associated with falling in older, community-dwelling, chronic stroke survivors 1 year after stroke and matched controls. Aging Clin Exp Res 2005;17:74–81.
- Wood J, Connelly D, Maly M. "Getting back to real living": a qualitative study of the process of community reintegration after stroke. Clin Rehabil 2010;24:1045–56.
- van de Port IG, Kwakkel G, Lindeman E. Community ambulation in patients with chronic stroke: how is it related to gait speed? J Rehabil Med 2008;40:23–7.
- Desrosiers J, Malouin F, Bourbonnais D, et al. Arm and leg impairments and disabilities after stroke rehabilitation: relation to handicap. Clin Rehabil 2003;17:666–73.
- Leardini A, Benedetti MG, Catani F, et al. An anatomically based protocol for the description of foot segment kinematics during gait. Clin Biomech 1999;14:528–36.
- Menz H, Morris M, Lord, S. Foot and ankle characteristics associated with impaired balance and functional ability in older people. J Gerontol A Biol Sci Med 2005;60:1547–52.
- Spink MJ, Fotoohabadi M, Wee E, et al. Foot and ankle strength, range of motion, posture, and deformity are associated with balance and functional ability in older adults. Arch Phys Med Rehabil 2011; 92:68–75.
- Forghany S, Tyson S, Nester, C, et al. Foot posture after stroke: frequency, nature and clinical significance. Clin Rehabil 2011;25: 1050–5.
- Connell L, Lincoln N, Radford K. Somatosensory impairment after stroke: frequency of different deficits and their recovery. Clin Rehabil 2008;22:758–67.
- 16. Lee M-J, Kilbreath S, Refshauge K. Movement detection at the
- ankle following stroke is poor. Aust J Physiol 2005;51:19-24.
  Lamontagne A, Malouin F, Richards C, Dumas F. Mechanisms of disturbed motor control in ankle weakness during gait after stroke. Gait Posture 2002:15:244-55
- Laurent G, Valentini F, Loiseau K, et al. Claw toes in hemiplegic patients after stroke. Ann Phys Rehabil Med 2010;53:77–85.
- Yelnik A, Colle F, Bonan I, et al. Disabling overactivity of the extensor hallucis longus after stroke: clinical expression and efficacy of botulinum toxin type A. Arch Phys Med Rehabil 2003;84:147–9.
   Milo M-H, Nadeau S, Gravel D, Bourbonnais D. Effect of increases
- Milo M-H, Nadeau S, Gravel D, Bourbonnais D. Effect of increases in plantarflexor and hip flexor muscle strength on the levels of effort during gait in individuals with hemiparesis. Clin Biomech 2008;23: 415–23.
- Lin S-I. Motor function and joint position sense in relation to gait performance in chronic stroke patients. Arch Phys Med Rehabil 2005;86:197–203.
- Hsu A, Tang P, Jan M. Analysis of impairments influencing gait velocity and asymmetry of hemiplegic patients after mild to moderate stroke. Arch Phys Med Rehabil 2003;84:1185–93.
- Wutzke C, Mercer V, Lewek M. Influence of lower extremity sensory function on locomotor adaptation following stroke. Top Stroke Rehabil 2013;20:233–40.
- Ng S-S, Hui-Chan C. Contribution of ankle dorsiflexor strength to walking endurance in people with spastic hemiplegia after stroke. Arch Phys Med Rehabil 2012;93:1046–51.
- Tyson S, Chillala J, Hanley M, et al. Balance disability after stroke. Phys Ther 2006;86:30–8.

- Foot and ankle impairment in stroke (FAiMiS) 7
- Campbell M, Fitzpatrick R, Haines A, et al. Framework for design and evaluation of complex interventions to improve health. BMJ 2000;321:694–6.
- Burton C. Living with stroke: a phenomenological study. J Adv Nurs 2000;32:301-9.
   McKevitt C, Redfern J, Mold F, Wolfe C. Qualitative studies of
- McKevitt C, Redfern J, Mold F, Wolfe C. Qualitative studies of stroke: a systematic review. Stroke 2004;35:1499–505.
   Paterson B, Scott-Findlay S. Critical issues in interviewing
- people with traumatic brain injury. Qual Health Res 2002;12: 399-409.
- Lloyd V, Gatherer A, Kalsy S. Conducting qualitative interview research with people with expressive language difficulties. Qual Health Res 2006;16:1386–404.
- Ritchie J, Spencer L. Qualitative data analysis for applied policy research. In: Bryman A, Burgess R, eds. Analysing qualitative data. London: Routledge; 1993:173–94.
- QSR International. NVivo 9.2. 2013. Available from: www.qsrinternational.com.
   Srivastava A, Thomson S. Framework analysis: a qualitative
- Srivasava A, Induson S, Franework analysis: a quantative methodology for applied policy research. JOAAG 2009;4:72–9.
   Smith J, Firth J. Qualitative data analysis: the framework approach.
- Nurs Researcher 2011;18:52–62.
  Ritchie J. Lewis J. eds. Oualitative research practice: a guide for
- Ritchie J, Lewis J, eds. Qualitative research practice: a guide for social science students and researchers. London: Sage Publications; 2003.
- Richards L, ed. Working with the data: handling qualitative data. London: Sage Publications; 2005.
- Miles M, Huberman A. Early steps in analysis. An expanded sourcebook: qualitative data analysis. 2nd ed. London: Sage Publications; 1994.
- Creswell J, ed. Qualitative procedures. In: Research design: qualitative, quantitative and mixed methods approaches. 3rd ed. Thousand Oaks (CA): SAGE Publications 2009:173–201.
- Andersen G, Vestergaard K, Ingeman-Nielsen M, Jensen T. Incidence of central post-stroke pain. Pain 1995;61:187–93.
- Jönsson A, Lindgren I, Hallström B, et al. Prevalence and intensity of pain after stroke: a population based study focusing on patients' perspectives. J Neurol Neurosurg Psychiatr 2006;77:590–5.
   O'Donnell M, Diener H-C, Sacco R, et al. Chronic pain syndromes
- O'Donnell M, Diener H-C, Sacco R, et al. Chronic pain syndromes after ischemic stroke: PRoFESS trial. Stroke 2013;44:1238–43.
- Cattaneo D, Jonsdottir J. Sensory impairments in quiet standing in subjects with multiple sclerosis. Multiple Sclerosis 2009;15: 59–67.
- Courtemanche R, Teasdale N, Boucher P, et al. Gait problems in diabetic neuropathic patients. Arch Phys Med Rehabil 1996;77: 849–55.
- Connell L, McMahon N, Adams N. Stroke survivors' experiences of somatosensory impairment after stroke: an interpretative phenomenological analysis. Physiotherapy 2014;100:150–5.
- Tyson S, Hanley M, Chillala J, et al. Sensory loss in hospital admitted people with stroke: characteristics, associated factors, and relationship with function. Neurorehab Neur Rep 2008;22:166–72.
- Kalra L. Stroke rehabilitation: old chestnuts and new insights. Stroke 2009;41:e88–90.
- Feys H, de Weerdt W, Nuyens G, et al. Predicting motor recovery of the upper limb after stroke rehabilitation: value of a clinical examination. Physiother Res Int 2000;5:1–18.
- Moeller D, Carpenter C. Factors affecting quality of life for people who have experienced a stroke. Int J Ther Rehabil 2013;20:207–16.
- Wood J, Connelly D, Maly M. 'Getting back to real living': a qualitative study of the process of community reintegration after stroke. Clin Rehabil 2010;24:1045–56.
- Lord S, Rochester L, Weatherall M, et al. The effect of environment and task on gait parameters after stroke: a randomized comparison of measurement conditions. Arch Phys Med Rehabil 2006;87: 967–73.
- Shumway-Cook A, Patla A, Stewart A, et al. Environmental demands associated with community mobility in older adults with and without mobility disabilities. Phys Ther 2002;82:670–81.
- Park H-J, Oh D-W, Kim S-Y, Choi J-D. Effectiveness of communitybased ambulation training for walking function of post-stroke hemiparesis: a randomized controlled pilot trial. Clin Rehabil 2011; 25:451–9.
- Grose J, Freeman J, Skirton, H. Value of a confidant relationship in psychosocial care of people with multiple sclerosis. Int J MS Care 2012;14:115–22.

## 8 T. Gorst et al.

- 54. Naidoo S, Anderson S, Mills J, et al. "I could cry, the amount of Nadoo S, Anderson S, Milis J, et al. 1 could cry, the amount of shoes I can't get into'': a qualitative exploration of the factors that influence retail footwear selection in women with rheumatoid arthritis. J Foot Ankle Res 2011;4:21–9.
   Ng H, McGinley J, Jolley D, et al. Effects of footwear on gait and balance in people recovering from stroke. Age Ageing 2010;39: foot to
- 507-10.
- 56. Howes H, Edwards S, Benton D. Male body image following Andre S. M. Barkards, S. Bellour D. Male cody Image informing acquired brain injury. Brain Inj 2005;19:135–47.
   Ahuja S, Clark S, Morahan E, et al. The journey to recovery:
- experiences and perceptions of individuals following stroke. NZ J Phys 2013;41:36-43.

Disabil Rehabil, Early Online: 1-8

- 58. Chau J, Thompson D, Twinn S, et al. Determinants of participation restriction among community dwelling stroke survivors: a path analysis. BMC Neurol 2009;9:49.
- analysis. BMC Neurol 2009;2949.
  Intercollegiate Stroke Working Party. National clinical guideline for stroke. 4th ed. London: Royal College of Physicians; 2012.
  Galvin R, Cusack T, Stokes E. Physiotherapy after stroke in Ireland: a qualitative insight into the patients' and physiotherapists' experi-ulation of the Physician Science 2020. ence. Int J Rehabil Res 2009;32:238-44.
- Bulley C, Shield J, Wilkie K, Salisbury L. User experiences, preferences and choices relating to functional electrical stimulation and ankle foot orthoses for foot-drop after stroke. Physiotherapy 2011;97:226-33.

## 8.0. References

Aarons GA, Hurlburt M, Horwitz SM. Advancing a conceptual model of evidence-based practice implementation in child welfare. *Administration and Policy in Mental Health and Mental Health Services Research*. 2011; 38:4–23

Abboud R. Relevant foot biomechanics *Orthopaedics and Trauma* 2002; 16(3):165–179

Acar, M. & Karatas, G. K. 2010. The effect of arm sling on balance in patients with hemiplegia. *Gait Posture* 2010; 32(4): 641-644

Ackerley R, Borich M, Oddo C, Ionta S. Insights and Perspectives on Sensory-Motor Integration and Rehabilitation. *Multisensory Research* 2016. DOI:10.1163/22134808-00002530

Ackerley, R., Hassan, E., Curran, A., Wessberg, J., Olausson, H., McGlone, F. An fMRI study on cortical responses during active self-touch and passive touch from others. *Front. Behav. Neurosci.* 2012; 6, 51

Ackerley, R., Kavounoudias, A., The role of tactile afference in shaping motor behaviour and implications for prosthetic innovation. *Neuropsychologia* 2015

Adamson, J., Beswick, A. and Ebrahim, S. Stroke and Disability. *Journal of Stroke and Cerebrovascular Diseases* 2004 13(4);171-177

Ahuja S, Clark S, Morahan E, et al The journey to recovery: experiences and perceptions of individuals following stroke. *NZ J Phys* 2013; 41(1): 36-43

Allen JL, Kautz SA, Neptune RR. Step length asymmetry is representative of compensatory mechanisms used in post-stroke hemiparetic walking. *Gait Posture*. 2011;33(4):538-543.

Amaral D. The functional organization of perception and movement. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. p. 356-69 Alexander LD, Black SE, Patterson KK, Gao F, Danells CJ, McIlroy WE Association between gait asymmetry and brain lesion location in stroke patients. *Stroke*. 2009;40(2):537-44.

Alfuth, M., & Rosenbaum, D. (2012). Effects of changes in plantar sensory feedback on human gait characteristics: A systematic review. *Footwear Science*, 4(1), 1-22.

Anderson EK. Sensory impairments in hemiplegia. *Pract* Otorhinolaryngol (Basel). 1971;33(2):293-297.

Andersen G, Vestergaard K, Ingeman-Nielsen M, Jensen T. Incidence of central poststroke pain. *Pain.* 1995; 61: 187–193

Andresen EM. Criteria for assessing the tools of disability outcomes research. Arch *Phys Med Rehabil*. 2000;81:S15-S20.

Andersson O, & Grillner S Peripheral control of the cat's step cycle. II. Entrainment of the central pattern generators for locomotion by sinusoidal hip movements during "fictive locomotion". *Acta Physiol Scand.* 1983; 118: 229–239

Balasubramanian C, Bowden M, Neptune R, Kautz S. Relationship Between Step Length Asymmetry and Walking Performance in Subjects With Chronic Hemiparesis Arch Phys Med Rehabil. 2007 ; 88; 43-49

Bamford J, Sandercock P, Dennis, M et al Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet*; 1991 337(8756):1521-6

Barker-Collo S, Feigin VL, Parag V, Lawes CMM, Senior H. Auckland Stroke Outcomes Study Part 2: cognition and functional outcomes 5 years post stroke. *Neurology* 2010;75: 1608–18.

Bartesaghi M. Editorial. *Qualitative Research in Medicine & Healthcare* 2017; volume 1:i-ii

Batchelor F, Mackintosh S, Said C, Hill K. Falls after stroke. *Int J Stroke*. 2012; 7: 482–490

Behrmann, M., Geng, J. J., & Shomstein, S.. Parietal cortex and attention. *Current Opinion in Neurobiology*, 2004;14(2): 212-217

Belgen B, Beninato M, Sullivan PE, Narielwalla K. The association of balance capacity and falls self-efficacy with history of falling in community-dwelling people with chronic stroke. *Arch Phys Med Rehabil* 2006; 87:554–61.

Bensmaia S, Hollins M (2003): The vibrations of texture. Somatosens Mot Res 20:33-43

Bergmann Tiest WM (2010) Tactual perception of material properties. *Vision Res* 50(24):2775–2782

Bergmann Tiest W & Kappers A. Cues for Haptic perception of compliance. *IEEE Transactions on Haptics* 2010;2(4): 189-199

Berryhill, M. E., & Olson, I. R. (2008). Is the posterior parietal lobe involved in working memory retrieval? Evidence from patients with bilateral parietal lobe damage. *Neuropsychologia*, 46(7), 1767-1774.

Bernardi N, Darainy M, & Ostry D. Somatosensory Contribution to the Initial Stages of Human Motor Learning. *J Neurosci.*, 2015;35(42):14316–14326

Bi J. Sensory Discrimination Tests and Measurements: Statistical Principles, Procedures and Tables. 2006. Blackwell Publishing

Bing R. *Compendium of Regional Diagnosis in Affectations of the Brain and Spinal Cord*. 3rd Ed. St. Louis: F.S. Arnold; 1929

Bird T, Choi S, Goodman L, Schmalbrock P, Nichols-Larsen D. Sensorimotor Training Induced Neural Reorganization After Stroke: A Case Series. *J Neurol Phys Ther*. 2013; 37(1): 27–36

Bladh S., Nilson M., Hriz G-M et al. P Psychometric performance of a generic walking scale (Walk-12G) in multiple sclerosis and Parkinson's disease *J Neurol* 2012; 259:729–738

Blake DT, Hsiao SS, Johnson KO. Neural coding mechanisms in tactile pattern recognition: The relative contributions of slowly and rapidly adapting mechanoreceptors to perceived roughness. *J Neurosci* 1997 ;17(19):7480–7489.

Blanchard C, Roll R, Roll JP, Kavounoudias A. Combined contribution of tactile and proprioceptive feedback to hand movement perception. *Brain Res.* 2011 25; 1382 :219-29.

Bland M. *An introduction to medical statistics*. 4th edition. 2015. Oxford; Oxford University Press.

Bland M Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1: 307-310.

Blennerhassett JM, Dite W, Ramage ER, Richmond ME. Changes in balance and walking from stroke rehabilitation to the community: a follow-up observational study. *Arch Phys Med Rehabil* 2012;93:1782-7.

Blum L & Korner-Bitensky N. Usefulness of the Berg Balance Scale in stroke rehabilitation: a systematic review. *Phys Ther* 2008;88(5) 559-566

Bohannon RW, Andrews AW, Thomas MW. Walking speed: reference values and correlates for older adults. *J Orthop Sports Phys Ther*. 1996;24(2):86-90

Bohannon R, Andrews A, Smith M. Rehabilitation goals of patients with hemiplegia. *Int J Rehabit Res* 1988;11:181-183

Bonita R, Beaglehole R. "Modification of Rankin Scale: Recovery of motor function after stroke." *Stroke* 1988 Dec; 19(12): 1497-1500

Boisgontier MP, Olivier I, Chenu O, Nougier V. Presbypropria: the effects of physiological ageing on proprioceptive control. *Age (Dordr)* 2011.

Bonan, I.V., et al., Early post-stroke period: A privileged time for sensory re-weighting? *J Rehabil Med*, 2015. 47(6): p. 516-22. Bonan I, Colle FM, Guichard JP, Viacut E, Eisenfisz M, Huy TB, et al. Reliance on visual information after stroke. Part I: Balance on Dynamic Posturography. *Arch Phys Med Rehabil.* 2004;85:268-73

Bonan I, Derighetti F, Gellez-Leman, M et al. Visual dependence after recent stroke. Ann Readpt Med Phys 2006; 49:166-71

Bonan, I., et al., Sensory reweighting in controls and stroke patients. *Clin Neurophysiol*, 2013. 124(4): p. 713-22.

Borich M, Brodie S, Gray W, Ionta S, Boyd L. Understanding the role of the primary somatosensory cortex: Opportunities for rehabilitation *Neuropsychologia* 2015;79:246–255

Borstad A & Nichols-Larsen D. Assessing and Treating Higher Level Somatosensory Impairments Post Stroke. *Topics in Stroke Rehabilitation* 2014; 21(4): 290-295

Borstad A, Schmalbrock P, Choi S, Nichols-Larsen D. Neural correlates supporting sensory discrimination after left hemisphere stroke. *Brain Research* 2012;1460: 78–87

Bosco G & Poppele R. Proprioception From a Spinocerebellar Perspective *Physiological Reviews* 2001; 81(2):539-568

Boulton AJ, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, et al. (2005). Diabetic neuropathies: a statement by the American Diabetes Association. *Diabetes Care*, 28: 956-962

Bourgeon S, Dépeault A, Meftah E-M, Chapman E. Tactile texture signals in primate primary somatosensory cortex and their relation to subjective roughness intensity *J Neurophysiol* 2016; 115: 1767–1785,

Bowen C, Ashburn A, Cole et al. A survey exploring self-reported indoor and outdoor footwear habits, foot problems and fall status in people with stroke and Parkinson's. *Journal of Foot and Ankle Research* 2016; 9:39

392

Bowden M, Balasubramanian C, Behrman A et al. Validation of a Speed-Based Classification System Using Quantitative Measures of Walking Performance Post-Stroke. *Neurorehabil Neural Repair*. 2008 ; 22(6): 672–675.

Bowden J & McNulty P, Age-related changes in cutaneous sensation in the healthy human hand. *Age*, 2013:35; 1077-1089.

Bradford J, Lukos J, & Ferris D. Electrocortical activity distinguishes between uphill and level walking in humans. *J Neurophysiol* 2016; 115:958-966

Bramble D & Lieberman D. Endurance running and the evolution of Homo. *Nature* 2004; 432: 345-352

Brindle T, Lebiedowska M, Miller J, Stanhope S. The influence of ankle joint movement on knee joint kinesthesia at various movement velocities *Scand J Med Sci Sports* 2010: 20: 262–267

Bringoux L, Scotto DiCesare C, Borel L, MacalusoT and Sarlegna FR Do Visual and Vestibular Inputs Compensate for Somatosensory Loss in the Perception of Spatial Orientation? Insights from a Deafferented Patient. *Front. Hum.Neurosci*.2016 10:181.

Brunnstrom S. Movement therapy in hemiplegia. New York: Harper & Row; 1970.

Bulley C, Shiels J, Wilkie K, and & Salisbury L. User experiences, preferences and choices relating to functional electrical stimulation and ankle foot orthoses for footdrop after stroke. *Physiotherapy* 2011; 97(3): 226–33.

Burdett R. Forces predicted at the ankle during running. *Med Sci Sports Exerc* 1981; 14: 308e16.

Burnard P., Gill P., Stewart K., et al. Analysing and presenting qualitative data. *British Dental Journal* 2008; 204: 429-432

Burton C. Living with stroke: a phenomenological study. J Adv Nurs 2000; 32(2): 301-9.

Busse M & Tyson S. How many body locations need to be tested when assessing sensation after stroke? An investigation of redundancy in the Rivermead Assessment of Somatosensory Performance. *Clinical Rehabilitation* 2009; 23: 91–95

Butler AA, Lord SR, Taylor JL, Fitzpatrick RC. Ability versus hazard: risk-taking and falls in older people. *Gerontol A Biol Sci Med Sci*. 2015 May;70(5):628-34.

Byl N, Roderick J, Mohamed O, Hanny M, Kotler J, Smith A, Tang M, Abrams G. Effectiveness of sensory and motor rehabilitation of the upper limb following the principles of neuroplasticity: patients stable poststroke. *Neurorehabil Neural Repair* 2003;17:176-191

Byl NN, Pitsch EA, Abrams GM. Functional outcomes can vary by dose: learning-based sensorimotor training for patients stable poststroke. *Neurorehabil Neural Repair.* 2008; 22(5):494

Callaghan B, Kerber K, Langa KM, Banerjee M, Rodgers A, McCammon R, et al. (2015). Longitudinal patient-oriented outcomes in neuropathy: Importance of early detection and falls. *Neurology*, 85: 71-79

Campbell N, Murray E, Darbyshire J, et al. Designing and evaluating complex interventions to improve health care. *British Medical Journal* 2007; 334:455-459.

Carey LM, Matyas TA, Oke LE. Evaluation of impaired fingertip texture discrimination and wrist position sense in patients affected by stroke: comparison of clinical and new quantitative measures. J Hand Ther 2002; 15: 71–82.

Carey L & Matyas T. Frequency of Discriminative Sensory Loss in the Hand after Stroke in a Rehabilitation Setting. *J Rehabil Med* 2011; 43: 257–263

Carey L & Matyas T. Training of Somatosensory Discrimination After Stroke: Facilitation of Stimulus Generalization. *Am J Phys Med Rehabil.* 2005;84:428-442.

Carey L, Macdonell R & Matyas T. SENSe: Study of the Effectiveness of Neurorehabilitation on Sensation: A Randomized Controlled Trial. *Neurorehabil Neural Repair* 2011; 25(4): 304–313

Carey, L. Somatosensory loss after stroke. Crit Rev Phys Rehabil Med 1995;7:51-91

Carey LM, Oke LE and Matyas TA. Impaired limb position sense after stroke: A quantitative test for clinical use. *Arch Phys Med Rehabil* 1996; 77: 1271–78.

Carey LM, Oke LE and Matyas T. Impaired touch discrimination after stroke: a quantitative test. *J Neuro Rehab* 1997; 11: 219–32.

Carey, L.M., Abbott, D.F., Puce, A., Seitz, R.J., Donnan, G.A. Same intervention-Different reorganisation: The impact of lesion location on training-facilitated somatosensory recovery after stroke. *Neurorehabilitation and Neural Repair* 2016; 1– 13

Carey L, Abbott D, Harvey M, Puce A, Seitz R, Donnan G. Relationship Between Touch Impairment and Brain Activation After Lesions of Subcortical and Cortical Somatosensory Regions. *Neurorehabilitation and Neural Repair* 2011; 25(5): 443–457

Carpenter M & Bloem B. Postural control in Parkinson patients: A proprioceptive problem? Experimental *Neurology* 227 (2011) 26–30

Carpenter C, Suto M. *Qualitative Research for Occupational Therapists and Physical Therapists: A Practical Guide*. Oxford: Blackwell Publishing, 2008.

Carroll M, Joyce W, Brenton-Rule A, Dalbeth N, and Rome K. Assessment of foot and ankle muscle strength using hand held dynamometry in patients with established rheumatoid arthritis. *Journal of Foot and Ankle Research* 2013, 6:10

Castelloe E. Finding myself in Medicine. Qualit Res Med Healthc 2017;1:6301

Cattaneo D and Jonsdottir J. Sensory impairments in quiet standing in subjects with multiple sclerosis. *Multiple Sclerosis* 2009; 15(1): 59–67.

Chan B, Marshall L, Winters K et al. Incident Fall Risk and Physical Activity and Physical Performance among Older Men: The Osteoporotic Fractures in Men Study. *Am J Epidemiol* 2006; 165 (6): 696-703.

Chartered Society of Physiotherapy. Core standards of physiotherapy practice. London: Chartered Society of Physiotherapy, 2005.

Chau J, Thompson D, Twinn S, et al. Determinants of participation restriction among community dwelling stroke survivors: A path analysis. *BMC Neurology* 2009; 9:49

Chisholm A, Domingo A, Jeyasurya J, and Lam T. Quantification of Lower Extremity Kinesthesia Deficits Using a Robotic Exoskeleton in People with a Spinal Cord Injury. *Neurorehabilitation and Neural Repair* 2016, 30(3) 199–208

Chien JH, Eikema, D-J, Mukherjee M & Stergiou N. Locomotor sensory organisation test: a novel paradigm for the assessment of sensory contributions in gait. *Ann Biomed Eng.* 2014; 42(12): 2512–2523.

Clark N, Roijezon U, Treleaven J. Proprioception in musculoskeletal rehabilitation. Part 2: Clinical assessment and intervention *Manual Therapy* 2015 20: 378-387

Cohen J. (1988). Statistical Power Analysis for the Behavioral Sciences. New York, NY: Routledge Academic

College of Occupational Therapists. Professional standards for occupational therapy practice. London: COT, 2007.

Collins S, Visscher P, De Vet HC, Zuurmond WW, Perez RS. Reliability of the Semmes Weinstein Monofilaments to measure cutaneous sensibility in the feet of healthy subjects. *Disabil Rehabil*. 2010;32: 2019–2027.

Collings R, Paton J, Chockalingam N, Gorst T, Marsden J. Effects of the site and extent of plantar cutaneous stimulation on dynamic balance and muscle activity while walking. *The Foot* 2015; 25(3):159-163

Connell L. (2007) *Sensory Impairment and recovery After Stroke*. PhD thesis, University of Nottingham.

Connell, L. Lincoln, N., and Radford, K. Somatosensory impairment after stroke: frequency of different deficits and their recovery. *Clin Rehabil* 2008; 22(8): 758–67.

Connell, L & Tyson, S. Measures of sensation in neurological conditions; a systematic review. *Clin Rehabil* 2012; 26: 68

Connell L, McMahon N, and Adams N. Stroke survivors' experiences of somatosensory impairment after stroke: An Interpretative Phenomenological Analysis. *Physiotherapy* 2014; 100(2):150-5

Connor CE, Johnson KO. Neural coding of tactile texture: Comparison of spatial and temporal mechanisms for roughness perception. *J Neurosci* 1992; 12(9):3414–3426

Conway, B.A., Hultborn, H. & Kiehn, O. Proprioceptive input resets central locomotor rhythm in the spinal cat *Exp Brain Res* (1987) 68: 643.

Courtemanche, R. Teasdale N, Boucher P, et al. Gait problems in diabetic neuropathic patients. *Arch Phys Med Rehabil* 1996; 77(9): 849-855

Cowan, N. Attention and memory: an integrated framework. Oxford: Oxford University Press 1995

Craig A, Strauss M, Daniller A et al. Foot Sensation Testing in the Patient With Diabetes: Introduction of the Quick & Easy Assessment Tool *WOUNDS*. 2014;26(8):221-231.

Creswell J. Qualitative procedures In: Research Design: Qualitative, Quantitative and Mixed Methods Approaches (3rd edition). USA: SAGE Publications 2009

Cresswell, JW. & Plano Clark, VL. *Designing and conducting mixed method research*. 2<sup>nd</sup> Edition 2011. Sage; Thousand Oaks, CA

Crichton S, Bray B, McKevitt C, Rudd A & Wolfe C, et al. J Patient outcomes up to 15 years after stroke: survival, disability, quality of life, cognition and mental health. *Neurol Neurosurg Psychiatry* 2016;87:1091–1098

Cronin N, Ishikawa M, Grey M, et al. Mechanical and neural stretch responses of the human soleus muscle at different walking speeds *J Physiol* 2009; 587; 13:3375–3382

Dannenbaum RM, Michaelsen SM, Desrosiers J and Levin MF. Development and validation of two new sensory tests of the hand for patients with stroke. *Clin Rehabil* 2002; 16: 630–39.

de Jong A, Kilbreath SL, Refshauge KM, Adams R. Performance in different proprioceptive tests does not correlate in ankles with recurrent sprain. *Arch Phys Med Rehabil* 2005;**86**:2101–5.

Delbaere K, Close J, Mikolaizak S, Sachdev P, Brodaty H, Lord S. The Falls Efficacy Scale International (FES-I). A comprehensive longitudinal validation study. *Age Ageing* 2010; 39 (2): 210-216

Demeurisse. G, Demol. O, Robaye. E. Motor evaluation in vascular hemiplegia. *Eur Neurol* 1980; 19: 382–89

Den Otter AR, Geurts AC, de Haart M, Mulder T, Duysens J. Step characteristics during obstacle avoidance in hemiplegic stroke. *Exp Brain Res* 2005; **161:**180–92.

Department of Health (2008) *High quality care for all–NHS Next Stage Review Final Report.* Department of Health, UK

Deshpande N, Metter EJ, Ferrucci L. et al. Validity of clinically derived Cumulative Somatosensory Impairment Index. *Arch Phys Med Rehabil* 2010;91:226-32.

Deshpande N, Metter EJ, Ferrucci L et al. Association of Lower Limb Cutaneous Sensitivity with Gait Speed in the Elderly: The Health ABC Study. *Am J Phys Med Rehabil*. 2008; 87(11): 921–928

Deshpande N, Connelly D, Culham E, Costigan P. Reliability and Validity of Ankle Proprioceptive Measures. *Arch Phys Med Rehabil* 2003; 84; 883-889

Desrosiers J, Malouin F, Bourbonnais D, et al. Arm and leg impairments and disabilities after stroke rehabilitation: relation to handicap. *Clin Rehabil* 2003; 17(6): 666–673.

Dimitrijevic, M.R., Gerasimenko, Y., and Pinter, M.M. (1998). Evidence for a spinal central pattern generator in humans. *Ann.N.Y. Acad. Sci.* 860, 360–376

Dietz V: Interaction between central programs and afferent input in the control of posture and locomotion. *Journal of biomechanics* 1996, 29:841-844

Dixon J, Gamesby H, Robinson J, Hodgson D, Hatton AL, et al. (2012) The effect of textured insoles on gait in people with multiple sclerosis: An exploratory study. *Physiother Res Int* 17: 121–122.

Dixon-Woods M, Agarwal S, Young B, Jones D, Sutton A. *Integrative approaches to qualitative and quantitative evidence*. London: 2004.

Domingo A, Lam T. Reliability and validity of using the Lokomat to assess lower limb joint position sense in people with incomplete spinal cord injury. *J Neuroeng Rehabil*. 2014;11:167.

Donaghy A, DeMott T, Allett L et al. Accuracy of clinical techniques for evaluating lower limb sensorimotor function associated with increased fall risk. *PM R* 2016; 8:331-339

Doros G and Lew R. Design Based on Intra-Class Correlation Coefficients. American *Journal of Biostatistics* 2010;1 (1): 1-8,

Doyle S, Bennett S, Fasoli SE, McKenna KT. Interventions for sensory impairment in the upper limb after stroke. *Cochrane Database of Systematic Reviews* 2010, Issue 6. Art. No.: CD006331.

Duclos, N.C., et al., Hemispheric specificity for proprioception: Postural control of standing following right or left hemisphere damage during ankle tendon vibration. *Brain Res*, 2015. 1625: p. 159-70.

Dukelow S, Herter T, Moore K, Demers M, Glasgow J, Bagg S, et al. Quantitative assessment of limb position sense following stroke. *Neurorehabil Neural Repair* 2010; 24: 178–87.

Duncan PW, Studenski S, Chandler J et al. Functional reach: predictive validity in a sample of elderly male veterans. *J Gerontol*. 1992;47(3):M93-8.

Dunn, W., Griffith, J. W., Sabata, D., et al. Measuring change in somatosensation across the lifespan. *American Journal of Occupational Therapy*, 2015; 69 (3):1-9

Durcan S, Flavin E, Horgan F. Factors associated with community ambulation in chronic stroke, *Disability and Rehabilitation* 2016; 38(3): 245-249

Duysens J, Pearson KG (1980) Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Res 187*: 321–332

Eckstrand E, Lexell J, & Brogardh C. Test-retest reliability of the Shape/Texture Identification test in people with chronic stroke. *Clinical Rehabilitation* 2016;30(11):1120-1127

Eek E and Engardt M. Assessment of the perceptual threshold of touch (PTT) with highfrequency transcutaneous electric nerve stimulation (Hf/TENS) in elderly patients with stroke: a reliability study. *Clin Rehabil* 2003; 17: 825–34.

Elangovan N, Herrmann A, Konczak J. Assessing proprioceptive function: evaluating joint position matching methods against psychophysical thresholds. *Phys Ther*. 2014;94:553–561.

Engen, T. Psychophysics: Discrimination and Detection. In: Kling J, Riggs L eds. Woodworth and Schlosbergs experimental psychology. Rev. ed. New York:Holt, Rinehart & Winston, 1971:11-46

Era P, Sainio P, Koskinen S, Haavisto P, Vaara M, Aromaa A. Postural balance in a random sample of 7,979 subjects aged 30 years and over. *Gerontology* 2006;52(4):204–13.

Fallon JB, Bent LR, McNulty PA, et al. Evidence for strong synaptic coupling between single tactile afferents from the sole of the foot and motoneurons supplying leg muscles. *J Neurophysiol*. 2005; 94:3795–804.

Fawcett A (2007) *Principles of assessment and outcome measurement for Occuptaional therapists and physiotherapists: Theory, skills and application*. Wiley & Sons: Chichester Feigin V, Forouzanfar M, Krishnamurthi R, et al. Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) and the GBD Stroke Experts Group. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *Lancet* 2014;383:245–54

Feng, Y., Schlosser, F. J., Sumpio, B. E., The Semmes Weinstein monofilament examination as a screening tool for diabetic peripheral neuropathy, *Journal of Vascular Surgery*, 2009; 50(3):675-682.

Ferrucci L, Bandinelli S, Benvenuti E, et al. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. *J Am Geriatr Soc* 2000;48:1618-25.

Feys H, de Weerdt W, Nuyens G, et al. Predicting motor recovery of the upper limb after stroke rehabilitation: value of a clinical examination. *Physiother Res Int* 2000; 5: 1-18.

Fitzpatrick R, Taylor, J & McCLoskey D. Ankle stiffness of standing humans in response to imperceptible perturbation: reflex and task-dependent components. *Journal of Physiology* 1992; 454, 533–547.

Flansbjer, U. B., Holmback, A. M., et al. (2005). "Reliability of gait performance tests in men and women with hemiparesis after stroke." *J Rehabil Med* 37(2): 75-82

Floel, A, Nagorsen, U, Werhahn K et al. Influence of Somatosensory Input on Motor Function in Patients with Chronic Stroke. *Annals of Neurology* 2004; 56( 2) ; 206-212

Forghany S, Tyson S, Nester, C, et al The effect of stroke on foot biomechanics; underlying mechanisms and the functional consequences *Journal of Foot and Ankle Research* 2014, 7(Suppl 1):A18

Forghany S, Tyson S, Nester, C, et al. Foot posture after stroke: frequency, nature and clinical significance. *Clin Rehabil* 2011; 25(11): 1050–5.

Fournier Belley A, Bouffard J, Brochub K et al. Development and reliability of a measure evaluating dynamic proprioception during walking with a robotized ankle-foot orthosis, and its relation to dynamic postural control *Gait & Posture* 2016;49: 213–218

Franchignoni F, Horak FB, Godi M, Nardone A, Giordano A. Using psychometric techniques to improve the Balance Evaluation Systems Test: the mini-BESTest. J Rehabil Med. 2010;42(4):323–331.

Friedman P. The Star cancellation test in acute stroke. *Clinical Rehabilitation* 1992; 6(1);23-30

Friedman RM, Hester KD, Green BG, LaMotte RH. Magnitude estimation of softness. *Experimental brain research*. 2008; 191:133–142.

Fugl-Meyer A, Jaasko L, Leyman I, Olsson S and Steglind S. The post-stroke hemiplegic patient: a method for evaluation of physical performance. *Scand J Rehab Med* 1975; 7: 13–31.

Fulk G, Reynolds C, Mondal S, & Deutsch J Predicting Home and Community Walking Activity in People With Stroke. *Arch Phys Med Rehabil* 2010: 91: 1582-1586

Fusch P. & Ness L. Are We There Yet? Data Saturation in Qualitative Research. The Qualitative Report 2015; 20 (9): 1408-1416

Gale N, Heath G, Cameron E. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Medical Research Methodology* 2013, 13:117

Galvin R, Cusack T, Stokes E. Physiotherapy after stroke in Ireland: a qualitative insight into the patients' and physiotherapists' experience. *Int J Rehabil Res* 2009; 32: 238–44

Ganz DA, Higashi T, Rubenstein LZ. Monitoring falls in cohort studies of communitydwelling older people: Effect of the recall. *J Am Geriatr Soc*. 2005; 53:2190–2194.

Garcia-Perez, M. Forced-choice staircases with fixed step sizes: asymptotic and smallsample properties. *Vision Research* 1998;38: 1861–1881 Gardner E. & Johnson K . The somatosensory system: Receptors and central pathways. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013a. p. 475-497.

Gardner E. & Johnson K. Sensory Coding. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013b. p. 449-474.

Gatev, P., Thomas S., Thomas K. & Hallett M. Feedforward ankle strategy of balance during quiet stance in adults. *Journal of Physiology* 1999; 514, 915–928.

Ghiasi F, Akbari A. Comparison of the effects of open and closed kinematic chain and different target position on the knee joint position sense. *J Med Sci* 2007;7: 969–76.

Giavarina D. Understanding Bland Altman analysis. *Biochemia Medica* 2015;25(2):141–51

Gibson JJ. *The senses considered as perceptual systems*. London: George Allen & Unwin Ltd.; 1966.

Gilman S. Joint position sense and vibration sense: anatomical organisation and assessment. *J Neurol Neurosurg Psychiatry* 2002;73:473–477

Gilsing MG, Van den Bosch CG, Lee SG, et al. Association of age with the threshold for detecting ankle inversion and eversion in upright stance. *Age Ageing*. 1995; 24(1):58-66.

Goble DJ, Brown SH. Dynamic proprioceptive target matching behavior in the upper limb: effects of speed, task difficulty and arm/hemisphere asymmetries. *Behav Brain Res* 2009; 200: 7–14.

Goble DJ. Proprioceptive acuity assessment via joint position matching: from basic science to general practice. *Phys Ther.* 2010;90:1176–1184.

Goble DJ, Coxon JP, Van Impe A, De Vos J, Wenderoth N, Swinnen SP. The neural control of bimanual movements in the elderly: brain regions exhibiting age-related

increases in activity, frequency-induced neural modulation, and task-specific compensatory recruitment. *Hum Brain Mapp* 2010; 31: 1281–95.

Goble et al Brain activity during ankle proprioceptive stimulation predicts balance performance in young and older adults. *J Neurosci.* 2011; 31(45):16344 –16352

Gold J & Ding L. How mechanisms of perceptual decision-making affect the psychometric function. *Progress in Neurobiology* 2013; 103: 98–114

Goldberg, M, Walker M & Hudspeth A. The Vestibular system. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. p. 917- 934.

Goldberg M & Walker, M. The control of gaze. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. p. 894-916.

Goodyear, M, Krleza-Jeric K, Lemmens T. The Declaration of Helsinki. *BMJ* 2007. 335 (7621): 624-5

Gordon J, Ghilardi MF, Ghez C. Impairments of reaching movements in patients without proprioception. I. Spatial errors. *J Neurophysiol* 1995;73:347–360

Gorst T, Lyddon A, Marsden J et al Foot and ankle impairments affect mobility and balance in stroke (FAiMiS): the views of people with stroke. *Disabil Rehabil*. 2016;38(6):589-96.

Gowers WR. A *Manual of Disease of the Nervous System*. Vol. 1. London: Churchill; 1888

Graham Brown T. The intrinsic factors in the act of progression in the mammal. *Philos.Trans.R.Soc.* Lond.B Biol.Sci. 1911;84: 309–319

Gravano S, Ivaneko Y, Maccioni G, et al. A novel approach to mechanical foot stimulation during human locomotion under body weight support. *Human Movement Science* 2011; 30: 352–367 Gregory JE, Morgan DL, Proske U. After effects in the responses of cat muscle spindles and errors of limb position sense in man. *J Neurophysiol* 1988;**59**:1220–30.

Green D & Swets J. *Signal detection theory and psychophysics* 1974 (Rev Ed). Huntingdon: New York

Grefkes C & Ward N. Cortical Reorganization After Stroke How Much and How Functional? *The Neuroscientist* 2015; ; 20(1): 56-70

Grey MJ, Mazzaro N, Nielsen JB & Sinkjaer T. Ankle extensor proprioceptors contribute to the enhancement of the soleus EMG during the stance phase of human walking. *Can J Physiol Pharmacol.* 2004; **82:** 610–616.

Grose J, Freeman J and Skirton, H. Value of a Confidant Relationship in Psychosocial Care of People with Multiple Sclerosis *Int J MS Care* 2012; 14: 115–122.

Grillner, S., Wallen, P., Saitoh, K., Kozlov, A., Robertson, B., Neural bases of goaldirected locomotion in vertebrates — an overview. *Brain Res. Rev.* 2008;57: 2–12.

Grissom R & Kim J. *Effect Sizes for Research: Univariate and Multivariate Applications*. 2012 Taylor & Francis Group; NY

Guertin P. The mammalian central pattern generator for locomotion. *Brain Res. Rev.* 2009;62: 45–56.

Guertin P. Central pattern generator for locomotion; anatomical, physiological, and pathophysiological considerations. *Frontiers in neurology* 2013;3:183;1-15

Guest, G., Bunce, A., & Johnson, L. (2006). How many interviews are enough? An experiment with data saturation and variability. *Field Methods*, 18(1), 59-82.

Gunn, H, Creanor, S, Haas, B, Marsden, J & Freeman, J. Risk factors for falls in multiple sclerosis: an observational study. *Multiple Scler Jnl* 2013; 0(0); 1-10

Haegens S, Osipova D, Oostenveld R & Jensen O. Somatosensory working memory performance in humans depends on both engagement and disengagement of regions in a distributed network. *Human Brain Mapping* 2010; 31: 26-35

Halasi T, Kynsburg A, Tallay A, Berkes I. Changes in joint position sense after surgically treated chronic lateral ankle instability. *Br J Sports Med* 2005;39:818–24.

Han J, Waddington G, Adams R, Anson J & Liu Y. Assessing proprioception: A critical review of methods. *Journal of Sport and Health Science* 2016; 5: 80–90

Han J, Waddington G, Adams R, Anson. Proprioceptive performance of bilateral upper and lower limb joints: side-general and site-specific effects *Exp Brain Res* 2013; 226:313–323

Han J, Anson J, Waddington G and Adams R. Sport attainment and proprioception. International Journal of Sports Science and Coaching, 2014; 9(1): 159–170.

Han J, Waddington G, Anson J, Adams R. Level of competitive success achieved by elite athletes and multi-joint proprioceptive ability. *J Sci Med Sport* 2015;18:77–81.

Han L & Law-Gibson. Key neurological impairments influence function-related group outcomes after stroke. *Stroke.* 2002;33:1920-1924

Hartmann, S., Missimer, J.H., Stoeckel, C., Abela, E., Shah, J., Seitz, R.J., 2008. Functional connectivity in tactile object discrimination: a principal component analysis of an event related fMRI-study. *PLoS One 3.* 

Hedman L. Sullivan J. An initial exploration of the perceptual threshold test using electrical stimulation to measure arm sensation following stroke. *Clin Rehabil* 2011; 25(11): 1042–1049

Hegeman J, Weerdesteyn V, van den Bemt B, Nienhuis B, et al. Dual-tasking interferes with obstacle avoidance reactions in healthy seniors. *Gait Posture*. 2012; 36(2):236-40.

Hellstrom, K. and Lindmark, B. Fear of falling in patients with stroke: a reliability study. *Clinical rehabilitation* 1999; 13(6): 509-517.

Hennig, M and Sterzing, T. Sensitivity Mapping of the Human Foot: Thresholds at 30 Skin Locations. *Foot Ankle Int* 2009 30: 986-991 Hernandez ME, Goldberg A, Alexander NB. Decreased muscle strength relates to selfreported stooping, crouching, or kneeling difficulty in older adults. *Phys Ther*. 2010;90(1):67-74

Hicks C. *Research Methods for Clinical Therapists: Applied Project Design and Analysis*. 4<sup>th</sup> Edition. Churchill Livingston.

Hillier S, Immink M, Thewlis D. Assessing proprioception: a systematic review of possibilities. *Neurorehabil Neural Repair* 2015;29:933–49.

Hilier S & Dunsford A. A pilot study of sensory retraining for the hemiparetic foot poststroke. *International Journal of Rehabilitation Research* 2006; 29(3): 237-242

Hoang P, Baysan M, Gunn H, Cameron M, Freeman J, Nitz J Low Choy, N, Lord S. Fall risk in people with MS: A Physiological Profile Assessment study. *Multiple Sclerosis Journal- Experimental, Translational and Clinica*. 2016; 2: 1-10

Hobart JC, Riazi A, Lamping DL, Fitzpatrick R, Thompson AJ (2003) Measuring the impact of MS on walking ability: the 12-Item MS Walking Scale (MSWS-12). *Neurology* 60(1):31–36

Holland A, O'Connor RJ, Thompson AJ et al. Talking the talk on walking the walk: a 12item generic walking scale suitable for neurological conditions? *Journal of Neurology*. 2006;253(12):1594-602.

Hollins M, Faldowksi R, Rao S, Young F. Perceptual dimensions of tactile surface texture: a multidimensional scaling analysis. *Perception & Psychophysics* 1993; 54(6): 697-705

Hollins M & Risner SR (2000): Evidence for the duplex theory of tactile texture perception. *Percept Psychophys* 62:695–705

Hollins M, Bensmaia SJ, Washburn S (2001): Vibrotactile adaptation impairs discrimination of fine, but not coarse, textures. *Somatosens Mot Res* 18:253–262.

Hollins, M & Bensmaïa, S.J., 2007. The coding of roughness. *Can. J. Exp. Psycyhol*. 61, 184–195.

Holmes G. Disorders of sensation produced by cortical lesions. Brain 1927; 50:413-427.

Hohne A, Ali S, Stark C, Bruggemann GP. Reduced plantar cutaneous sensation modifies gait dynamics, lower-limb kinematics and muscle activity during walking. *Eur J Appl Physiol.* 2012;112:3829-3838.

Horak FB. Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? *Age Ageing*. 2006 Sep;35 Suppl 2:ii7-ii11.

Howes H, Edwards S, Benton D. Male body image following acquired brain injury. *Brain Inj.* 2005; 19(2): 135-47.5.

Howe J, Inness E, Venturini A, Williams JI, Verrier MC. The Community Balance and Mobility Scale: A balance measure for individuals with traumatic brain injury. *Clinical Rehabilitation*, 2006; 20, 885-95.

Hsieh CL, Hsueh IP, Chiang FM and Lin PH. Interrater reliability and validity of the Action Research Arm Test in stroke patients. *Age Ageing* 1998; 27: 107–114

Hsu A, Tang P, Jan M. Analysis of impairments influencing gait velocity and asymmetry of hemiplegic patients after mild to moderate stroke. *Arch Phys Med Rehabil* 2003; 84: 1185-93.

Hsu L-J, Lin S-I, Li S-W et al. Effect of weight bearing on ankle joint position sense. *Journal of biomechanics* 2006 39 (suppl 1)

Hu J, Ding X, Wang R et al (2009) Mechanistic principles of sensory analysis on object softness by touch means Chinese. *J Theor Appl Mech* 41(5):761–768

Hu J, Zhao Q, Jiang R et al. Responses of cutaneous mechanoreceptors within fingerpad to stimulus information for tactile softness sensation of materials *Cogn Neurodyn* 2013; 7:441–447

Huxhold O, Li SC, Schmiedek F, et al.: Dual-tasking postural control: aging and the effects of cognitive demand in conjunction with focus of attention. *Brain Res Bull*, 2006, 69: 294–305

Hyndman D, Ashburn A, Stack E. Fall events among people with stroke living in the community: circumstances of falls and characteristics of fallers. *Arch Phys Med Rehabil* 2002; 83:165–70

Hyndman D, Ashburn A. Stops walking when talking as a predictor of falls in people with stroke living in the community. J Neurol Neurosurg Psychiatry. 2004;75(7):994–97.

Hyndman D, Ashburn A, Yardley L, Stack E. Interference between balance, gait and cognitive task performance among people with stroke living in the community. Disabil Rehabil. 2006;28(13–14):849–56

Jaeschke R, Singer J and Guyatt G (1989) Ascertaining the Minimal Clinically Important Difference. *Controlled Clinical Trials* 10:407-415 1989

Jayaram G, Tang B, Pallegadda R, Vasudevan E1, Celnik P and Bastian. Modulating locomotor adaptation with cerebellar stimulation. *J Neurophysiol*. 2012 Jun 1; 107(11): 2950–2957.

Jenkins ME, Almeida QJ, Spaulding SJ, van Oostveen RB, Holmes JD, et al. (2009) Plantar cutaneous sensory stimulation improves single-limb support time and EMG activation patterns among individuals with Parkinson's disease. *Parkinsonism Relat Disord* 15: 697–702.

Johnson KO, Hsiao SS, Yoshioka T (2002) Neural coding and the basic law of psychophysics. *Neuroscientist* 8:111–121.

Jönsson A, Lindgren I, Hallström B, et al. Prevalence and intensity of pain after stroke: a population based study focusing on patients' perspectives. *J Neurol Neurosurg Psychiatr* 2006; 77: 590–595. Kahn J & Hornby T. Rapid and long term adaptations in gait symmetry following unilateral step training in people with hemiparesis. *Phys Ther.* 2009; 89(5):474-483

Kalra L. Stroke Rehabilitation: old chestnuts and new insights. *Stroke* 2009; 41(2) e88-e90

Kalron, A, Pasitselsky D, Greenberg-Abrahami, M et al. Do Textured Insoles Affect Postural Control and Spatiotemporal Parameters of Gait and Plantar Sensation in People With Multiple Sclerosis? *PM & R* 2015; 7: 17-25

Kamon N. Quantitative measurement of vibratory perception threshold using a new vibrometer TM-31A. *J Occup Med* 1994; 36: 989–96.

Kandel E. From Nerve Cells to Cognition: The Internal Representations of Space and Action In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. p. 370-391

Kandel E, Schwartz J, & Jessel T, Siegelbaum S & Hudspeth A. *Principles of Neural Science*. 5<sup>th</sup> Edition. 2013. McGraw Hill Professional

Kato H & Izumiyama M. Impaired motor control due to proprioceptive sensory loss in a patient with cerebral infraction localized to the postcentral gyrus. *J Rehabil Med*. 2015;47(2):187-90

Kavounoudias A, Roll R, & Roll J-P. Foot sole and ankle muscle inputs contribute jointly to human erect posture regulation *Journal of Physiology* 2001:**532.3**:869–878

Kavounoudias A, Roll R, & Roll J-P. The plantar sole is a 'dynamometric map' for human balance control. *Neuroreport.* 1998; 9(14):3247-52.

Keats D. Interviewing: a practical guide for students and professionals. Open University Press: Buckingham.

Kelleher KJ, Spence WD, Solomonidis S, Apatsidis D (2010) The effect of textured insoles on gait patterns of people with multiple sclerosis. *Gait Posture* 32: 67–71.

Kessner S, Bingel U, Thomalla G. Somatosensory deficits after stroke: a scoping review. *Topics In Stroke Rehabilitation* 2016;23(2):136-146

Kiefer G, Forwell L, Kramer J, Birmingham T. Comparison of sitting and standing protocols for testing knee proprioception. *Physiother Can* 1998;50:30–4

Kim, C.M., Eng, J.J. Magnitude and pattern of 3D kinematic and kinetic gait profiles in persons with stroke: relationship to walking speed. *Gait Posture* 2004; 20 (2): 140–146

Kim, C. M. and J. J. Eng (2003). "Symmetry in vertical ground reaction force is accompanied by symmetry in temporal but not distance variables of gait in persons with stroke." *Gait Posture* **18**(1): 23-28.

Kim JS & Choi-Kwon S. Discriminative sensory dysfunction after unilateral stroke. *Stroke.* 1996;27(4):677–682.

Kingdom F & Prins N. *Psychophysics: a practical introduction* 1<sup>st</sup> edition. 2009. Academic Press

Kluding P, Cajewski B. Lower extremity strength differences predict activity limitations in people with chronic stroke. *Phys Ther.* 2009,89:73-81

Knorr S, Brouwer B, Garland J. Validity of the Community Balance and Mobility Scale in community-Dwelling Persons After Stroke. *Arch Phys Med Rehabil* ;2010: 91: 890-896

Ko S-K, Simonsick E, Deshpande N & Ferrucci. Sex-specific age associations of ankle proprioception test performance in older adults: results from the Baltimore Longitudinal Study of Aging. *Age and Ageing* 2015; 44: 485–490

Kottner J, Audige L, Brorson S, et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. *Journal of Clinical Epidemiology* 2011; 64: 96-106

Krewer C, Van de Winckel A, Elangovan N et al. Commentary on: "Assessing proprioception: A critical review of methods" by Han et al. *Journal of Sport and Health Science* 2016; 5:91–92

Kunkel D, Potter J, Mamode L. A cross-sectional observational study comparing foot and ankle characteristics in people with stroke and healthy controls. *Disabil Rehabil*. 2017;39(12):1149-1154.

Kunkel D, Pickering R & Ashburn A. Comparison of retrospective interviews and prospective diaries to facilitate fall reports among people with stroke. Age & Ageing 2011; 40 (2): 277-280

Kynsburg A, Halasi T, Tallay A, Berkes I. Changes in joint position sense after conservatively treated chronic lateral ankle instability. *Knee Surg Sports Traumatol* Arthrosc 2006;14:1299–306.

Lajoie K, Bloomfield L, Nelson F, Suh J, Marigold D. The contribution of vision, proprioception, and efference copy in storing a neural representation for guiding trail leg trajectory over an obstacle. *J Neurophysiol* 2012; 107:2283–2293.

Lam T & Dietz V. Transfer of Motor Performance in an Obstacle Avoidance Task to Different Walking Conditions *Neurophysiol* 2004: 92: 2010–2016

Lam T, Luttman K, Houldin A, Chan C. Treadmill-based locomotor training with leg weights to enhance functional ambulation in people with chronic stroke: a pilot study. *J neurol Phys Ther*. 2009; 33(3):129-135

Lamb GD. Tactile discrimination of textured surfaces: psychophysical performance measures in humans. *J Physiol (Lond)*, 1983; 338: 551–565

Lamb SE, Jørstad-Stein EC, Hauer K, Becker C; Prevention of Falls Network Europe and Outcomes Consensus Group. Development of a common outcome data set for fall injury prevention trials: the Prevention of Falls Network Europe consensus *J Am Geriatr Soc* 2005 Sep;53(9):1618-22.

Lamontagne A, Malouin F, Richards C, and Dumas F. Mechanisms of disturbed motor control in ankle weakness during gait after stroke. *Gait & Posture* 2002; 15: 244–255.

412

Laufer Y, Elboim-Gabyzon M. Does Sensory Transcutaneous Electrical Stimulation Enhance Motor Recovery Following a Stroke? A Systematic Review. *Neurorehabil Neural Repair* 2011 ; 25(9) : 799–809

Laurent G, Valentini F, Loiseau K et al. Claw toes in hemiplegic patients after stroke. Ann Phys Rehabil Med 2010 ; 53(2): 77-85

Lauzière S, Betschart M, Aissaoui R, Nadeau S (2014) Understanding Spatial and Temporal Gait Asymmetries in Individuals Post Stroke . Int J Phys Med Rehabil 2014; 2: 201

Laybourne A, Biggs S, & Martin F. Falls exercise interventions and reduced falls rate: Always in the patient's interest? *Age and Ageing* 2008; 37: 10–13

Lederman SJ, Klatzky RL. Haptic aspects of motor control. In: Boller F, Grafman J, editors. *Handbook of neuropsychology*. Amsterdam: Elsevier Science; 1997. p 131-47

Lederman, S. J.& Klatzky, R. L. Haptic perception: A tutorial. *Attention Perception & Psychophysics* 71, 1439–1459 (2009).

Lee, M.-J, Kilbreath S and Refshauge, K. Movement detection at the ankle following stroke is poor. *Australian J of Physio* 2004; 51(1): 19–24.

Lee KB, Lim SH, Ko EH, Kim YS, Lee KS, Hwang BY. Factors related to community ambulation in patients with chronic stroke. *Top Stroke Rehabil*. 2015;22(1):63-71.

Leek M. Adaptive procedures in psychophysical research. *Perception & Psychophysics* 2001, 63 (8), 1279-1292

Leibowitz N, Levy N, Weingarten S, Grinberg Y, Karniel A, Sacher Y, et al. Automated measurement of proprioception following stroke. *Disabil Rehabil* 2008; 30: 1829–36.

Lemay J-F, Gagnon D, Duclos C, Grangeon M, Gauthier C, Nadeau S. Influence of visual inputs on quasi-static standing postural steadiness in individuals with spinal cord injury. *Gait & Posture* 2013;38(2):357–60
Lin P-Y, Yang y-R, Cheng S-J et al. The Relation Between Ankle Impairments and Gait Velocity and Symmetry in People With Stroke *Arch Phys Med Rehabil* 2006; 87: 562-568

Lin S.-I. Motor function and joint position sense in relation to gait performance in chronic stroke patients. *Arch Phys Med Rehabil* 2005; 86(2): 197–203.

Lin S-I, Hsu L-J, Wang H-C. Effects of ankle proprioceptive interference on locomotion after stroke. *Arch Phys Med Rehabil* 2012;93:1027-33.

Lin J, Hsueh I, Sheu C and Hsieh C. Psychometric properties of the sensory scale of the Fugl-Meyer Assessment in stroke patients. *Clin Rehabil* 2004; 18: 391–97.

Lin C-H, Lien YH, Wang SF, Tsauo JY. Hip and knee proprioception in elite, amateur and novice tennis players. *Am J Phys Med Rehabil*. 2006;85:216-221.

Lin C-H, Chiang S-L, Lu L-H et al Validity of an ankle joint motion and position sense measurement system and its application in healthy subjects and patients with ankle sprain. *Computer Methods and Programs in Biomedicine* 2016; 131:89–96

Lincoln N, Leadbitter D. Assessment of motor function in stroke patients. *Physiotherapy* 1979; 65: 48–51.

Lincoln NB, Crow JL, Jackson JM, Waters GR, Adams SA and Hodgson P. The unreliability of sensory assessment. *Clin Rehabil* 1991; 5: 273–82.

Lincoln NB, Jackson JM and Adams SA. Reliability and revision of the Nottingham Sensory Assessment for Stroke Patients. *Physiotherapy* 1998; 84: 358–65.

Li JX, Xu DQ, Hong Y. Effects of 16-week Tai Chi intervention on postural stability and proprioception of knee and ankle in older people. *Age Ageing* 2008; 37: 575–8.

Lisberger S, Thach T. The cerebellum. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. p. 960-981. Liu J, Song AG (2008) Discrimination and memory experiments on haptic perception of softness. *Percept Mot Skills* 106(1):295–306

Lloyd V, Gatherer A, and Kalsy S. Conducting qualitative interview research with people with expressive language difficulties. *Qual Health Res* 2006; 16(10): 1386–404.

Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther*. 2003 Mar;83(3):237-52

Lord S, McPherson K, McNaughton H, et al. Community ambulation after stroke: how important and obtainable is it and what measures appear predictive? *Arch Phys Med Rehabil* 2004: 85(2) 234–239.

Lord S, Murray S, Chapman K, Munro B, Tiedemann A. Sit-to-stand performance depends on sensation, speed, balance, and psychological status in addition to strength in older people. *J Gerontol A Biol Sci Med Sci*. 2002;57(8):M539-43.

Lord S, Rochester L, Weatherall M et al. The effect of environment and task on gait parameters after stroke: A randomized comparison of measurement conditions. *Arch of Phys Med Rehabil*, 2006; 87(7): 967–73.

Lord S, Clark R, Webster I. Physiological factors associated with falls in an elderly population. *J Am Geriatr Soc*. 1991;39(12):1194-200.

Lowrey C, Strzalkowski N, & Bent L. Skin sensory information from the dorsum of the foot and ankle is necessary for kinesthesia at the ankle joint. *Neuroscience Letters* 485 (2010) 6–10

Lynch EA, Hillier SL, Stiller K, Campanella RR, Fisher PH. Sensory retraining of the lower limb after acute stroke: a randomized controlled pilot trial. *Arch Phys Med Rehabil* 2007;88:1101-7.

Lu L, Barrett A, Cibula J, Gilmore R et al. Proprioception more impaired distally than proximally in subjects with hemispheric dysfunction. *Neurology* 2000; 55: 596-597

Mackintosh S, Goldie P, Hill K. Falls incidence and factors associated with falling in older, community-dwelling, chronic stroke survivors 1 year after stroke and matched controls. *Aging Clin Exp Res* 2005; 17:74–81

Macpherson J. & Horak F. Posture. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. p. 935-959.

Mackenzie L, Byles J, D'Este C. Validation of self-reported fall events in intervention studies. *Clin Rehabil.* 2006 Apr;20(4):331-9

MacLellan, M.J. & Patla, A.E. Adaptations of walking pattern on a compliant surface to regulate dynamic stability. *Exp Brain Res* 2006; 173: 521.

Macmillan, N. A., & Creelman, C. D. (2005). *Detection theory: A user's guide* (2nd ed.). New York: Psychological Press

Makin S, Turpin S, Dennis M, Wardlaw J. Cognitive impairment after lacunar stroke: systematic review and meta-analysis of incidence, prevalence and comparison with other stroke subtypes. *J Neurol Neurosurg Psychiatry*. 2013 Aug;84(8):893-900.

Malterud, K. Qualitative research: standards, challenges, and guidelines. *The Lancet* 2001; 358; 483-488.

Malhotra, P., Coulthard, E. J., & Husain, M. Role of right posterior parietal cortex in maintaining attention to spatial locations over time. *Brain* 2009; 132(3): 645-660.

Marigold DS, Andujar JE, Lajoie K, Drew T. Motor planning of locomotor adaptations on the basis of vision: the role of the posterior parietal cortex. *Prog Brain Res* 188: 83– 100, 2011

Marsden, J.F., E.D. Playford, and B.L. Day. The Vestibular control of balance following stroke. *Journal of Neurology and Neurosurgery*, 2005. 76(5): p. 670-678

Marks R. Muscle Spindles and Locomotor Control-An Unrecognized Falls Determinant? International Journal of Orthopaedics 2015; 2(6): 445-451

416

Masanic CA, Bayley MT. Interrater reliability of neurologic soft signs in an acquired brain injury population. *Arch Phys Med Rehabil* 1998;79:811-5.

Masani A, Vette A, Abe M. Center of pressure velocity reflects body acceleration rather than body velocity during quiet standing *Gait & Posture* 39; 2014: 946–952

Maschke M, Gomez C, Tuite P, Konczak J. Dysfunction of the basal ganglia, but not the cerebellum, impairs kinaesthesia. *Brain* 2003; 126:2312-2322

Mason, M. Sample size and saturation in PhD studies using qualitative interviews. Forum: *Qualitative Social Research*, 2010; 11(3)

McDonnell, M.N. and S.L. Hillier, Vestibular rehabilitation for unilateral peripheral vestibular dysfunction. *Cochrane Database Syst Rev*, 2015. 1: p. Cd005397

Mecagni C, Smith JP, Roberts KE, O'Sullivan SB Balance and ankle range of motion in community-dwelling women aged 64 to 87 years: a correlational study. *Phys Ther*. 2000;80(10):1004-11.

Meesen RL, Cuypers K, Rothwell JC, Swinnen SP and Levin O. The effect of long-term TENS on persistent neuroplastic changes in the human cerebral cortex. *Hum Brain Mapg* 2011: 32; 872–882

Mentiplay BF, Adair B, Bower KJ, Williams G, Tole G, Clark RA. Associations between lower limb strength and gait velocity following stroke: a systematic review. *Brain Inj*. 2015;29(4):409-22

Menz, H, Morris, M., Lord, S. Foot and ankle characteristics associated with impaired balance and functional ability in older people. *J Gerontol A Biol Sci* Med 2005; 60A:1547-52

Menz H, Morris M, Lord S. Foot and ankle risk factors for falls in older people: a prospective study. *J Gerontol A Biol Sci Med Sci*. 2006;61(8):866-70.

Meyer S., De Bruyn N., Lafosse C. et al. Somatosensory Impairments in the Upper Limb Poststroke: Distribution and Association With Motor Function and Visuospatial Neglect *Neurorehabilitation and Neural Repair* 2016; 30(8): 731–742

McGlone F & Spence C. The cutaneous senses: Touch, temperature, pain/itch, and pleasure. *Neuroscience and Biobehavioral Reviews* 34 (2010) 145–147

McKevitt C, Redfern J, Mold F, and Wolfe C. Qualitative studies of stroke: a systematic review. *Stroke* 2004; 35(6): 1499–505.

Miles M. & Huberman A. *Early Steps in Analysis. An Expanded Sourcebook: Qualitative Data Analysis* (2nd edition). USA: Sage Publications

Miller K, Phillips B, Martin C, Wheat H, Goodwin and Galea M. The AsTex : clinimetric properties of a new tool for evaluating hand sensation following stroke. *Clin Rehabil* 2009; 23: 1104–15.

Milo M.-H, Nadeau S, Gravel D and Bourbonnais D. Effect of increases in plantarflexor and hip flexor muscle strength on the levels of effort during gait in individuals with hemiparesis. *Clin Biomech* 2008; 23(4): 415–23

Moeller D and Carpenter C. Factors affecting quality of life for people who have experienced a stroke. *Int J Ther Rehabil* 2013; 20(4): 207-216

Morley J, Goodwin A, Darians Smith I. Tactile Discrimination of gratings. *Experimental Brain Research* 1983; 49(2): 291-299

Morton SM, Bastian AJ. Cerebellar contributions to locomotor adaptations during splitbelt treadmill walking. *J Neurosci* 2006;26:9107–9116

Morioka S & Yagi F. Effects of perceptual learning exercises on standing balance using a hardness discrimination task in hemiplegic patients following stroke: a randomized controlled pilot trial. *Clinical Rehabilitation* 2003; 17: 600–607

Moskowitz E, Lightbody FE, Freitag NS. Long-term follow-up of the poststroke patient. *Arch Phys Med Rehabil*. 1972;53(4):167–172 Muir-Hunter S-W, Wittwer J. Dual-task testing to predict falls in community-dwelling older adults: a systematic review. *Physiotherapy* 2016; 102:29–40

Mullie Y, & Duclos C. Role of proprioceptive information to control balance during gait in healthy and hemiparetic individuals. *Gait Posture*. 2014;40(4):610-5

Naidoo S, Anderson S, Mills J, et al. (2011). "I could cry, the amount of shoes I can't get into": A qualitative exploration of the factors that influence retail footwear selection in women with rheumatoid arthritis. *J Foot Ankle Res* 2011; 4(1): 21.

Niam S, Cheung W, Sullivan P et al. Balance and physical impairments after stroke. Arch Phys Med Rehabil. 1999;80:1227-1233

Nieuwenhuys R. The insular cortex: a review Prog Brain Res. 2012;195:123-63..

NIHR INVOLVE. Briefing notes for researchers: public involvement in NHS, public health and social care research. 2012

Ng H, McGinley J, Jolley D et al. Effects of footwear on gait and balance in people recovering from stroke. *Age Ageing* 2010; 39(4): 507-10.

Ng S and Hui-Chan C. (2012). Contribution of ankle dorsiflexor strength to walking endurance in people with spastic hemiplegia after stroke. *Arch Phys Med Rehabil* 2012; 93(6): 1046–51

Ng S & Shepherd R. Weakness in patients with stroke: implications for strength training in neurorehabilitation. *Phys Ther Rev* 2000;5:227-38.

Niessen M, Veeger D, Koppe P, Konijnenbelt M, van Diee<sup>"</sup>n J and Janssen T. Proprioception of the shoulder after stroke. *Arch Phys Med Rehabil* 2008; 89: 333–38.

Nurse M, Nigg B. The effect of changes in foot sensation on plantar pressureand muscle activity. *Clin Biomech* 2001;16:719–27.

O'Donnell M, Diener H-C, Sacco R. et al. Chronic pain syndromes after ischemic stroke: PRoFESS trial. *Stroke* 2013; 44(5): 1238–43.

Okamoto S, Nagano H, Yamada Y. Psychophysical Dimensions of Tactile Perception of Textures. *IEEE Transactions on Haptics* 2012; 6(1): 81-93

Olsson L, Lund H, Henriksen M, Rogind H, Bliddal H, Danneskiold-Samsoe B. Test-retest reliability of a knee joint position sense measurement method in sitting and prone position. *Adv Physiother* 2004;6:37–47.

O'Doherty, J. E. et al. Active tactile exploration using a brain-machine-brain interface. *Nature* 479, 228–U106 (2011).

O'Reilly, M., & Parker, N. Unsatisfactory saturation: A critical exploration of the notion of saturated sample sizes in qualitative research. *Qualitative Research Journal*, 2012: 1-8

Orth D, Davids K, Wheat J, Seifert L, Liukkonen J, et al. (2013) The Role of Textured Material in Supporting Perceptual-Motor Functions. *PLoS ONE* 8(4): e60349.

Palastanga N & Soames R. *Anatomy and Human Movement: Structure and Function*. 6<sup>th</sup> edition 2012, Churchill Livingstone: Elsevier

Palinkas LA, Holloway IW, Rice E, Fuentes D, Wu Q, Chamberlain P. Social networks and implementation of evidence-based practices in public youth-serving systems: A mixed methods study. *Implementation Science*. 2011; 6:113

Pallant J. SPSS Survival manual; a step by step guide to data analysis. 5<sup>th</sup> edition 2013. Open University Press.

Park H.-J, Oh D-W, Kim S.-Y, & Choi J.-D. (2011). Effectiveness of community-based ambulation training for walking function of post-stroke hemiparesis: a randomized controlled pilot trial. *Clinical Rehabil* 2011; 25(5): 451–9.

Patel A, Duncan P, Lai S, Studenski S. The relation between impairments and functional outcomes poststroke. *Arch Phys Med Rehabil*. 2000; 81(10):1357-63

Patla A. Mobility in complex environments: implications for clinical assessment and rehabilitation. *Neurol Rep* 2001;25:82-90

Paterson B and Scott-Findlay S. Critical issues in interviewing people with traumatic brain injury. *Qual Health Res* 2002; 12: 399–409.

Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE. Evaluation of gait symmetry after stroke: a comparison of current methods and recommendations for standardization. *Gait Posture*. 2010;31(2):241-246.

Patterson KK, Parafianowicz I, Danells CJ, et al. Gait asymmetry in communityambulating stroke survivors. *Arch Phys Med Rehabil*. 2008; 89(2):304-10.

Paton J, Hatton AL, Rome K, Kent B. Effects of foot and ankle devices on balance, gait and falls in adults with sensory perception loss: a systematic review. *Jbi Database of Systematic Reviews and Implementation Reports*. 2016;14(12):127-162.

Patton, MQ. *Qualitative research and evaluation methods*. 3<sup>rd</sup> Edition 2002. Sage Publications; Thousand Oaks, CA.

Pavlou, M., A.M. Bronstein, and R.A. Davies, Randomized trial of supervised versus unsupervised optokinetic exercise in persons with peripheral vestibular disorders. *Neurorehabil Neural Repair*, 2013. 27(3): p. 208-18.

Pearson K, Gordon J. Spinal reflexes. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors.. *Principles of neural science*. New York: McGraw Hill; 2013. p. 790-811

Perry, S, Mcllroy, B Maki, E. The role of plantar cutaneous mechanoreceptors in the control of compensatory stepping reactions evoked by unpredictable, multi-directional perturbation. *Brain Research* 2000; 877:401–406

Perry, J and Burnfield, JM, 2010, *Gait Analysis. Normal and pathological function*. SLACK, Thorofare, NJ

Perruchoud D, Murray M, Lefebvre J, Ionta S. Focal dystonia and the Sensory-Motor Integrative Loop for Enacting (SMILE). *Front Hum Neurosci*. 2014; 20(8):458. 2014 Peterka RJ. Sensorimotor integration in human postural control. *J Neurophys* 2002; 88: 1097–118.

Petty N., Thomson O. & Stew G. Ready for a paradigm shift? Part 1: Introducing the philosophy of qualitative research. *Manual Therapy* 2012;17: 267-274

Piriyaprasarth P, Morris ME, Delany C, Winter A, Finch S () Trials needed to assess knee proprioception following stroke. *Physiother Res Int* 2009; 14:6–16

Plummer P, Eskes G, Wallace S, Giuffrida C et al on behalf of the American Congress of Rehabilitation Medicine Stroke Networking Group Cognition Task Force. Cognitive-Motor Interference during Functional Mobility after Stroke: State of the Science and Implications for Future Research. *Arch Phys Med Rehabil*. 2013; 94(12):1-17

Pope C & Mays N. (Eds) *Qualitative Research in Health Care*, 3rd Edition 2006. BMJ Books.

Portney LG, Watkins MP. *Foundations of Clinical Research: Applications to Practice.* Upper Saddle River, NJ: Pearson Prentice Hall; 2009

Prescott RJ, Garraway WM, Akhtar AJ. Predicting functional outcome following acute stroke using a standard clinical examination. *Stroke*. 1982;13:641-647

Preusser S, Thiel S, Rook C et al. The perception of touch and the ventral somatosensory pathway. *Brain* 2015;138:540-548

Proske U & Gandevia S. The proprioceptive senses: their roles in signalling body shape, body position and movement, and muscle force. *Physiol Rev* 2012; 92: 1651–1697.

Pumpa L., Cahill L., & Carey L. Somatosensory assessment and treatment after stroke: An evidence-practice gap. *Aust Occ Ther J*. 2015; 62(2):93-104

Qaiser T, Chisholm A, & Lam T. The relationship between lower limb proprioceptive sense and locomotor skill acquisition. *Exp Brain Res* 2016 ;234(11):3185-3192

Qui F, Cole M, Davids K, Hennig E, Silburn P, Netscher H, et al. Enhanced somatosensory information decreases postural sway in older people. *Gait Posture* 2012;35:630–5.

Radovanovic S, Korotkov A, Ljubisavljevic M, et al. Comparison of brain activity during different types of proprioceptive inputs: a positron emission tomography study. *Exp Brain Res*. 2002;143:276–285

Rankin G & Stokes m. Reliability of assessment tools in rehabilitation: an illustration of appropriate statistical analyses. *Clin Rehabil*. 1998: 12:187-199

Refshauge K, Chan R, Taylor J, McCloskey D. Detection of movements imposed on human hip, knee, ankle and toe joints. *Journal of Physiology* 1995; 488.1: 231-241

Reisman D, Wityk R, Silver K, Bastian A. Split-belt treadmill adaptation transfers to overground walking in persons poststroke. *Neurorehabil Neural Repair* 2009;23(7):735-744

Reisman D, Bastian A, Morton S. Neurophysiologic and rehabilitation insights from the split-belt and other locomotor adaptation paradigms. *Phys Ther* 2010; 34(4):202-207.

Rhea CK, Rietdyk S. Influence of an unexpected perturbation on adaptive gait behavior. *Gait Posture* 34: 439–441, 2011.

Ribeiro FO, Oliveira J. Aging effects on joint proprioception: the role of physical activity in proprioception preservation. *Eur Rev Aging Phys Act* 2007; 4: 71–6.

Richards L (Ed) *Working with the Data: Handling Qualitative Data*. London: Sage Publications 2005.

Ritchie J, and Spencer L. Qualitative data analysis for applied policy research. In: Bryman A, Burgess R, editors. *Analysing qualitative data*. London: Routledge; 1993. pp. 173–194.

Ritchie J and Lewis J (Eds) *Qualitative Research Practice: A Guide for Social Science Students and Researchers*. London: Sage Publications 2003

Rizzolatti G & Kalaski J. Voluntary Movement: The parietal and premotor cortex. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. 790-811

Robson C. *Real World Research: a resource for social scientists and practitionerresearchers.* 2nd Ed. Oxford: Blackwell Publishers. 2002

Robbins SM, Houghton PE, Woodbury MG, Brown JL. The therapeutic effect of functional and transcutaneous electric stimulation on improving gait speed in stroke patients: a meta-analysis. *Arch Phys Med Rehabil*. 2006; 87(6):853-9

Robbins SE, Waked EG, MacClaran J. Proprioception and stability: foot position awareness as a function of age and footwear. *Age Ageing* 1995; 24: 67-72.

Robinson C, Shumway-Cook A, Matsuda P, & Ciol M. Understanding physical factors associated with participation in community ambulation following stroke. *Disab Rehabil* 2011;33(12):1033-1042

Roijezon U, Clark N, & Treleaven J. Proprioception in musculoskeletal rehabilitation. Part 1: Basic science and principles of assessment and clinical interventions. *Manual Therapy* 2015 20 368-377

Romo R, Hernandez A, Zainos A, Lemus L, Brody CD (2002): Neuronal correlates of decision-making in secondary somatosensory cortex. *Nat Neurosci* 5:1217–1225.

Romo, R., Salinas, E., 2001. Touch and go: decision-making mechanisms in somatosensation. *Annu. Rev. Neurosci.* 24, 107–137.

Romo R & Lafuente V. Conversion of sensory signals into perceptual decisions. *Progress in Neurobiology* 2013; 103:41-75

Rothwell J, Traub M, Day L, Obeso J et al Manual motor performance in a deafferented man *Brain*. 1982 105 (Pt 3):515-42.

Royal College of Physicians Intercollegiate Stroke Working Party. 2012 *National clinical guideline for stroke*, 4th Edition. London.

Royal College of Physicians Intercollegiate Stroke Working Party. 2016 *National clinical guideline for stroke,* 5th Edition. London.

Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategies for prevention. *Age Ageing* 2006;35 Suppl 2:ii37-ii41.

Ruhe A., Fejer R., Walker B. The test–retest reliability of centre of pressure measures in bipedal static task conditions – A systematic review of the literature. *Gait & Posture* 32;2010: 436–445

Said C, Goldie P, and Patla A. Balance during obstacle crossing following stroke. *Gait & Posture* 2008; 27:23–30.

Said, C. M., Galea Mp Fau - Lythgo, N. & Lythgo, N. People with stroke who fail an obstacle crossing task have a higher incidence of falls. *Phys Ther* 2013; 93: 334-344.

Sacco et al. AHA/ASA Expert Consensus Document: An updated definition of stroke for the 21<sup>st</sup> Century. *Stroke*. 2013; 44:2064-2089

Saka A, McGuire A Wolfe, C, The cost of stroke in the United Kingdom. Age & Ageing 2009 38: 27-32

Salbach N, O'Brien K, Brooks D. et al. Speed and Distance Requirements for Community Ambulation: A Systematic Review. *Arch Phys Med Rehab* 2014; 95:117-28

Salter K, Hellings C, Foley N, Teasell R. The experience of living with stroke: A qualitative meta-synthesis. Journal of Rehabilitation Medicine. 2008;40(8):595–602

Sanes J, Mauritz KH, Evarts E, Dalakas M Chu A Motor deficits in patients with largefiber sensory neuropathy *Proc. Nail. Acad. Sci.* 1984 81: 979-982

Sato M, Takahashi N, Yoshimura S et al. A new device for foot sensory examination employing auto-presentation of shear force stimuli against the skin. *Journal of Biomechanical Science and Engineering*, 2015;10(2): 1-11

Saradjian A. Sensory modulation of movement, posture and locomotion. *Clinical Neurophysiology* 2015; 45: 255—267

Schabrun S & Hillier S. Evidence for the retraining of sensation after stroke: a systematic review *Clin Rehabil* 2009; 23: 27-39

Schmid A, Yaggi K, Burrus N et al. Circumstances and consequences of falls among people with chronic stroke. *JRRD* 2013; 50(9):1277-1286

Schmid A, Duncan P, Studenski S. Improvements in speed-based gait classifications are meaningful. *Stroke* 2007; 38:2096-2100.

Schmid, A. A., & Rittman, M. Consequences of poststroke falls: Activity limitation, increased dependence, and the development of fear of falling. American Journal of Occupational Therapy, 2009; 63, 310–316.

Semmes J, Weinstein S, Ghent L, Teuber H. *Somatosensory changes after penetrating brain wounds in man*. Cambridge, MA: Harvard University Press; 1960

Shamay S, Ng M and Hui-Chan CWY. Transcutaneous electrical nerve stimulation combined with task-related training improves lower limb functions in subjects with chronic stroke. *Stroke* 2007; 38; 2953–2959.

Sherrington CS. *The integrative action of the nervous system*. Cambridge: Cambridge University Press; 1906.

Shoukri M, Asayli M, Donner A. Sample size requirements for the design of reliability study: review and new results. *Statistical Methods in Medical Research* 2004; 13: 1:21

Shumway-Cook A, Patla A, Stewart A, et al; Environmental demands associated with community mobility in older adults with and without mobility disabilities. *Phys Ther* 2002; 82: 670–81.

Shumway-Cook A. & Wollacott, M (eds) *Motor Control: Translating Research Into Clinical Practice* – 4<sup>th</sup> edition 2012. Wolters Kluwer, Lippincott Williams & Wilkins,

Sillar KT, Skorupski P, Elson RC, Bush BM. Two identified afferent neurones entrain a central rhythm generator. *Nature* 1986; 323: 440–443

Sipp AR, Gwin JT, Makeig S, Ferris DP. Loss of balance during balance beam walking elicits a multifocal theta-band electrocortical response. J Neurophysiol 2013; 110: 2050–2060.

Silverman D. Interpreting Qualitative Data. 4<sup>th</sup> edition. SAGE; London. 2011

Simoes-Franklin C, Whitaker T, Newell F. Active and Passive Touch Differentially Activate Somatosensory Cortex in Texture Perception. *Human Brain Mapping* 2011; 32:1067–1080

Skedung, L. et al. Feeling Small: Exploring the Tactile Perception Limits. *Sci. Rep.* 2013; 3: 2617;

Smith T, Davies L, Hing C. A systematic review to determine the reliability of knee joint position sense assessment measures. *The Knee* 2013; 20: 162–169

Smith PS, Hembree JA, Thompson ME. Berg Balance Scale and Functional Reach: determining the best clinical tool for individuals post acute stroke. *Clin Rehabil*. 2004;18(7):811-8.

Smith J and Firth J. Qualitative data analysis: the framework approach. *Nurse Researcher* 2011; 18(2): 52–62.

Smith KD, Emerzian GJ, Petrov O. A comparison of calibrated and non-calibrated 5.07 nylon monofilaments. *Foot Ankle Int*. 2000;21(10):852-855

Smania N, Picelli A, Gandolfi M, et al. Rehabilitation of sensorimotor integration deficits in balance impairment of patients with stroke hemiparesis: a before/after pilot study. *Neurol Sci* 2008; 29:313-9.

Smulders K, van Swigchem R, de Swart B et al. Community-dwelling people with chronic stroke need disproportionate attention while walking and negotiating obstacles. *Gait Posture*. 2012; 36 (1): 127–132

Smulders K, Esselink RA, Cools R, Bloem BR (2014) Trait Impulsivity Is Associated with the Risk of Falls in Parkinson's Disease. PLoS ONE 9(3): e91190

Soyuer F, Oztürk A. The effect of spasticity, sense and walking aids in falls of people after chronic stroke. *Disabil Rehabil* 2007;29(9):679-87

Spink, M. J., Fotoohabadi, M., Wee, E., et al. Foot and ankle strength, range of motion, posture, and deformity are associated with balance and functional ability in older adults. *Arch Phys Med Rehabil* 2011; 92(1): 68–75.

Srinivasan M, LaMotte RH (1995) Tactual discrimination of softness. *J Neurophysiol* 73(1):88–101

Srivastava, A and Thomson S. Framework Analysis: A Qualitative Methodology for Applied Policy Research. *JOAAG* 2009; 4(2): 72–79.

Stark, T., Walker, B., Phillips, J., Fejer, R. & Beck, R. Hand-held dynamometry correlation with the gold standard isokinetic dynamometry: A systematic review. *Physical Medicine and Rehabilitation* 2011; 3(5): 472–479.

Stillman BC and McMeeken JM. The role of weightbearing in the clinical assessment of knee joint position sense. *Australian Journal of Physiotherapy* 2001; 47: 247-253

Stolk-Hornsveld F, Crow JL, Hendriks EP, van der Baan R and Harmeling-van der Wel BC. The Erasmus MC modifications to the (revised) Nottingham Sensory Assessment: a reliable somatosensory assessment measure for patients with intracranial disorders. *Clin Rehabil* 2006; 20: 160–72.

Stoesz, M.R., Zhang, M., Weisser, V.D., Prather, S.C., Mao, H., Sathian, K., 2003. Neural networks active during tactile form perception: common and differential activity during macrospatial and microspatial tasks. *Int. J. Psychophysiol*. 50, 41–49.

Styles E. The Psychology of Attention. Taylor & Francis: Psychology press

Sullivan K, Tilson J, Cen S. Et al. Fugl-Meyer Assessment of Sensorimotor Function After Stroke: Standardized Training Procedure for Clinical Practice and Clinical Trials *Stroke*. 2011;42:427-432. Sullivan J & Hedman L. Sensory dysfunction following stroke: Incidence, significance, examination and intervention. *Top Stroke Rehabil*. 2008;15(3):200-217

Suetterlin K & Sayer A. Proprioception: where are we now? A commentary on clinical assessment, changes across the life course, functional implications and future interventions. *Age and Ageing* 2014; 43: 313–318

Sun, W Qipeng Song, Bing Yu, Cui Zhang & Dewei Mao. Test-retest reliability of a new device for assessing ankle joint threshold to detect passive movement in healthy adults, *Journal of Sports Sciences*, 2015; 33(16): 1667-1674,

Svensson E. Guidelines to statistical evaluation of data from rating scales and questionnaires. *J Rehabil Med* 2001; 33: 47–48

Tabachnick B. & Fidell L. *Using multivariate statistics* 6<sup>th</sup> edition. Boston: Pearson Education

Tarricone R. Cost-of-illness analysis. What room in health economics? *Health Policy* 2006; 77: 51–63.

Thies SB, Richardson JK, Ashton-Miller JA. Effects of surface irregularity and lighting on step variability during gait: a study in healthy young and older women. *Gait Posture*. 2005; 22(1):26–31.

Thomson MP, Potter J, Finch PM, Paisey RB. Threshold for detection of diabetic peripheral sensory neuropathy using a range of research grade monofilaments in persons with Type 2 diabetes mellitus. *J Foot Ankle Res*, 2008; 1: 9

Tiedemann A, Sherrington C., & Lord S.R. Physiological and Psychological Predictors of Walking Speed in Older Community-Dwelling People. *Gerontology* 2005;51:390–395

Tinetti, M., Richman, D., et al. (1990). "Falls efficacy as a measure of fear of falling." *J Gerontol* 45(6): 239-243 Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a. 32-item checklist for interviews and focus groups. International Journal for Quality in Health Care. 2007. Volume 19, Number 6: pp. 349 – 357

Townsend N, Wickramasinghe K, Bhatnagar P, et al *Coronary heart disease statistics* 2012 edition. British Heart Foundation: London. P57

Tjernstrom F, Bjorklund M, Malmstrom E-M. Romberg ratio in quiet stance posturography—Test to retest reliability. Gait & Posture 2015; 42: 27-31

Tyson S, DeSouza L. Reliability and validity of functional balance tests post-stroke. *Clin Rehabil*. 2004;18:916–923.

Tyson S, Crow L, Connell L, Winward C, & Hilier S. Sensory Impairments of the lower limb after stroke; A pooled analysis of individual patient data. *Topics in Stroke Rehabilitation* 2013a; 20(5): 441-449

Tyson S, Sadeghi-Demneh E, & Nester C. The effects of transcutaneous electrical nerve stimulation on strength, proprioception, balance and mobility in people with stroke: a randomized controlled cross-over trial. *Clinical Rehabilitation* 2013b; 27(9): 785–791

Tyson S & Connell L. The psychometric properties and clinical utility of measures of walking and mobility in neurological conditions: a systematic review. *Clin Rehabil*. 2009;23:1018-33.

Tyson S, Hanley M, Chillala J et al. Sensory loss in hospital admitted people with stroke: characteristics, associated factors, and relationship with function. *Neurorehabil Neural Repair* 2008; 22:166–72.

Tyson S, Chillala J, Hanley M, et al. Balance disability after stroke. *Phys. Ther.* 2006; 86(1): 30-38.

Uswatte G, Taub E, Morris D, Vignolo M and McCulloch K. Reliability and validity of the upper extremity motor activity log-14 for measuring real world use. *Stroke* 2005; 36: 2493–2496.

Uszynski M, Purtill H, Coote, S. Interrater Reliability of Four Sensory Measures in People with Multiple Sclerosis. *Int J MS Care*. 2016;18 :86–95.

van de Port I G, Kwakkel G and Lindeman E. Community ambulation in patients with chronic stroke: how is it related to gait speed? *J Rehabil Med* 2008; 40 (1): 23–27

van Mierlo ML, van Heugten CM, Post MWM, et al. A longitudinal cohort study on quality of life in stroke patients and their partners: restore4stroke cohort. *Int J Stroke* 2014;9:148–54.

van Swigchem R, van Duijnhoven H, den Boer J et al Deficits in Motor Response to Avoid Sudden Obstacles During Gait in Functional Walkers Poststroke. *Neurorehabil Neural Repair* 2013; 27(3):230-239

Vaz S, Falkmer T, Passmore AE, Parsons R, Andreou P (2013) The Case for Using the Repeatability Coefficient When Calculating Test–Retest Reliability. *PLoS ONE* 8(9): e73990.

Veerbeek J, Kwakkel G, van Wegan E, et al. Early prediction of outcome of activities of daily living after stroke: a systematic review. *Stroke* 2011;42:1482–8.

Vidoni E, Acerra N, Dao E, et al. Role of the primary somatosensory cortex in motor learning: An rTMS study. *Neurobiology of Learning and Memory* 2010; 93: 532–539

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, et al. (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. *PLoS Med* 4(10): e296

von Holst E, Mittelstaedt H (1950) The reafference principle: interaction between the central nervous system and the periphery. *Die Naturwissenschaften* 37:464 –476

Waddington G and Adams R. Discrimination of active plantarflexion and inversion movements after ankle injury. *Australian Journal of Physiotherapy* 1999; 45:7-13

Wade DT, Collin C. The Barthel ADL Index: a standard measure of physical disability? *Int Disabil Stud* 1988; 10: 64–67.

Wagner J, Solis-Escalante T, Griefshofer P. et al. Level of participation in roboticassisted treadmill walking modulates midline sensorimotor EEG rhythms in ablebodeied subjects. *Neuroimage* 2012;63:1203-1211

Walker E, Hyngstrom A, Schmit B. Sensory electrical stimulation improves foot placement during targeted stepping post-stroke *Exp Brain Res*. 2014 ; 232(4): 1137– 1143

Ward R, Caserotti P, Cauley J et al. Mobility-Related Consequences of Reduced Lower-Extremity Peripheral Nerve Function with Age: A Systematic Review. *Aging and Disease*. 2016;7(4): 466-478,

Ward N, Brown M, Thompson A, Frackowiak R. Neural correlates of motor recovery after stroke: a longitudinal fMRI study. *Brain* 2003; 126: 2476-2496

Ward-Griffin C, Hobson S, Melles P et al. Falls and Fear of Falling among Community-Dwelling Seniors: The Dynamic Tension between Exercising Precaution and Striving for Independence. Canadian Journal on Aging 2004 ; 23 (4): 307-318.

Weber A, Saala H, Lieber J et al. Spatial and temporal codes mediate the tactile perception of natural textures *PNAS* 2013; 110 (42): 17107–17112

Weerdesteyn V, de Niet M, van Duijnhoven H, Geurts A. Falls in individuals with stroke. *JRRD* 2008; 45 (8): 1195–1214

Weerdesteyn V, Schillings AM, van Galen GP, Duysens J. Distraction affects the performance of obstacle avoidance during walking. *J Mot Behav* 2003;35:53-63.

Weiner, D. K., Duncan, P. W., et al. "Functional reach: a marker of physical frailty." *J Am Geriatr Soc* 1992; 40(3): 203-207

Westlake K, Wu Y, Culham E. Sensory-Specific Balance Training in Older Adults: Effect on Position, Movement, and Velocity Sense at the Ankle. *Phys Ther*. 2007;87:560–568.

Whelan, P., Bonnot, A., and O'Donovan, M. J. (2000). Properties of rhythmic activity generated by the isolated spinal cord of the neonatal mouse. *J. Neurophysiol*. 84, 2821–2833.

Willems T, Witvrouw E, Verstuyft J, Vaes P, De Clercq D. Proprioception and muscle strength in subjects with a history of ankle sprains and chronic instability. *J Athl Train* 2002;37:487–93

Williams P, Basso M, Case-Smith J and Nichols-Larsen D. Development of the Hand Active Sensation Test: reliability and validity. *Arch Phys Med Rehabil* 2006; 87: 1471–77.

Wingert J, Welder C, Foo P. Age-Related Hip Proprioception Declines: Effects on Postural Sway and Dynamic Balance. *Arch Phys Med Rehabil* 2014;95:253-61

Wingert J, Burton H, Sinclair R, Brunstrom J and Damiano D. Joint-position sense and kinesthesia in cerebral palsy. *Arch Phys Med Rehabil* 2009; 90: 447–53.

Winter D., Patla A, Prince F, et al, Stiffness control of balance in quiet standing. *Journal of Neurophysiology* 1998: 80, 1211–1221.

Winward CE, Halligan PW and Wade DT. Somatosensory recovery: A longitudinal study of the first 6 months after unilateral stroke. *Disab Rehabil*. 2007;29(4):293-299

Winward CE, Halligan PW and Wade DT. Current practice and clinical relevance of somatosensory assessment after stroke. *Clin Rehabil* 1999a; 13: 48–55.

Winward C, Halligan P and Wade D. Somatosensory Assessment after central nerve damage: the need for standardised assessments. *Phys Ther Rev* 1999b; 4: 21–28.

Winward CE, Halligan PW and Wade DT. The Rivermead Assessment of Somatosensory Performance (RASP): standardisation and reliability data. *Clin Rehabil* 2002; 16: 523–33

Witchalls J, Waddington G, Blanch P, Adams R. Ankle Instability Effects on Joint Position Sense When Stepping Across the Active Movement Extent Discrimination Apparatus. *Journal of Athletic Training* 2012;47(6):627–634 Witchalls J, Waddington G, Blanch P, Adams R. Chronic ankle instability affects learning rate during repeated proprioception testing. *Physical Therapy in Sport* 2014;15:106-111

Wolpert D. Pearson K & Ghez C. The Organization and planning of movement. In: Kandel E, Schwartz J, Jessell T, Siegelbaum S, Hudspeth A, editors. *Principles of neural science*. New York: McGraw Hill; 2013. p. 743-767.

Wolpert DM, Diedrichsen J, Flanagan JR. Principles of sensorimotor learning. *Nat Rev Neurosci* 2011;12(12):739e51.

Wood J, Connelly D, & Maly M. "Getting back to real living": A qualitative study of the process of community reintegration after stroke. *Clin Rehabil* 2010; 24(11):1045–56.

Woods AJ, Mennemeier M, Garcia-Rill E, Meythaler J, Mark VW, Jewel GR, Murphy H. Bias in magnitude estimation following left hemisphere injury. *Neuropsychologia*. 2006;44:1406–1412.

World Health Organization (WHO). *International Classification of Functioning, Disability and Health*. Geneva: World Health Organization; 2001.

Wright W, Ivanenko & Gurfinkel V. Foot anatomy specialization for postural sensation and control *J Neurophysiol* 2012; 107: 1513–1521,

Wutzke C, Mercer V, and Lewek M. Influence of Lower Extremity Sensory Function on Locomotor Adaptation Following Stroke. *Top Stroke Rehabil* 2013; 20(3): 233-240

Xu DQ, Li JX, Hong Y. Effect of regular Tai Chi and jogging exercise on neuromuscular reaction in older people. *Age Ageing* 2005; 34: 439–44.

Yalcin E, Akyuz M, Onder B, et al Position Sense of the hemiparetic and nonhemiparteic ankle after stroke: is the non-hemiparetic ankle also affected? *Eur Neurol* 2012; 68:294-299 Yan T and Hui-Chan CWY. Transcutaneous electrical stimulation on acupuncture points improves muscle function in subjects after acute stroke: a randomised controlled trial.*J Rehab Med* 2009; 41: 312–316.

Yardley, L., Beyer, N., Hauer, K., et al Development and initial validation of the Falls Efficacy Scale-International (FES-I). *Age and Ageing*, 2005 34(6), 614-619.

Yasuda K, Sato Y, limura N, Iwata H. Allocation of attentional resources toward a secondary cognitive task leads to compromised ankle proprioceptive performance in healthy young adults. *Rehabil Res Prac* 2014;2014:7.

Yelnik A, Colle F, Bonan I et al. Disabling overactivity of the extensor hallucis longus after stroke: clinical expression and efficacy of botulinum toxin type A. Arch Phys Med Rehabil 2003; 84(1): 147-9

Yelnik, A.P., et al., Postural visual dependence after recent stroke: assessment by optokinetic stimultaion. *Gait & Posture*, 2006. 24(3): p. 262-269.

Yekutiel M. (Ed). Sensory Re-education of the hand after stroke. 2000. Wiley.

Yong R, Karas TJ, Smith KD, Petrov O. The durability of the Semmes-Weinstein 5.07 monofilament. *J Foot Ankle Surg*. 2000;39(1):34-38.

Yoshioka, T., Bensmaia, S. J., Craig, J. C.&Hsiao, S. S. Texture perception through direct and indirect touch: An analysis of perceptual space for tactile textures in two modes of exploration. *Somatosensory And Motor Research* 2007; 24:53–70.

You S-H Joint Position Sense in Elderly Fallers: A Preliminary Investigation of the Validity and Reliability of the SENSERite Measure. *Arch Phys Med Rehabil* 2005;86:346-52.

Youden, W.J. Index for rating diagnostic tests. Cancer. 1950; 3: 32–35

Zanto T Gazzaley A. Neural Suppression of Irrelevant Information Underlies Optimal Working Memory Performance. *Journal of Neuroscience*, 2009; 29(10):3059–3066 Zehr E, Nakajima T, Barss T et al. Cutaneous stimulation of discrete regions of the sole during locomotion produces "sensory steering" of the foot. *BMC Sports Science, Medicine, and Rehabilitation* 2014, 6:33

Zhang S & Li L The differential effects of foot sole sensory on plantar pressure distribution between balance and gait. *Gait & Posture* 2013;37: 532–535

Zweig MH, Campbell G (1993) Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clinical Chemistry* 39:561-577