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The effect of an exercise intervention on peripheral sensorimotor function in neuropathic diabetics

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2011

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy
Abstract

Peripheral neuropathy is the first and most common microvascular complication of diabetes mellitus, and involves the distal-to-proximal necrosis of peripheral nerves. Loss of peripheral sensory function, combined with confounding autonomic and neuromuscular complications, leads to an increase in the risk of plantar ulceration due to traumatic or repetitive loading. The evidence for the effectiveness of an exercise intervention in improving sensorimotor function in this population is building, but care is needed when implementing these interventions due to the risk of exacerbating associated neuropathic complications. Therefore the purpose of the current thesis was to investigate the effect of a low-impact balance and lower limb strength training intervention on the sensorimotor complications of peripheral diabetic neuropathy. Ten diabetics with peripheral neuropathy (age 61 ± 9 yrs, BMI 32 ± 5) underwent a twice-weekly supervised low-impact exercise intervention for 12 weeks, which comprised of balance board, isolated ankle strength and passive strength training components. Two pre-intervention (0-weeks and 4-weeks), and two post-intervention (16-weeks and 28-weeks) biomechanical assessments were performed to assess the effectiveness of the intervention. During these assessments six experimental components were investigated, each of which addressed a different aspect of sensorimotor function. These components included sensory threshold, postural stability, gait, foot morphology and plantar loading, muscle strength and quality of life. Despite the observation of low group homogeneity in terms of sensory function, significant improvements in this measure were observed following the intervention; however it was observed that those participants with the most severe sensory loss exhibited no change. It was theorised that these findings were best explained by an improvement in the function of pre-existing sensory nerves, most probably due to improved vascular flow. Due to a low sample size, the current study lacks the statistical power to make any definitive statements regarding the efficacy of the intervention in improving sensory function in a wider neuropathic population. No significant group improvements in the multiple measures of motor function were observed as a result of the intervention. It was theorised that these findings were best explained by a combination of an absence of severe motor pathology in most instances and the inability of the current low-intensity exercise intervention to cause motor adaptation in the instances where dysfunction was found. No significant group improvements in quality of life were
observed following the intervention, possibly due to relatively high quality of life levels in the
current participants prior to the intervention. This is the first study to exhibit quantifiable
changes in sensory function as a result of a low-impact balance and strength training
intervention in a neuropathic diabetic population. This is also the first study to investigate the
effect of an exercise intervention on the kinematic and kinetic qualities of neuropathic gait, as
well as the first study to investigate the effect of an exercise intervention on foot morphology
and plantar loading in this population. Future research should incorporate advanced
peripheral and cortical neural imaging techniques, as well as measures of peripheral vascular
flow, in order to further understand the observed changes in sensory function.
For my family
Acknowledgements

This body of work would not have been possible without the contribution of an incredible group of people. First and foremost, I am eternally grateful to the study participants who gave so much of their time and energy. It is people like them that make health research possible. My main supervisor for most of my PhD studies, Dr. Sharon Walt, provided me with consistent accountability. Our meetings were an invaluable source of feedback and encouragement, especially during the tough times. The inspiration for this study was Assoc. Prof. Uwe Kersting, without whom I would not be following this career path. His passion for research and optimistic manner are truly infectious qualities that I hope to emulate. Prof. Dr. Dieter Rosenbaum, my other academic ‘Dad’ and prolific researcher had no good reason to provide the level of attention to me that he has over this process, but he did anyway. I think it’s because of my Hobbit feet. Dr. Paul Marshall, the inspiration for the intervention employed in this study, is my yardstick for academic quality – if Paul is happy, then I am happy. My lab friends Nico Kurpiers, Paul McAlpine and Megan Moreau have provided me with great support, and were always happy to volunteer for pilot experiments.

The Health Research Council of New Zealand provided the funding for this study, as did the University of Auckland through the brilliant PReSS account scheme. I am eternally grateful to these sources, without which I could not have completed the current study. From the Department of Sport and Exercise Science I gratefully acknowledge the support of Bruce Rattray, Kathleen Rushworth, Mandie Barber and Phil Lacey.

My Mum and Dad always reinforced that I could have anything that I want if I worked hard enough for it. This thesis is proof of their honesty. My brother Dallas has always provided a vast shadow under which I could develop my own interests without Mum and Dad worrying too much about what I was doing with my life. My sister Nicole is my constant inspiration, and the reason why I am passionate about helping those with pathological conditions. My Nana and Papa have always provided a loving welcome whenever I needed to get out of Auckland for a couple of days at the beach. Thank you all so much for your love and support. Finally, to my wife Sarah and daughter Olivia – my little family. This thesis was as hard on them as it was on me. Their love, encouragement and ability to listen to my rants were as important in finishing this study as all of the biomechanical tools combined. This thesis really belongs to them.
# Table of Contents

Abstract ...................................................................................................................................... i
Acknowledgements .................................................................................................................. iv
Table of Contents ..................................................................................................................... v
List of Tables .......................................................................................................................... viii
List of Figures ........................................................................................................................... x
Glossary ................................................................................................................................... xii

**Chapter One: Introduction** ................................................................................................... 14
  The Problem ......................................................................................................................... 15
  Thesis Background ............................................................................................................... 15
  Purpose of Thesis ................................................................................................................. 16
  Overview of Thesis .............................................................................................................. 17
  General Aims and Hypotheses ............................................................................................. 18

**Chapter Two: General Literature Review** ........................................................................... 19
  Overview of General Literature Review .............................................................................. 20
  Diabetes and its Complications ............................................................................................ 21
  Pathogenesis of Diabetic Neuropathy .................................................................................. 22
  Epidemiology of Diabetic Neuropathy ................................................................................. 24
  Symptoms of Diabetic Neuropathy ...................................................................................... 25
  Current Treatment Modalities ............................................................................................. 33
  Low-Impact Exercise Interventions ..................................................................................... 37
  Summary of General Literature Review .............................................................................. 41

**Chapter Three: The Intervention** ......................................................................................... 43
  Introduction .......................................................................................................................... 44
  Exercise Modalities .............................................................................................................. 45
  Frequency of Intervention .................................................................................................... 53
  Intensity of Intervention ....................................................................................................... 53
  Supervision of Intervention ................................................................................................. 54
  Participant Recruitment ........................................................................................................ 56
  Overview of Study Design ................................................................................................... 61
  Conclusion ............................................................................................................................ 63

**Chapter Four: Effect of the Intervention on Sensory Function** ........................................ 64
Discussion .......................................................................................................................... 199
Conclusions ........................................................................................................................ 202

Chapter Ten: General Discussion, Recommendations and Conclusions ............... 203

General Discussion ............................................................................................................. 204
Recommendations .............................................................................................................. 212
Final Conclusions ............................................................................................................... 219
Originality of Research ..................................................................................................... 220

Appendices ............................................................................................................................ 221

Appendix 1: Kinematic and Kinetic Model ................................................................. 222
Appendix 2: Centre of Pressure Calculations ................................................................. 245
Appendix 3: Balance Results Omitted from Chapter Five ............................................. 253
Appendix 4: Gait Results Omitted from Chapter Six ....................................................... 264
Appendix 5: Monofilament Protocol Sheet ................................................................. 279
Appendix 6: Participant Information Sheet and Consent Form .................................... 281
Appendix 7: Pressure Distribution System Reliability Study ...................................... 291

References ............................................................................................................................. 300
List of Tables

Table 3.1: Progression of exercise difficulty and repetition. .......................................................... 53
Table 4.1: Participant demographic information ............................................................................ 69
Table 4.2: Sensory threshold results ............................................................................................. 73
Table 5.1: List of static, dynamic and virtual markers and their anatomical placement ............... 95
Table 5.2: Postural stability outcome measures and formula(e) ..................................................... 99
Table 5.3: List of segments with the markers and joint centres ..................................................... 101
Table 5.4: Root mean square of CoP distance to the mean for AP and ML directions ............... 104
Table 5.5: CoP displacement for AP and ML directions ............................................................... 105
Table 5.6: Velocity of CoP for AP and ML directions ................................................................... 106
Table 5.7: CoP ellipse area ......................................................................................................... 107
Table 5.8: Root mean square of CoP - CoM ............................................................................. 109
Table 6.1: Participant demographic information ......................................................................... 129
Table 6.2: Temporal-spatial results ............................................................................................. 134
Table 6.3: CoP - CoM results for the AP and ML directions during gait ...................................... 142
Table 7.1: Foot morphology results ........................................................................................... 161
Table 8.1: Peak isometric torque results ...................................................................................... 184
Table 9.1: SF-36 quality of life results .......................................................................................... 198
Table A3.1: Romberg ratio results for standard and foam surface conditions .......................... 255
Table A3.2: Foam ratio results for eyes open and eyes closed .................................................... 256
Table A3.3: Cross-correlation and latency between hip I/E rotation moment and ML CoP movement ....................................................................................................................... 258
Table A3.4: Cross-correlation and latency between hip Abd/Add moment and ML CoP movement ................................................................................................................................. 259
Table A3.5: Cross-correlation and latency between hip F/E moment and AP CoP movement ................................................................................................................................. 260
Table A3.6: Cross-correlation and latency between knee F/E moment and AP CoP movement ................................................................. 261
Table A3.7: Cross-correlation and latency between ankle I/E moment and ML CoP movement ........................................................................................................ 262
Table A3.8: Cross-correlation and latency between ankle F/E moment and AP CoP movement ........................................................................................................ 263
Table A4.1: Trunk and pelvis range of movement during gait .......................................................... 266
Table A4.2: Hip range of movement during gait ............................................................................. 267
Table A4.3: Knee range of movement during gait .......................................................................... 268
Table A4.4: Ankle range of movement during gait ....................................................................... 269
Table A4.5: Peak hip moment during stance phase of gait ............................................................ 271
Table A4.6: Timing of peak hip moment during stance phase of gait ............................................. 272
Table A4.7: Peak knee moment during stance phase of gait ......................................................... 273
Table A4.8: Timing of peak knee moment during stance phase of gait ......................................... 274
Table A4.9: Peak ankle moment during stance phase of gait ....................................................... 275
Table A4.10: Timing of peak ankle moment during stance phase of gait ....................................... 276
Table A4.11: Peak joint powers during stance phase of gait ....................................................... 277
Table A4.12: Timing of peak joint powers during stance phase of gait ......................................... 278
List of Figures

Figure 2.1: Pathogenesis of diabetic neuropathy ................................................................. 23
Figure 2.2: Stages of diabetic neuropathy ......................................................................... 24
Figure 2.3: Example of ‘clawing’ of toes ........................................................................... 29
Figure 2.4: Contributing factors to the ulceration of the diabetic foot .............................. 31
Figure 3.1: Balance board exercises ................................................................................. 46
Figure 3.2: Isolated ankle strength exercises ................................................................. 49
Figure 3.3: Passive stretching exercises ........................................................................... 51
Figure 3.4: Reasons for exclusions and corresponding numbers of excluded patients ....... 60
Figure 3.5: Overview of study design .............................................................................. 62
Figure 4.1: The 20-monoﬁlament Semmes-Weinstein set ................................................. 70
Figure 4.2: A typical 4-2-1 Semmes-Weinstein testing protocol ........................................ 72
Figure 5.1: Four conditions for standing balance trials ................................................... 92
Figure 5.2: Marker placement for modiﬁed Cleveland Clinic model ................................. 94
Figure 5.3: Cross-correlation coefﬁcient (r) results between AP CoP movement and ankle, knee and hip F/E moments during the SS condition for the dominant limb .......... 110
Figure 5.4: Cross-correlation coefﬁcient (r) results between ML CoP movement and ankle I/E, hip Ab/Ad and hip rotation moments during the SS condition for the dominant limb… 111
Figure 5.6: Time to cross a beam (left) and balance index (right) results from Allet et al. (2010b) .................................................................................................................. 113
Figure 6.1: Walkway and force platform setup for collection of gait trials ....................... 130
Figure 6.2: Trunk, pelvis and hip joint angle during gait cycle ......................................... 136
Figure 6.3: Knee and ankle joint angle during gait cycle .................................................. 137
Figure 6.4: Joint moments during gait cycle ..................................................................... 139
Figure 6.5: Joint powers during gait cycle ....................................................................... 140
Figure 7.1: Novel EMED-AT pressure distribution platform ........................................... 156
Figure 7.2: The PRC mask: division of the foot into regions, with geometry lines .......... 158
Figure 7.3: Average values for plantar loading measures for all foot regions ............... 163
Figure 7.4: Within-session variability results for plantar loading measures ............... 165
Figure 7.5: Peak pressure beneath the dominant lateral forefoot ............................... 166
Figure 7.7: Peak pressure beneath the non-dominant hallux of the participant that sustained an ulcer post-intervention, plotted alongside the group average for this region .......... 171
Figure 8.1: The Biodex isokinetic dynamometer .......................................................... 180
Figure 9.1: Typical questions from the SF-36 related to physical functioning .......... 195
Figure 9.2: SF-36 results for bodily pain ................................................................. 197
Figure A1.1: Figure showing the line C and the angles $\beta$ and $\theta$ .......................... 229
Glossary

**Abd/Add:** Abduction / Adduction.

**ADA:** American Diabetes Association.

**AP:** Anterior / Posterior.

**ATP:** Adenosine tri-phosphate.

**BMI:** Body mass index.

**BW:** Body weight in kilograms.

**CMDHB:** Counties-Manukau District Health Board. All participants in the current study were recruited within the CMDHB catchment area.

**CoM:** Centre of mass.

**CoP:** Centre of pressure.

**CoV:** Coefficient of variation.

**CVD:** Cardiovascular disease.

**Diabetes mellitus:** A metabolic dysfunction characterised by consistent hyperglycaemia, caused by deficits in insulin activity and/or proliferation from the pancreas.

**F/E:** Flexion / Extension.

**FL:** Foot length.

**Foot morphology:** Refers in the current thesis to the structural and geometric characteristics of the foot under dynamic plantar loading conditions.

**HbA1c:** Glycosylated haemoglobin.

**I/E:** Internal / External.
JC: Joint centre.

kPa: KiloPascals, a unit of pressure.

ML: Medio / Lateral.

Motor function: Refers in the current thesis to the extent of ability in utilising motor actuators to perform given dynamic tasks.

Neuropathy: Refers in the current thesis to the peripheral, bilateral loss of sensorimotor function as a result of nerve death due to diabetic complications.

Nm: Newton-metres, a unit of torque.

Postural stability: Refers in the current thesis to the extent of ability in maintaining upright standing balance.

QoL: Quality of life.

Sensory function: Generally refers in the current thesis to peripheral touch sensation.

SF-36: Short-form, 36-item quality of life questionnaire.

SW: Semmes-Weinstein monofilament.
Chapter One

Introduction
Introduction

The Problem

In 2009, Bharara et al. proposed a “call to arms” in the battle against diabetes. The authors cited epidemiological evidence that while death or injury worldwide from landmines occurred every thirty minutes, a limb is amputated due to diabetic complications every thirty seconds (Bharara et al., 2009). Peripheral neuropathy is the first and most common microvascular complication experienced by diabetics (Yasuda et al., 2007), and involves the necrosis of peripheral nerves in a distal to proximal fashion (Ziegler, 2008). The loss of peripheral sensory function, combined with confounding autonomic and neuromuscular complications (Boulton, 1992; Tavee & Zhou, 2009), leads to an increase in the risk of plantar ulceration due to traumatic or repetitive loading (Quattrini, Tavakoli, et al., 2007). These ulcers can become infected, and due to reduced healing capacity (Cunha, 2000) infected wounds can become gangrenous and lower limb amputation may be required (Boulton, 1992).

Thesis Background

There are no pharmaceutical cures for peripheral neuropathy, and the best that can be achieved with this type of treatment is the cessation of painful neuropathic symptoms (Yuen et al., 2002). While the evidence for the effectiveness of an exercise intervention in these populations is growing, there is a hesitancy to conduct these interventions due to the risk of exacerbating their condition. Considering the possibility of causing plantar tissue damage or aggravating autonomic conditions, it is of vital importance that the modus of exercise that is employed in this population is either non- or only moderately-weight-bearing and low-impact in nature (Colberg et al., 2010; Zinman et al., 2004). A small-scale study by Fisher et al. (2007) exhibited improvements in peripheral sensorimotor nerve conduction measures following an aerobic training programme in five neuropathic diabetics; however their exercise intervention involved cardiovascular training up to 75% of maximum oxygen uptake. The authors argue that it was safe to conduct their intervention since no participants sustained complications as a result of it; however this is unsound reasoning that could have placed the participants of that study at increased risk of adverse complications. However, this research
Introduction

did show that it is possible to improve peripheral neural function via an exercise intervention in neuropathic diabetic populations.

Recent work by Allet et al. (2010a; 2010b) has built on the work of Richardson et al. (2001) by exhibiting improvements in clinical measures of gait and balance in neuropathic diabetics via a low-impact exercise intervention. These interventions reduce the likelihood of a patient sustaining plantar injury, and are therefore highly desirable for use in neuropathic populations. However these studies are lacking in terms of sophistication of outcome measures that may have helped explain their findings, offering no insight regarding sensorimotor function beyond clinical measures such as walking speed and unipedal balance time.

Purpose of Thesis

Based on previous research, it appears possible that a structured exercise intervention could have significant clinical benefit to neuropathic diabetic populations. However caution must be employed when designing exercise modalities for this population, due to the risk of overloading an insensate foot and exacerbating any underlying autonomic conditions. The implementation of a low-impact exercise intervention which reduces stress on these tissues has been shown to be effective at improving some clinical measures of gait and balance in neuropathic populations. However it remains unknown whether such an intervention can improve sensory function, and in cases where motor improvements have been observed following these interventions the mechanisms behind these improvements also remain unknown.

Therefore the purpose of the current thesis was to investigate the effect of a low-impact exercise intervention on the sensorimotor complications of peripheral diabetic neuropathy.
Introduction

Overview of Thesis

The current thesis is comprised of six experimental components, each of which addresses the effect of the exercise intervention on different aspects of sensorimotor function. Prior to these components, the current introductory chapter provides an overview of the problem, thesis background and purpose, and general experimental aims and hypotheses. Each component also has its own set of specific aims and hypotheses, and these are exhibited in their respective chapters.

Chapter 2 provides a general review of the literature regarding diabetes and its complications, an overview of the epidemiology, pathogenesis and symptoms of diabetic neuropathy, and finishes with a review of current and potential treatment modalities.

Chapter 3 provides a detailed description of the design of the current exercise intervention, as well as a description of the recruitment process and an overview of the study design.

Chapters 4 through 9 contain each of the six experimental components, with their own review of literature pertinent to the component as well as methodology, results and discussion sections.

Following the presentation of these experimental components, Chapter 10 of this thesis combines all findings into discussion points, recommendations and conclusions. The appendices include a full description of the kinematic and kinetic model and centre of pressure calculations, as well as postural stability and gait results omitted from their respective chapters. These are all included as appendices for the sake of brevity in the main thesis body.
General Aims and Hypotheses

There were six general aims of the current study:

1. To design and implement an exercise intervention that is low-impact in nature but relevant in terms of expected benefits to neuropathic diabetic populations;
2. To recruit a group of neuropathic diabetic participants that have no other peripheral complications, to ensure validity of any improvements caused as a result of the exercise intervention;
3. To assess whether the low-impact intervention is able to cause significant improvements in peripheral sensorimotor function;
4. To use kinematic, kinetic and other advanced biomechanical techniques to investigate mechanisms behind any changes in sensorimotor function;
5. To assess the holistic effect of the intervention on health-related quality of life;
6. To remove the intervention and assess its long-term effect at a follow-up assessment.

There were six general hypotheses of the current study:

1. Peripheral sensory function will significantly improve as a result of the intervention;
2. Postural stability will significantly improve as a result of the intervention;
3. Dynamic lower limb function, as measured by gait analysis, will significantly improve as a result of the intervention;
4. Dynamic foot function, as measured by foot morphology and plantar loading analysis, will significantly improve as a result of the intervention;
5. Lower limb muscle strength will significantly improve as a result of the intervention;
6. Health-related quality of life will significantly improve as a result of the intervention;

It was hypothesised that all improvements would return to baseline by the follow-up assessment, following an A-B-A format where A = pre-intervention and B = intervention.
Chapter Two

General Literature Review
Overview of General Literature Review

In the current chapter, a general literature review will be presented. In addition, each experimental component (Chapters 4 – 9) begins with a literature review pertinent to that component. In this chapter, a brief overview of diabetes and its complications will be presented. This will be followed by a description of diabetic neuropathy and its pathogenesis, epidemiology and symptoms. Finally, current and potential treatments of these neuropathic symptoms will be described.
Diabetes and its Complications

In order to understand diabetic neuropathy, we must first understand its cause. Diabetes mellitus is a metabolic dysfunction characterised by consistent hyperglycaemia, or high concentration of glucose within blood, caused by deficits in insulin activity and/or proliferation from the pancreas (ADA, 2005; Desphande et al., 2008) or resistance by tissue to respond to insulin (Colberg, et al., 2010). Diabetes mellitus is categorised as either Type-1 or Type-2.

Type-1 and Type-2 diabetes

Type-1 and Type-2 diabetes differ in their causal roots. Type-1 diabetes, typically diagnosed early in life, is a disorder directly affecting the pancreas, whereby the beta cells which produce insulin in this organ are destroyed (ADA, 2005; Desphande, et al., 2008). Type-2 diabetes is characterised by resistance to insulin, a deficit in beta cell secretion as well as a confounding increase in glucose production by the kidneys (ADA, 2005; Perkins & Bril, 2003). The cause of Type-2 diabetes, while still contentious, can be summarised as being the result of a combination of lifestyle, environment and genetic factors (Aaberg et al., 2008; ADA, 2005). When researchers, as well as popular press, refer to the international proliferation of diabetes as an ‘epidemic’, they are referring to the dramatic increase in rates of Type-2 diabetes (Caballero, 2009). Worldwide incidence of Type-2 diabetes is increasing at a near-exponential rate (Horowitz, 2006).

Complications of diabetes mellitus

Newly-diagnosed diabetics may have very few if any symptoms at all prior to their diagnosis (Aaberg, et al., 2008). The complications of diabetes can be divided into two categories: macrovascular, which include cardio- and cerebrovascular diseases, and microvascular, which include retinopathy, nephropathy and neuropathy (Amini & Parvaresh, 2009). Diabetic neuropathy is the first and most common microvascular complication experienced by diabetics (Yasuda, et al., 2007), and it is this complication which will be the focus of this thesis.
**General Literature Review**

**Diabetic Neuropathy**

The official American Diabetes Association definition of diabetic neuropathy is the presence of peripheral neural dysfunction in diabetic patients following the exclusion of causes other than diabetes (Boulton et al., 2005). The neuropathies associated with diabetes can either be symmetrical or asymmetrical in nature (Perkins & Bril, 2003). The most typical form of diabetic neuropathy is bilateral, symmetrical and peripheral neuropathy, otherwise known as polyneuropathy (Booya et al., 2005; Boulton, et al., 2005) and referred to in the current thesis as diabetic neuropathy.

Diabetic neuropathy involves a gradual ‘dying back’ of nerves, starting from the distal most points of the periphery and progressing proximally, sometimes even as far as the trunk (Tavee & Zhou, 2009; Ziegler, 2008). It is still not completely understood which nerve fibres are the first to be affected by neuropathy; however some evidence suggests that it is the small, unmyelinated fibres which are first affected, resulting in painful symptoms prior to the actual loss of sensation or any decreases in nerve conduction velocity which are linked to large fibre destruction (Yagihashi et al., 2007; Ziegler, 2008). Small peripheral nerve fibres (particularly A-delta and C fibres) are highly sensitive to damage as a result of even short-term hyperglycaemia (Horowitz, 2006).

**Pathogenesis of Diabetic Neuropathy**

The pathogenesis of diabetic neuropathy is multifaceted, comprising of metabolic, neural and vascular alterations to normal peripheral function. Ziegler (2008) provided a summary of the factors which combine to cause the structural and functional alterations to the peripheral nervous system which are typical of diabetic neuropathy (Yagihashi, et al., 2007). These are summarised in Fig. 2.1.
Hyperglycaemia leads to increases in activity of the polyol pathway, the process by which glucose is converted to sorbitol by the enzyme aldose reductase (Yagihashi et al., 2007).

This leads to a surplus of sorbitol and fructose within cells, as well as a decrease in Sodium-Potassium ATPase activity which regulates the concentration of sodium and potassium inside cells (Ziegler, 2008).

These disruptions to metabolic processes result in damage to microvascular and neural structures, including Schwann cells which sheath peripheral neurons to allow increased nerve conduction velocity along the axon.

Microvascular disruption causes a reduction in oxygen supply to tissue (hypoxia) and a lack of adequate blood supply (ischemia).

End-products of glycation, the process where glucose or fructose molecules are bound to proteins without enzyme activity, accumulate on nerve and blood vessel proteins (Horowitz, 2006; Sima, 2003).

Expression of nerve growth factor and insulin-like growth factor is reduced.

Axonal transport is ultimately disrupted.
While the progression of neuropathic symptoms will be described later in this chapter, the chronological stages of diabetic neuropathy were simplified by Boulton et al. (2004) and these are summarised in Fig. 2.2.

![Figure 2.2: Chronological presentation of the stages of diabetic neuropathy according to Boulton et al. (2004), Table 2, p1460.](image)

**Epidemiology of Diabetic Neuropathy**

It is estimated that approximately 100 million people worldwide are diabetic (Jagodic et al., 2007). Estimates of neuropathy incidence are vague, with reported incidence ranging between 12-60% of diabetics (Amini & Parvaresh, 2009; Horowitz, 2006; Kramer et al., 2005; Tesfaye et al., 2007; Yagihashi et al., 2007). Diabetics with poor glycaemic control, exhibited by high levels of glycosylated haemoglobin (HbA1c), are 30% more likely to suffer from neuropathy at some stage in their lives than those with good glycaemic control (Booya, et al., 2005). The risk of the development of diabetic neuropathy has been shown to be proportional to diabetes and hyperglycaemia duration (Aaberg, et al., 2008); however there have been reported incidences of neuropathy in adolescents with Type-2 diabetes (Karabouta et al., 2008).

The rate of ulceration among diabetics is as high as 25% (Gupta et al., 2010), while an astonishing 60-70% of all these ulcers are primarily caused by neuropathic complications (Gordois et al., 2003). Neuropathy is therefore the principal cause of plantar ulceration in diabetics, and a great majority (80%) of lower limb amputations are preceded by a foot ulcer (Quattrini, et al., 2007). Diabetics are 15 times more likely to require lower limb amputation than non-diabetics (Ziegler, 2008), and 15% of diabetics with neuropathy will require foot
amputation (Booya, et al., 2005; Feldman et al., 1999). These alarming statistics highlight the need for pre-ulceration intervention in this population.

**Symptoms of Diabetic Neuropathy**

The symptoms of diabetic neuropathy are often divided into two groups: positive symptoms, such as pain, and negative symptoms, such as loss of sensation. Linking the word ‘positive’ to pain seems to be a conflict in terms, however it is the so-called ‘negative’ symptoms which are the most dangerous to the function and morbidity of the diabetic foot (Horowitz, 2006; Yagihashi, et al., 2007).

**Neuropathic Pain**

The painful symptoms of diabetic neuropathy can be attributed to nerve impulses caused by nerve fibre degeneration, as well as by nerve fibres which are attempting to regenerate but are unable to. Specifically, there is irregular activity of peripheral nerves and the dorsal root ganglia, the portion of the spine which contains the cell bodies of sensory neurons (Benbow et al., 1999; Spruce et al., 2003). This central sensitisation results in allodynia or hyperaesthesia, a condition where very light stimuli cause disproportionate amounts of pain to the sufferer (Andreasen et al., 2006). Once these nerve fibres cease activity or are degenerated, it follows that sensation from that region will also be lost (Baba et al., 2006; Yagihashi, et al., 2007).

Pain is the principal reason why diabetics with neuropathy initially seek medical attention (Tesfaye et al., 2007). Pain is a protective mechanism, the purpose of which is to prevent further injury by forcing a volitional response. The insensate foot that results from diabetic neuropathy is therefore the most dangerous factor in the ultimate amputation of the lower limb (Levin, 1998; Quattrini, et al., 2007); in the absence of pain, patients will not seek medical attention and foot complications will go unnoticed (Boulton, 1992). For example, a non-diseased individual who steps on a sharp object will immediately remove the object to prevent further pain; however a neuropathic diabetic who has lost sensation will not sense that they have stepped on the object, and therefore worsen the outcome of the original insult.
General Literature Review

Levin (1998) described an occurrence where a neuropathic diabetic was alerted to the presence of a foot wound by their spouse, when the latter discovered blood-soaked socks and bed sheets.

Loss of Peripheral Neural Function

The symptoms of diabetic neuropathy are linked to functional and physical changes in peripheral nerves. As mentioned, this includes a distal-to-proximal loss of nerve fibres (Yagihashi, et al., 2007), generally beginning with small fibres and progressing to larger fibres. Kramer et al. (2005) described the neural abnormalities associated with diabetic neuropathy as including nerve demyelination, increases in distal latency and axonopathy, which includes the reduction of sensorimotor nerve action potentials.

The loss of neural function due to diabetic neuropathy leads to symptoms such as loss of motor strength and reflexes – particularly in the lower limb – as well as reduced proprioception, decreased thermal and pressure sensation and a regression in vibration detection threshold (Park et al., 2007; Tesfaye, et al., 2007). Diabetes has been correlated with an annual 0.5 – 1% decrease in sensorimotor nerve conduction velocities (Brown et al., 2004), and there is a relationship between poor glycaemic control and decreases in motor nerve conduction velocity (Almeida et al., 2008). Regarding loss of sensation, patients with neuropathy affecting sensorimotor function generally have a ‘stocking’ loss of sensation, where the pattern of sensory loss mimics the shape of a stocking (Boulton, 1992).

Damage to neural structures is not solely limited to patients who are deemed to be beyond some ‘threshold’ of neuropathy. An individual who exhibits pre-diabetic symptoms, such as irregular hyperglycaemia and evidence of insulin resistance, may already be suffering damage to peripheral nerves (Singleton & Smith, 2008).

Autonomic Dysfunction

In this thesis, autonomic dysfunction refers to the cardio- and cerebrovascular dysfunctions that result from diabetic neuropathy. It has been approximated that 54% of Type-1 diabetics and 73% of Type-2 diabetics will suffer from some form of autonomic
dysfunction (Horowitz, 2006). Autonomic neuropathy is highly dangerous in terms of mortality, particularly if cardiovascular autonomic neuropathy is present (Boulton, et al., 2005).

There are several signs that autonomic dysfunction has occurred in diabetic patients. These include thermal alterations to the foot, dry skin and the presence of callous under high-pressure plantar surfaces (Boulton, et al., 2005). Lower limb blood flow can be altered in neuropathic diabetics, which in turn causes a decrease in the transport of blood-carried nutrients to the periphery (Varkonyi & Kempler, 2008). Autonomic dysfunction in neuropathic patients has been shown to cause arterio-venous shunting, a mechanism where blood travels directly from arteries to veins, bypassing the capillary network. As a result, there is a decrease in the flow of blood-carried nutrients to peripheral tissue, and the neuropathic foot may be warm to touch and veins may be prominent (Boulton, 1992; Boulton, et al., 2005).

Due to autonomic dysfunction, neuropathic diabetics may lose the ability to produce sweat at the feet. This causes skin to dry and harden, increasing the risk of callous and ulcer development (Boulton, 1992; Ziegler, 2008). The symptoms of diabetic autonomic neuropathy also include exercise intolerance, tachycardia at rest (>100bpm), as well as motor and neurovascular dysfunction (Boulton, et al., 2005). These complications are a serious consideration when designing any type of exercise intervention in these populations, since autonomic neuropathy may be present but undiagnosed.

**Motor Dysfunction**

It has been proposed that the symptoms of peripheral neuropathy follow a ‘staging’ process, where initial sensory neuropathy is followed by autonomic neuropathy, and then finally motor neuropathy (Yasuda, et al., 2007). Diabetic neuropathy has a considerable effect on lower limb musculature. These muscles may become progressively weak and atrophied in neuropathic diabetics, and ankle reflexes may regress or disappear (Horowitz, 2006; Ziegler, 2008). This muscle weakness may be caused by the demyelination of the nerves which supply them (Andreassen, et al., 2006). Atrophy of the small muscles of the foot is common (Andersen et al., 2004; Greenman, Khaodhian, et al., 2005) and leads to
conditions such as ‘claw’ toes (Boulton, 1992). It has been shown that the strength of ankle musculature decreases at a rate of 3% per year in neuropathic diabetics, but does not decline in diabetic patients with no neuropathy (Horowitz, 2006). Studies examining lower limb muscle strength have shown a clear impairment of ankle and knee strength compared to healthy controls (Andersen et al., 1998). It has been shown that muscle weakness and dysfunction are more likely to occur in the later stages of diabetic neuropathy (Horowitz, 2006).

Functionally, muscle weakness in neuropathic diabetics is linked to gait abnormalities and an increase in the risk of a fall occurring due to postural instability (Andreassen, et al., 2006). It is known that postural stability is severely reduced in neuropathic diabetics, due to dysfunctions in afferent feedback, lower limb proprioception and joint mobility (Kim & Robinson, 2006; Lafond, Corriveau et al., 2004; Nardone et al., 2006; Richardson & Ashton-Miller, 1996; Simoneau et al., 1996; Simoneau et al., 1994; Uccioli et al., 1997; Vanya et al., 2002). The severity of this instability was illustrated by Boucher et al. (1995), who discovered that neuropathic participants in their study exhibited similar postural stability during quiet standing with their eyes open than that exhibited by non-neuropathic participants who had their eyes shut.

The reflex response of lower limb musculature to unexpected perturbation has been shown to take significantly longer in neuropathic diabetics compared to non-neuropathic diabetics and non-diabetics (Di Nardo et al., 1999). This increase in muscle latency results in an increase in the likelihood of a fall occurring in these populations (Meyer et al., 2004). Gutierrez et al. (2001) found that neuropathic diabetics had a reduced ability to recover from a 5% or 10% lean, and suggested that this was due to a loss of ‘rapidly-available’ ankle strength.

Foot abnormalities and increases in plantar pressure

The neuropathic diabetic foot is at high risk of developing a number of different foot abnormalities additional to ulceration. These include osteomyelitis (bone infection), neuropathic osteoarthropathy (popularly referred to as Charcot foot), edema (swelling) of the foot, calcification (hardening) of the medial artery and the emergence of hallux valgus,
General Literature Review

whereby the hallux points severely lateral toward the second toe (Lavery et al., 1998; Prior, 2001; Thomson et al., 1991; Ziegler, 2008). Foot abnormalities such as ‘clawing’ of the toes and the appearance of ‘gutters’ between the metatarsals due to intrinsic foot muscle atrophy are also common (Boulton, 1992), and may lead to potentially harmful increases in plantar pressure (Bus et al., 2005; Fig. 2.3).

Figure 2.3: Example of ‘clawing’ of toes (left) due to neuropathic diabetic complications compared to no clawing (right); from Bus et al. (2009), Fig. 2, p1066.

Diabetic patients, regardless of neuropathy status, may also exhibit significantly thicker plantar fascia tissue than non-diabetics, again potentially leading to increases in plantar pressure (D'Ambrogi et al., 2003; Duffin et al., 2002). The combination of a flat foot and diabetic neuropathy has been linked with an increase in the likelihood of plantar ulcer occurrence (Sacco et al., 2008).

The elevation of peak plantar loading experienced by the neuropathic diabetic foot has been well documented (Boulton, 2004; Bus et al., 2005; P.R. Cavanagh et al., 1998), as has the correlation between elevated plantar loading and plantar ulceration (P.R. Cavanagh et al., 1998; P.R. Cavanagh & Ulbrecht, 1994; Frykberg et al., 1998). Plantar loading patterns are known to be altered in neuropathic diabetic populations, caused by a combination of structural, muscular and sensory abnormalities (Boulton, 1992; Bus et al., 2005; D'Ambrogi et
General Literature Review

al., 2003; Duffin et al., 2002; Fernando et al., 1991). Therefore the measurement of plantar loading patterns is of particular interest as a diagnostic tool; following a plantar loading assessment, it is possible to diagnose patients as either being at high risk of plantar ulceration or low risk (P.R. Cavanagh & Ulbrecht, 1994).

Ulceration and amputation

The complications of neuropathy each serve to increase the likelihood of foot ulceration (Quattrini, et al., 2007). A likely mechanism of injury can be described.

Neuropathy-derived deficiencies in foot proprioception may cause the foot to load irregularly during gait, raising peak pressures under regions such as the heel, metatarsal heads and toes (Fernando et al., 1991). These increases in pressure are not felt by the neuropathic foot, since it is insensate. These pressures eventually cause the foot to callous under these areas, the formation of which is assisted by the autonomic dysfunction associated with diabetic neuropathy (Boulton, et al., 2005). The presence of callous causes the localisation of loading to very small areas, leading to extreme peak pressures in the area of the callous which again cannot be felt by the neuropathic patient. These extreme pressures are likely to be sufficient to cause damage to the soft tissue underlying the callous. Finally, whether by trauma, friction via incorrect footwear (Boulton & Jude, 2004) or other insult, the callous can break, exposing the damaged underlying tissue. The resulting wound is referred to as an ulcer (Booya, et al., 2005).

Boulton (1992) concisely summarised the multiple contributors to ultimate foot ulceration in diabetic patients. This summary has been adapted and is shown in Figure 2.4.
Figure 2.4: Contributing factors to the ulceration of the diabetic foot. Adapted from Boulton (1992)

Diabetic foot ulcers are the leading cause of non-traumatic amputation in the world (Eldor et al., 2004). The direct link between diabetic neuropathy and 60-70% of these ulcers (Gordois, et al., 2003) is a vivid reminder of the risk of this diabetic complication, and a strong incentive for the implementation of pre-ulceration interventions.

Quality of life

The pain associated with diabetic neuropathy has a considerable impact on the health-related quality of life of the patient (Happich et al., 2008; Ziegler, 2008). There is good evidence for an association between diabetic neuropathy and psychological depression in diabetic patients (Vileikyte et al., 2005). Painful diabetic neuropathy is also linked with great disturbances to normal sleep (Ziegler, 2008), which would also have a detrimental effect on quality of life. It has been shown that health-related quality of life is significantly related to
severity of neuropathic symptoms, whereby as symptoms increase, quality of life decreases (Currie et al., 2006).

**Summary of symptoms**

As diabetic neuropathy progresses, patients may experience painful symptoms such as allodynia. As peripheral nerves die, this pain dissipates and losses in sensorimotor neural function progress. Linked to these losses is dysfunction of autonomic processes, which include a compromised ability of the foot to sweat in order to provide moisture to dermal tissue, and a reduction in vascular flow to the periphery. Also linked to peripheral neural necrosis is loss of motor function, including reductions in muscle strength and postural stability. Alterations in sensorimotor function ultimately place the foot at higher risk of overloading during gait, due to reductions in ankle proprioception and absence of sensation of potentially harmful external loads. All these symptoms place the plantar surface of the foot at increased risk of ulceration following repetitive or extreme loading. These ulcers, left untreated, can lead to amputation of the lower limb.

This section has illustrated the effect of diabetic neuropathy on sensorimotor function, as well as its effect on health-related quality of life. Considering these complications and the proliferation of diabetes worldwide, it is highly desirable to improve these symptoms via an appropriate intervention which does not exacerbate diabetic complications. In terms of the lower limb, the critical goal in neuropathic populations is the prevention of limb morbidity. The improvement of any of the symptoms which ultimately culminate in limb amputation could serve to prevent this occurrence. A number of interventions of differing modality have been employed to improve these symptoms, and these will now be addressed.
Current Treatment Modalities

The current treatment methods for diabetic neuropathy are largely unsatisfactory (Horowitz, 2006). Treatments should principally focus on the causal roots of the condition (Boulton, et al., 2005); unfortunately, it is difficult to design such a therapy since the causal roots of diabetic neuropathy are complex and multi-factorial in nature. However, previous research has shown that it may be possible to systematically improve some of the neuromuscular symptoms that result from this condition, and a variety of treatment modalities have been employed to this effect.

Variety of treatment modalities

The most simple and cost-effective intervention is the effective education of neuropathic patients (Boulton, 1992; Vinik, 2003; Waine, 1992). Boulton et al. (2005) state that education is an important factor in the prevention of ulceration and amputation among neuropathic diabetics.

In contrast to this simplicity, an extreme means of reversing the progression of diabetic neuropathy is a complete transplant of the pancreas. A fully-functioning pancreas would effectively solve the problem of metabolic dysfunction associated with diabetes, and assuming that the patient adheres to a healthy lifestyle this could be effective in reversing their neuropathic condition. However this transplant procedure has many inherent problems (Kramer, et al., 2005), and if a patient has severe loss of peripheral neural function this may not be reversible (Allet, et al., 2010b; Yasuda, et al., 2007). Less extreme but still invasive, some researchers have shown that surgical procedures which decompress the peripheral nerves of the lower extremity may reduce neuropathic pain and restore sensation (Dellon, 2004).

The improvement of vascular function in neuropathic diabetics is linked to an improvement in neuropathic symptoms. Leonard et al. (2004) found that a device known as the Anodyne Therapy System, which increases circulation by dilating arteries and veins, causes improvements in sensation, balance and a reduction in pain in neuropathic patients.
General Literature Review

This research highlights the fact that an improvement in vascular flow via an intervention can lead to improvements in neural function.

Electromagnetic nerve stimulation, as well as external muscle stimulation, have been shown to reduce neuropathic pain (Andreassen, et al., 2006). A novel method of improving balance in neuropathic patients is the use of insoles which vibrate below the threshold of human detection (Priplata et al., 2006). However research on the effectiveness of these treatment modalities is still in its infancy.

Pharmaceutical Treatments

In addition to the control of blood glucose, pharmaceutical therapies are used to aid in the cessation of painful neuropathic symptoms. Various medications, including antiarrythmics, anticonvulsants, antidepressants and vasodilators have been used to this effect (Andreassen, et al., 2006; Varkonyi & Kempler, 2008; Yuen, et al., 2002). Since the previously-discussed polyol pathway is implicated in the progression of neuropathic symptoms, aldose reductase-inhibitors are often prescribed in order to suppress activity of the polyol pathway (Hotta et al., 2006). However, drug therapies also have negative side effects which need to be taken into consideration. Intensive pharmaceutical treatment of diabetes is typically associated with moderate weight gain and hypoglycaemia (Ziegler, 2008).

There are no pharmaceutical therapies which can improve lower limb sensory or motor function, other than by causing an improvement in painful symptoms. In order to improve lower limb dysfunction associated with diabetic neuropathy, the evidence for the efficacy of lifestyle interventions is building.

Lifestyle Treatments

While the merits of physical activity in preventing or managing diabetes have been well documented (Albright et al., 2000; Colberg, et al., 2010; Zinman, et al., 2004), the non-pharmaceutical treatment of diabetic neuropathy has received very little coverage in the literature. In a comprehensive review article by Ziegler (2008) discussing the treatment of
diabetic neuropathy, barely a paragraph is dedicated to alternatives to pharmaceutical treatment.

Sensorimotor recovery following peripheral nerve damage can be improved and hastened by exercise training or some form of physical activity (Seo et al., 2006). Multiple studies have shown improvements in neural function as a result of an exercise intervention in animals with peripheral nerve damage (Cui et al., 2004; L. M. Doyle & Roberts, 2006; Gardiner et al., 1984; Marqueste et al., 2004; Molteni et al., 2004; Pachter & Eberstein, 1989; Sarikcioglu & Oguz, 2004; van Meeteren et al., 1997). However it should be noted that the subjects of these studies were non-human and peripheral nerve damage was caused by the experimenter, as opposed to being a chronic condition with other associated complications.

Some small-scale human studies have shown that diet and exercise may serve to improve the symptoms of neuropathy, including improvements in peripheral nerve function. Smith et al. (2006) showed improvements in cutaneous re-innervation, as well as a reduction in pain, via a simple diet and exercise counselling programme in patients with pre-diabetic neuropathy. However, in this study improvements tended to be short-term after the intervention was removed (Singleton & Smith, 2008). Fisher et al. (2007) conducted an aerobic exercise intervention with a group of neuropathic diabetics, and measured sensorimotor peripheral nerve conduction velocity before and after the intervention. They found significant improvements in these measures as a result of the exercise programme, again showing that it is possible to improve peripheral nerve function via an exercise intervention. However, their selected method of intervention may have placed their neuropathic diabetics at increased risk of complications, a point which will be discussed later in this section.

In a study conducted by Balducci et al. (2006), the researchers showed that a long-term exercise intervention may be able to prevent the onset of diabetic neuropathy. Their study, conducted over four years, showed a significantly greater progression of neuropathic symptoms, such as reductions in nerve conduction velocity and vibration perception, in the group that received no exercise intervention compared to the group that did. It should be noted that no participants had diabetic neuropathy at the beginning of the study, yet 6.5% of the exercise group were diagnosed with this condition at some point in the four-year period; however this is compared 30% of the control group, and therefore incidence rates were significantly improved by the intervention.
Praet et al. (2008) examined the effect of a 10-week resistance and interval training programme on Type-2 diabetics with neuropathy. Their intervention included upper and lower limb resistance exercises using weights, as well as cycling. Outcome measures included body composition, blood pressure, glycaemic control, predicted VO$_2$ max and upper and lower limb strength. It was found that the exercise intervention significantly improved blood pressure and both upper and lower limb strength. The authors of this study suggested that the strength improvements gained by such a short-duration exercise intervention could be an effective catalyst for the continued pursuit of a healthy and active lifestyle by neuropathic patients.

It is also possible to improve autonomic function in diabetic patients via the introduction of an exercise intervention. It has been shown that endothelial function can be improved in diabetics via exercise (N. D. Cohen et al., 2008; Sonne et al., 2007). Several studies have shown improvements in vascular flow (Brandenburg et al., 1999; Colberg et al., 2003), as well as improvements in resting heart rate and heart rate variability (Carnethon et al., 2006). However these studies have primarily been conducted on diabetic patients without neuropathy, so it remains unclear if the same improvements can be gained in this population.

Exercise programmes have generally been discouraged as a treatment modality for patients with diabetic neuropathy, owing to the fact that this population are at a greater risk of sustaining injury from weight-bearing exercises (Albright, et al., 2000; Zinman, et al., 2004). As is obvious from the few articles listed above, there is a lack of well-constructed exercise interventions with appropriate exercise modalities which fulfil the unique requirements of an individual with neuropathic complications. An example of this is the studies conducted by Fisher et al. (2007) and Tesfaye et al. (1992), the latter of which trained neuropathic diabetics up to 80% of their age-predicted maximum heart rate on a treadmill. There are two critical factors which are erroneous in the design of this study: firstly, they trained individuals which may have had underlying cardiovascular autonomic dysfunction up to 80% of their maximum heart rate; and secondly, their training modality was a treadmill, which involves repetitive loading of the plantar surface of the foot. As discussed, this surface is at increased risk of ulcerating in this population and therefore any intervention which repetitively stresses this tissue should not be employed (Zinman, et al., 2004). Tesfaye et al. (1992) did not report whether or not any ulcers or autonomic damage occurred as a result of their study. Likewise, Fisher et al. (2007) state that since no participants suffered any negative consequences as a
result of their cardiovascular exercises – which trained participants up to 75% of their maximum oxygen uptake – the intervention they employed was safe for use in other neuropathic populations. Such reasoning is unsound, and could have placed these patients at risk of developing serious complications as a result of an intervention which should be attempting to improve health and quality of life.

Due to the autonomic and neuromuscular complications of diabetic neuropathy, American College of Sports Medicine and American Diabetes Association position papers state that extreme caution needs to be exercised when stressing these systems in this population (Albright, et al., 2000; Ziegler, 2008). It is therefore of interest to examine the efficacy of low-impact exercise interventions which minimise the risk of exercise-associated complications in improving sensorimotor function in neuropathic diabetics.

**Low-Impact Exercise Interventions**

Due to the increasing awareness of the high risk of limb morbidity in neuropathic populations, the employment of low-impact exercise interventions is gaining credence. Allet et al. (2010a; 2010b) recently showed significant improvements in clinical measures of gait and balance – such as walking speed and time taken to cross a beam – in neuropathic diabetics following a simple, low-impact exercise intervention conducted in a clinical setting. While their outcome measures lacked the sophistication required to investigate the mechanisms behind any observed changes, their results prove that it is possible to cause clinically-relevant improvements in neuromuscular function with an exercise intervention that does not place the neuropathic diabetic at increased risk of developing complications.

There is increasing evidence for the effectiveness of low-impact interventions which focus almost exclusively on the lower limb in improving peripheral motor function. The populations in which these interventions have been employed include those with some form of lower limb motor dysfunction, whether by acute or chronic injury. Such interventions generally include balance and/or lower limb strengthening exercises, and these will now be described.
**Balance training**

Laufer et al. (2007) implemented a balance training intervention in a group of participants who had recently sustained an ankle injury, and investigated the effect of the intervention on postural stability. The balance training programme, as well as measurements of postural stability, were conducted using the Biodex Stability System (BSS), which is essentially a balance or wobble board with the ability to sense and record position. Following three training sessions using the BSS, the authors found improvements in overall and anterior-posterior stability, and this effect lasted for at least two days after the last session. This study shows that ankle instability can be improved with balance training over a very compressed period of time, and that this improvement can last beyond the intervention period. Using a similar training device, Couillandre et al. (2008) conducted a two-month balance training programme on 12 healthy participants. They found improvements in centre of pressure displacement beneath the base of support, and these improvements were particularly evident in the condition where participants were standing on foam to remove cutaneous sensation.

Clark and Burden (2005), intervening in a group of participants with ankle instability, investigated the effect of a balance training programme on the latency of lower limb muscle onset in response to perturbation. The onset latency of peroneus longus and tibialis anterior following a sudden 20° inversion was compared between ten participants who received the intervention and nine who did not. Balance training consisted of 4-weeks of monitored wobble board exercises, performed three times per week, with each session lasting approximately 10 minutes. Significant decreases in tibialis anterior latency (approx. 30%) following perturbation were observed in the exercise group following the intervention, while the control group showed no significant change.

These studies show a positive relationship between neuromuscular function and balance training in healthy populations and those who have a pre-intervention loss of ankle function.

**Low-intensity strength training**

Docherty et al. (1998) trained a group of 10 participants with ankle instability using Thera-Band as a strength training device. Participants conducted 10-minute ankle strength
exercise sessions three times per week for six weeks. Following this intervention, comparisons in ankle strength and joint position sense were made between the intervention group and 10 controls who received no intervention. It was found that this intervention not only improved muscle strength, but also improved the ability of BMI-the participants to sense ankle joint position. This study shows that a specific strength training programme, using simple Thera-Band exercises, is able to improve neuromuscular function in populations who have loss of ankle function. The efficacy of combining the aforementioned balance training techniques with low-intensity strength training at improving neuromuscular function will now be addressed.

**Balance training plus low-impact strength training**

In a study conducted with healthy populations, Linford et al. (2006) conducted a 6-week training programme and investigated latency of peroneus longus onset following ankle perturbation during gait via a trap-door mechanism. Comparisons were made with a control group who received no intervention. The training programme consisted of stretching, balance board and single-leg balance exercises, strength exercises using Thera-Band and power exercises involving single-leg hopping. This programme was supervised and was completed three times per week, with each session lasting approximately 40 minutes. A significant reduction in peroneus longus onset latency following perturbation was observed in the exercise group following the intervention, while the control group remained unchanged.

Richardson et al. (2001) conducted a lower limb-specific strength and balance training programme in 10 neuropathic diabetics (invention group), and compared outcome measures to 10 neuropathic diabetics who received a upper limb strength training programme (control group). The intervention programme consisted of toe and heel raises, inversion and eversion stretches, wall slides and one-legged standing balance exercises. In order to assess postural stability, time in tandem stance (where one foot is placed in front of the other), time in one-legged stance and functional reach length were measured. The exercises were performed daily for a period of three weeks. It was found that the intervention group significantly improved across all of these outcome measures while the control group remained unchanged; in particular, time in one-legged stance improved by more than 100%. This study shows that a training programme specifically focussing on improving balance and lower limb strength
can be successful in neuropathic populations, and only requires a short period of intense training to exhibit benefits.

Matjacic & Zupan (2006) investigated the effect of a short-term dynamic balance training programme on 16 patients with hereditary sensory motor neuropathy. The intervention involved 12 sessions – completed over 13 days – comprised of passive stretching, muscle strengthening and standing balance while performing numerous dynamic tasks. Outcome measures were largely clinical, and included the Berg Balance Scale (based on largely qualitative clinical assessments), Up and Go test (a timed assessment of ability to get out of a chair, walk, turn and return to the chair) and a timed 10 metre walk. It was found that these outcome measures were significantly improved as a result of their intervention.

* * * *

The findings of Allet et al. (2010a; 2010b), Matjacic & Zupan (2006) and Richardson et al. (2001) show that it is possible to improve clinically-relevant measures of neuromuscular function in neuropathic populations via a low-impact balance and lower limb strength training programme. While clinical measures may have been most appropriate for the setting in which these studies took place – generally hospital environments – they lack the sophistication of outcome measures which would be required to help explain the improvements in function that were observed.

This absence of any further information regarding the mechanisms behind observed improvements in gross motor function leaves a gap in the literature which needs to be filled. Is it possible that the improvements obtained by these studies were the result of repetition of balance and strength tasks in populations that were previously unskilled at these tasks, rather than an improvement in peripheral sensorimotor function? Without quantitative measures of sensory function and more specific measures of motor function, this is a question which could not have been addressed by the authors of those previous studies.

Following a review of the relevant literature, the purpose of the current study became apparent; to conduct a low-impact balance and strength training intervention in a neuropathic
diabetic population, and to measure specific markers of peripheral sensorimotor function that could explain any improvements in gross motor function.

Six separate experimental components (Chapters 4 – 9) were included in the current study, each of which relates to an aspect of sensory, motor and quality of life dysfunction described in this general literature review. Chapter 4 investigates the effect of the intervention on quantitative sensory threshold at the foot, using Semmes-Weinstein monofilaments. Chapter 5 investigates the effect of the intervention on postural stability, using three-dimensional kinematic and kinetic techniques. Chapter 6 investigates the effect of the intervention on gait, using temporal spatial as well as three-dimensional kinematic and kinetic techniques. Chapter 7 investigates the effect of the intervention on dynamic plantar loading and foot morphology, using pedobarographic techniques. Chapter 8 investigates the effect of the intervention on muscle strength at the ankle, using dynamometric techniques. In the final experimental component, Chapter 9 investigates the effect of the intervention on health-related quality of life, using the quantifiable SF-36 questionnaire.

This concludes the general literature review. The next chapter will describe the design of the exercise intervention employed in the current study, as well as the recruitment process and overall study design.

Summary of General Literature Review

• The principle symptoms of diabetic neuropathy include loss of sensation, autonomic dysfunction, loss of lower limb proprioception and joint mobility, lower limb muscular atrophy and dysfunction, and alterations to foot morphology

• These symptoms manifest in functional complications such as postural instability, increased plantar loading during gait and reductions in quality of life

• These and associated symptoms can lead to ulceration and lower limb amputation

• While pharmaceutical treatments alleviate painful neuropathic symptoms, the evidence supporting the efficacy of lifestyle interventions in reversing the progression of neuropathy is building
General Literature Review

- Caution must be taken when designing exercise interventions for neuropathic diabetic populations due to their increased risk of autonomic dysfunction and foot morbidity.

- Low-impact exercise interventions have been shown to improve clinically-relevant gross markers of lower limb motor function in neuropathic diabetic populations, but more sophisticated measures of sensorimotor function are required to explain the mechanisms behind such improvements.
Chapter Three

The Intervention
Introduction

The exercise intervention employed in the current study was unique in both its design and in terms of the population to which it was applied. As discussed in Chapter 2, the application of an exercise intervention which focuses on lower limb balance and strength – particularly at the ankle joint – has previously been reserved for populations who exhibit ankle instability due to injury (Clark & Burden, 2005; Docherty, et al., 1998). In the neuropathic intervention study by Allet et al. (2010a; 2010b), some of the exercises employed did target the lower limb but most were daily activity-based, e.g. climbing stairs and moving from sitting to standing. Since improvements in lower limb function have been exhibited by individuals with ankle instability via the use of an intervention which focussed on the lower limb, it was theorised that such an intervention could have a positive effect on neuropathic diabetics who exhibit similar ankle dysfunction, albeit from a different aetiology.

The purpose of the current chapter is to describe the exercise intervention that was employed in the current study, in terms of modalities of exercise, frequency and intensity. Supervision of intervention sessions will also be described. Following this there is a description of the participant recruitment process, including inclusion/exclusion criteria and method of recruitment. This chapter concludes with a chronological overview of study events.
The Intervention

Exercise Modalities

The exercise intervention included a number of balance and strength exercises, designed to particularly stress the ankle joint. There were three main components of the intervention: balance exercises, isolated ankle strength exercises, and passive stretching exercises.

The balance exercises for the current intervention were derived from the paper by Clark and Burden (2005). In their study, the authors took a group of participants with functional ankle instability through a four-week balance board training intervention using these exercises, and showed significant improvements in lower limb motor function as a result. The exercises as they were employed in the current study are exhibited in Fig. 3.1.

The isolated ankle strength exercises for the current intervention were derived from the papers by Docherty et al. (1998) and Linford et al. (2006). Using these exercises, Docherty et al. (1998) showed significant improvements in ankle strength and joint position sense in participants with functional ankle instability, while Linford et al. (2006) showed reductions in latency of lower limb muscle onset following perturbation in healthy participants. The isolated ankle strength exercises as they were employed in the current study are exhibited in Fig. 3.2.

The passive stretching exercises for the current intervention were derived from the paper by Richardson et al. (2001). Using these exercises, the authors of that study showed significant improvements in clinical measures of balance in a neuropathic diabetic population. The passive stretching exercises as they were employed in the current study are exhibited in Fig. 3.3.
Figure 3.1: Balance board exercises (Clark & Burden, 2005)

B1: Feet parallel, anterior-posterior rock

B2: Feet parallel, medio-lateral rock

B3: Feet wide apart, board rotations
Figure 3.1 (cont): Balance board exercises (Clark & Burden, 2005)

B4: As for B1, with hands at top of buttocks

B5: As for B2, with hands at top of buttocks

B6: As for B3, with hands at top of buttocks
Figure 3.1 (cont): Balance board exercises (Clark & Burden, 2005)

**B7**: Left leg, single-limb balancing

**B8**: Right leg, single-limb balancing
**The Intervention**

Figure 3.2: Isolated ankle strength exercises (Docherty, et al., 1998; Linford, et al., 2006)

**S1:** Ankle dorsiflexion against resistance; start position (left) and end position (right)

**S2:** Ankle plantarflexion against resistance; start position (left) and end position (right)
Figure 3.2 (cont.): Isolated ankle strength exercises (Docherty, et al., 1998; Linford, et al., 2006)

**S3:** Ankle inversion against resistance; start position (left) and end position (right)

**S4:** Ankle eversion against resistance; start position (left) and end position (right)
The Intervention

Figure 3.3: Passive stretching exercises (Richardson, et al., 2001)

**P1:** Two-legged plantar/dorsiflexion raises

**P2:** Two-legged inversion/eversion
The Intervention

Figure 3.3 (cont.): Passive stretching exercises (Richardson, et al., 2001)

P3: One-legged plantar/dorsiflexion raises
The Intervention

Frequency of Intervention

The intervention was comprised of two sessions per week for 12 weeks. While this is one session per week less than that employed by Clark and Burden (2005), Linford et al. (2006) or Richardson et al. (2001), their training programmes did not last as long as the current intervention (four, six and three weeks, respectively). The choice of a 12-week intervention period was based on a desire to create an optimum length of intervention, one that was long enough to increase the possibility of causing an effect but not too long so as to avoid a significant loss of participants due to attrition.

Intensity of Intervention

As the intervention progressed, exercise difficulty was increased in order to maximise potential adaptation. Alterations were made to the programme in a step-wise fashion every four weeks. Tab. 3.1 shows this progression.

Table 3.1: Progression of exercise difficulty and repetition over the course of the intervention; numbers refer to exercises listed in Figs. 3.1 – 3.3.

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<th>Weeks 1 - 4</th>
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<td><strong>Thera-Band</strong></td>
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<td>+ 1 set each</td>
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<tr>
<td><strong>Passive</strong></td>
<td>P1 - P2</td>
<td>P2 - P3</td>
<td>P2 - P3</td>
</tr>
<tr>
<td><strong>Strength Exercises</strong></td>
<td></td>
<td></td>
<td>+ 1 set each</td>
</tr>
</tbody>
</table>
The Intervention

Two-legged balance board exercises (B1 – B6) were conducted for 30 seconds per set for two sets, with 30 seconds rest in between sets. At the 5-week mark, difficulty of these exercises was increased by placing the hands at the top of the buttocks (Clark & Burden, 2005). One-legged balance board exercises (B7 – B8) were conducted for 10 seconds per repetition, with 10 seconds rest, for six sets.

The isolated ankle strength exercises conducted with Thera-Band (S1 – S4) were conducted for 10 repetitions in each of the four movement directions for two sets, with one minute rest in between sets. At the 9-week mark, difficulty of these exercises was increased via the addition of a set for each movement direction, and therefore three sets of each exercise were conducted for the last four weeks of the intervention.

The passive stretching exercises (P1 – P3) were conducted for 10 repetitions in each movement direction for two sets, with 30 seconds rest in between sets. At the 5-week mark, the two-legged toe/heel raise stretch was replaced with a single-leg version, and at the 9-week mark an additional set for each movement direction was added (Richardson, et al., 2001).

Supervision of Intervention

Evidence for the effectiveness of self-administered and unsupervised exercise programmes for diabetic populations is poor (Praet, et al., 2008). In a large meta-analysis of the effect of supervision versus no supervision on the effectiveness of exercise interventions on the symptoms of peripheral arterial disease, it was found that supervised exercise was profoundly more effective at improving symptoms, physiological function and holistic quality of life (Shalhoub et al., 2009).

In order to ensure full participation in the intervention, all 24 exercise sessions were supervised by the current author. The supervised sessions were conducted at the homes or places of business of each participant, at the same time and on the same two weekdays for the entire 12-week intervention period. As well as ensuring 100% adherence rates across all participants, the individual supervision of each exercise session provided the opportunity to control the quality of exercise performance, and constant feedback was provided during sessions to this effect. For example, during two-legged balance board exercises participants
were constantly instructed to “keep the board off the ground” as much as possible, which anecdotally requires much greater control of balance than if the board is allowed to rest on the ground at the end of a movement.

Individual supervision also allowed for control of set duration, whereby the timings of sets or number of repetitions to be performed were controlled as per the intervention design. In this way, the amplitude of intervention was kept consistent across all participants. Footwear was standardised across participants for all exercise sessions to minimise the effect of use of footwear of differing construction; in addition, many participants lacked ownership of any athletic footwear appropriate for use in an exercise programme. Therefore all participants conducted the exercise intervention wearing Nike Pegasus athletic footwear. The supervision of participants ensured that this footwear was worn during exercise sessions.

Finally, individual supervision of every exercise session allowed for control of participant safety during the intervention period, of which there were three key aspects. Firstly, by being present during the exercise sessions, the current author was able to ensure that participants did not fall, which was of particular concern during the balance board exercises. As a result, no falls occurred during any exercise session in the current study. Secondly, the current author was also able to monitor exertion levels, to ensure that no participant over-exerted themselves and suffered an injury as a result of a given exercise. Lastly, the twice-weekly interaction with participants enabled the current author to inspect aspects of health relevant to their neuropathic condition, such as the plantar surface of the foot. While checks of the foot were not made at every exercise session, they were conducted intermittently as a means of examining foot health. Anecdotally, no observations were made of foot wounds or severe callous formation that would have required treatment.

The intervention employed in the current study was therefore conducted with utmost care and diligence in terms of avoiding the possibility of any negative consequences to the neuropathic diabetic participants. The intervention used in the current study was considered appropriate for implementation in this pathological population, since the risk of exacerbating the symptoms highlighted in Chapter 2 were minimised. The process of recruiting participants into the current study will now be detailed.
Participant Recruitment

Participants were recruited from the Counties-Manukau region of Auckland, New Zealand. Participants were referred for possible inclusion in the current study by clinicians from Counties-Manukau District Health Board (CMDHB). These clinicians included podiatrists, endocrinologists and specialist diabetes nurses, who practised from multiple clinics around the Counties-Manukau region. Following this referral, an appointment was made with the patient by the current author to further screen each candidate, where each individual inclusion/exclusion criteria was discussed in detail. Based on the outcome of this screening, patients were either included in or excluded from the current study.

Type-1 and Type-2 diabetics were included. Neuropathy status was determined according to the 10g Semmes-Weinstein monofilament test, whereby a monofilament which requires 10g of force to buckle is pressed against a given foot surface and an inability to feel this indicates a loss of protective sensory function (Armstrong, 2000). Participants unable to sense the 10g monofilament at one or more forefoot or toe sites were deemed neuropathic and considered for inclusion in the study. The heel was not used as an indicator of neuropathy based on discussions with CMDHB clinicians, who suggested that due to a thickening of the skin in this area from impact loading, false-positive monofilament results can occur.

A number of pathologies other than diabetic neuropathy could have potentially confounded the results of the current study. For example, a patient with a rheumatoid condition may also exhibit losses in peripheral sensory function (Rosenbaum et al., 2006) exclusive of any neuropathic diabetic condition. Neuropathic diabetic patients may also have severe cardiovascular conditions accessory to their neuropathy that could contraindicate them from participating in an exercise intervention. Therefore, a number of exclusion criteria were included in the current study, to ensure that the group were as homogeneous as possible in terms of their symptoms, and had no contraindications for participating in an exercise intervention. Exclusion criteria for this study included:

- a) Those with cardiovascular disease
- b) Those with current or recently-healed foot ulcers
- c) Those who had pain while walking
The Intervention

d) Those with rheumatism
e) Those with a partial or full amputation of the lower limb
f) Those with a severe lower limb injury or fracture within the past three years
g) Those with severe abnormalities of leg anatomy
h) Those who had recently suffered significant reductions in vision
i) Those who were pregnant

Reasoning for each of these exclusion criteria will now be summarised.

(a) Exclusion of patients with cardiovascular disease (CVD)

As previously mentioned, the exercise intervention employed in the current study was designed to be as low-impact as possible while still specifically targeting key symptoms of diabetic neuropathy. While the exercises undertaken by each participant could not be considered to be aerobic exercise, they were nonetheless acts of physical movement. While the likelihood of any negative cardiovascular consequences of the intervention occurring in patients with underlying CVD could be considered negligible, the risk of such consequences is still greater than in patients without CVD. For this reason, patients with underlying CVD, as diagnosed by CMDHB staff, were excluded from participation.

(b) Exclusion of patients with current or recently-healed foot ulcers

The reasoning for excluding patients with current or recent ulceration was two-fold: firstly, the exercise intervention required participants to complete multiple physical movements with their lower limb, several of which were completed with the participant in a standing position. The proper management of diabetic ulcers requires offloading of the ulcer site as much as possible to allow healing to occur (Bus, Duersen, et al., 2009). While the exercises were low-impact, loading of ulceration sites would occur nonetheless and the risk of re-ulceration or making an existing ulcer worse would increase. Secondly, the existence of an ulcer or recently healed ulcer could affect plantar loading measures taken from the ulcer region, and this may have confounded pre- and post-intervention comparisons of plantar loading since ulcers could have healed during this period, or vice-versa.
The Intervention

(c) Exclusion of patients who had pain during walking

Foot pain can negatively affect walking ability in neuropathic diabetics (Novak et al., 2004). For this reason, patients who reported any pain during walking were excluded from the current study, since any changes in gait over the course of the intervention period may have resulted from improvements in pain levels as opposed to absolute improvements in motor function.

(d) Exclusion of patients with rheumatism

As mentioned, rheumatoid conditions can reduce peripheral sensory function as well as limit lower limb mobility (Rosenbaum, et al., 2006). Therefore patients with rheumatoid conditions were excluded from the current study, since it would not be possible to determine if any improvements in sensorimotor function were a result of improvements in neuropathic or rheumatic symptoms.

(e) Exclusion of patients with full or partial amputation

Lower limb amputees were excluded from the current study due to the obvious alterations in gait exhibited by these individuals (Bateni & Olney, 2002), which among other factors would provide reasons other than the diabetic neuropathy itself for irregularities in lower limb motor function.

(f) Exclusion of patients with a recent severe lower limb injury or fracture

Fractures of the lower limb can significantly alter gait and plantar loading (Becker et al., 1995). For this reason, patients who had sustained a lower limb fracture or injury within three years were not included in the study.
The Intervention

(g) Exclusion of patients with severe lower limb abnormalities

The development of abnormalities to foot structure is a common diabetic complication which results in increases in plantar loading (Bus, 2008). In the current study, patients who had any severe foot deformity were excluded from participation due to their confounding influence on gait and plantar loading results. Minor deviations of the hallux were not considered abnormalities, but candidates with severe hallux valgus - where the hallux overlapped the 2\textsuperscript{nd} toe – or severe hallux varus were excluded.

(h) Exclusion of patients with recent significant reductions in vision

Retinopathy is a common complication of diabetes which results in substantial, progressive loss of vision (Crawford et al., 2009). Since the absence of vision can significantly alter postural stability (Ray et al., 2008), patients with diagnosed retinopathy or vision that had significantly deteriorated within the last year were excluded from the study.

(i) Exclusion of patients who are pregnant

In addition to the alterations in lower limb function exhibited by pregnant females (Ponnapula & Boberg, 2010), the fact that this was an intervention study with multiple assessments over the course of several months dictated that pregnancy was an exclusion criteria for the current study – whether pregnancy occurred before or during the study.

Exclusions following screening

A total of 60 neuropathic diabetic patients were referred for screening from CMDHB clinicians over a 14-month period. Following this screening process, 12 participants were included in the final intervention study. The reasons for the exclusion of the other 48 patients are shown in Fig. 3.4.
Therefore a significant proportion of the neuropathic diabetics referred by CMDHB clinicians were excluded from participation in the current study because of accessory complications which may have confounded the results of the current study. An overview of the study design will now be provided, including a chronological timeline of significant events.
Overview of Study Design

Numerous outcome measures related to sensorimotor function were assessed prior to and following the intervention, and these are detailed in Chapters 4 – 9. The design of the current study was a prospective cohort design, whereby neuropathic diabetic participants acted as their own control group. This design was chosen for two principle reasons. Firstly, in a prospective cohort design – often referred to as a ‘test-retest’ design – the homogeneity between compared ‘groups’ is assured, since we are in fact examining the same participants across a period of time. This is highly beneficial when the study population – neuropathic diabetics in the current case – may come from a pathologically diverse background, including differences in diabetes aetiology and level of symptom management. A prospective cohort design removes any likelihood of introducing heterogeneity between groups which are being compared. Also, in light of the small size of the current study and the number of likely participants which could have been recruited, a prospective cohort design removes the requirement to gather a sufficient number of participants before dividing them into control and intervention groups. Instead, a participant can begin their involvement in the study as soon as they are recruited, which has the double-benefit of maintaining their initial enthusiasm for participation, as well as ensuring that their general health status is the same as when they were recruited – an important consideration for a population at high risk of complication.

Secondly, it is recognised that a randomised controlled trial could be considered a highly desirable design with which to test hypotheses regarding the effectiveness of an intervention. When designing the current study, it was decided that it would be unethical to provide an intervention which was expected to improve sensorimotor function to some participants, but not deliver it to others. While the optimum situation would have been to offer the intervention to a control group at the conclusion of the study, this was not logistically possible due to resource constraints. Also, since participant recruitment took 14 months to complete, participants began their interventions at different times over the course of this period. To divide participants into intervention and control groups without knowing how many participants would be in the study would not have been efficacious for testing the validity of the intervention in this population.
In order to ensure that any changes observed following the intervention were actual intervention effects and not just natural variability, two baseline assessments separated by four weeks were conducted prior to the implementation of the intervention (1\textsuperscript{st} and 2\textsuperscript{nd} pre-intervention assessments). The 1\textsuperscript{st} post-intervention assessment was conducted one day after the last exercise session. Supervised exercise sessions, including access to wobble board and Thera-Band\textsuperscript{©} equipment, were removed and participants instructed to return to baseline levels of physical activity. Following a 12-week hiatus, a follow-up (2\textsuperscript{nd} post-intervention) assessment of all outcome measures was conducted in order to assess the long-term effect of the intervention. Therefore this study followed an A-B-A format, where A = no intervention and B = intervention (Fig. 3.5).

**Figure 3.5: Overview of study design**

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<table>
<thead>
<tr>
<th>Equipment reliability assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot experimentation</td>
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<tr>
<td>Participant recruitment</td>
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<tr>
<td>First baseline assessment</td>
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<tr>
<td>(Week 0)</td>
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<td>Second baseline assessment</td>
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<tr>
<td>(Week 4)</td>
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<tr>
<td>Start of intervention</td>
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<tr>
<td>Completion of intervention</td>
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<tr>
<td>(Week 16)</td>
</tr>
<tr>
<td>Effect of intervention assessment</td>
</tr>
<tr>
<td>Follow-Up Assessment</td>
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<tr>
<td>(Week 28)</td>
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</tbody>
</table>
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Conclusion

This chapter detailed the exercise intervention employed in the current study. The intervention was comprised of three components: balance, isolated ankle strength and passive stretching. A description of intervention frequency, intensity and supervision was provided. A description of the participant recruitment process was provided, including inclusion/exclusion criteria and rationale for each of these. Finally, an overview of the study design was provided.

The next six chapters contain the experimental components of the current study. As outlined at the conclusion of Chapter 2, each component investigates the effect of the intervention on different aspects of sensorimotor function relevant to diabetic neuropathy, as well as health-related quality of life. In the first of these components, Chapter 4 investigates the effect of the intervention on sensory function.
Chapter Four

Effect of the Intervention on Sensory Function
Effect of the Intervention on Sensory Function

Introduction

Overview

As discussed in Chapter 2, one of the chronic complications of diabetic neuropathy is the loss of peripheral sensation due to sensory nerve dysfunction or necrosis (Boulton, et al., 2004; Ziegler, 2008). This loss of protective sensation places a neuropathic diabetic at increased risk of developing foot wounds by reducing their ability to sense high peak loading (Bacarin et al., 2009; Boulton, 2004; Bus, et al., 2005; P.R. Cavanagh et al., 1998) or sudden trauma (P.R. Cavanagh et al., 2005) until a wound has already developed. The likelihood of foot ulcer occurrence can be reduced by the early assessment of sensory function and taking early preventative measures in high-risk patients (Valk et al., 1997).

Assessment of sensory function

Sensory function can be quantified using a variety of methods, including vibration tests with a tuning fork or biothesiometer, thermal sensitivity tests and pin-prick tests (Abbott et al., 2005; Armstrong et al., 1998; Batista et al., 2005; Boyko et al., 1999; Navarro & Kennedy, 1991; Young et al., 1994). Nerve conduction studies can also be undertaken; however it is often difficult to assess sensory nerve conduction velocity in neuropathic diabetics who may have already lost sensory function (Kramer, et al., 2005). The Semmes-Weinstein monofilament tests have been shown to be highly reproducible and applicable to a wide range of patients and examiners (Perkins & Bril, 2003). Klenerman et al. (1996) conducted a screening programme for peripheral neuropathy on more than 1000 diabetics, and compared vibration, pedal pulse and Semmes-Weinstein monofilament measurements. The latter was found to be the only measurement tool with adequate reproducibility for such a task, and the authors recommended it for widespread use.

The Semmes-Weinstein monofilament test involves the application of a plastic handle with an attached nylon monofilament which buckles when applied to the skin with the prescribed amount of force. For example, when a 10-gram (g) monofilament is employed, it will bend when a compressive force representing a weight of 10 grams is applied (Armstrong, 2000). The 10g (or 5.07, a logarithmic derivative) Semmes-Weinstein monofilament can be
used to determine whether sensory neuropathy is present (Dellon, 2004; Frykberg et al., 1998), since this has been shown to be an appropriate force level for indicating a loss of protective sensation (Batista, et al., 2005; Charanya et al., 2004; Laing, 1994). However, the use of a single monofilament or a simple pin-prick test does not allow for the detailed quantification of sensory thresholds; instead, it provides an unchanging stimulus which only produces a dichotomised response. Through the use of a set of multiple monofilaments, and the employment of a suitable testing protocol, a more detailed quantification of sensory threshold can be achieved (Jeng et al., 2000; Rosenbaum, et al., 2006).

Improving sensory function in pathological populations

Multiple studies have shown improvements in neural function as a result of an exercise intervention in animals with peripheral nerve damage (Cui et al., 2004; L. M. Doyle & Roberts, 2006; Gardiner et al., 1984; Marqueste et al., 2004; Molteni et al., 2004; Pachter & Eberstein, 1989; Sarikcioglu & Oguz, 2004; van Meeteren et al., 1997). In a study in which the peripheral nerves of eels were severed, Doyle and Roberts (2006) observed significant axonal growth following two weeks of forced swimming against a current. The control group, which was not forced to swim, exhibited no such neurogenesis.

In humans, Lynch et al. (2007) conducted an intervention study in stroke survivors in post-stroke rehabilitative care. Their study investigated the effect of sensory re-training techniques on touch sensitivity at seven foot regions using Semmes-Weinstein monofilaments, halluc proprioception and multiple clinically-relevant balance and gait tasks. The sensory re-training was incorporated into a patient’s normal rehabilitation programme, which involved lower limb strength and cardiovascular training for one hour per day over a short two-week period. Participants were randomly allocated to normal rehabilitation plus sensory re-training or normal rehabilitation plus relaxation techniques. While unable to detect significant differences between groups, the authors did find that sensory threshold improved at the heel, lateral border of the midfoot and the halluc in both groups immediately following the intervention. Proprioception did not improve in either group. It is unclear whether or not improvements in sensory function were the natural result of the passage of time following stroke incidence, since for obvious reasons no control group was employed in their study.
Previous research has also shown improvements in peripheral neural function in diabetic populations without neuropathy. Balducci et al. (2006) conducted a four-year exercise intervention with diabetics without peripheral neuropathy, with a view to investigating the effect of a long-term training programme on the natural progression of the disease. The intervention consisted of four hours per week of treadmill walking, and patients were randomly allocated into control and intervention groups. Outcome measures included lower limb nerve conduction velocity and vibration perception tests. It was discovered following the four-year period that the exercise intervention group exhibited significantly faster nerve conduction velocities than both their own baseline measurements and the control group, while the control group had regressed from baseline. In terms of vibration perception, while the control group regressed from baseline the intervention group either improved or stayed the same. The conclusion of the authors of this study was that exercise can prevent the onset of diabetic neuropathy, or at least significantly delay it.

Smith et al. (2006) showed improvements in cutaneous innervation via a simple diet and exercise counselling programme in patients with pre-diabetic neuropathy; however improvements tended to be short term following the removal of the intervention (Singleton & Smith, 2008). In a small-scale study investigating the effect of 24 weeks of a cardiovascular exercise programme on sensorimotor nerve conduction velocities in five neuropathic diabetics, Fisher et al. (2007) found improvements in these measures following the intervention. Their study suggests that it may be possible to improve peripheral neural function in neuropathic diabetic populations with an exercise intervention. As discussed in Chapter 2, Fisher et al. (2007) trained their participants at upwards of 75% of their maximal aerobic capacity, seemingly ignoring the possible risk of exacerbating underlying cardiac autonomic dysfunction in these populations. Their justification for this was retrospective, suggesting that their intervention was safe because no participants suffered complications as a result of it. It is the opinion of the current author that this is a dangerous approach, which could have resulted in serious consequences for the participants involved. Information regarding how these factors were monitored was not available.

Fortunately, some researchers have discovered that such potentially harmful interventions may not be required for causing improvements in peripheral sensory function in diabetic populations. Morrison et al. (2010) investigated the effect of a balance training intervention, not dissimilar to that employed in the current study, on risk of falling in a
diabetic population. The intervention was delivered three times per week for six weeks, and risk of falling was measured using a number of clinical measures including sensation and proprioception. The authors found a significant improvement in these measures following the intervention.

Following a review of relevant literature, it was clear that there was a fundamental lack of safely-executed exercise intervention studies which attempted to improve peripheral sensory function in neuropathic diabetic populations, despite such improvements being plausible based on research in other populations. It is likely that this lack of previous research is the result of a reasonable fear of causing further complications to this population. Therefore the purpose of this component of the current study was to investigate the effect of the exercise intervention (Chapter 3) on peripheral sensory function in a neuropathic diabetic population. If, as a result of the intervention, sensory threshold measures significantly improve, this is indicative of an improvement in protective afferent function and therefore a reduction in the likelihood of ulceration.

**Sensory function hypotheses**

It was hypothesised that sensory loss caused by peripheral sensory dysfunction in the current neuropathic population would improve as a result of the exercise intervention. These improvements would manifest as reductions in plantar sensory threshold, measured using Semmes-Weinstein monofilaments.

In summary it was hypothesised that, as a result of the intervention:

- Sensory threshold at all plantar sites measured will decrease, indicating an improvement in peripheral sensory function;
- Changes in sensory threshold will return to pre-intervention levels in the long-term follow up assessment, indicating that improvements were short-term due to the A-B-A format of the intervention.
Methodology

Participants

12 participants were initially recruited, two of whom dropped out during the exercise intervention due to unrelated clinical complications. Therefore 10 participants underwent sensory threshold assessment at 0 weeks (pre-1), 4 weeks (pre-2), 16 weeks (post-1) and 28 weeks (post-2). In the interim between 16 weeks (post-1) and 28 weeks (post-2), one participant developed a small ulcer under their right hallux and one participant underwent bariatric surgery. These participants were consequently excluded from the second follow-up assessment. Participant demographic information collected at the 1st pre-intervention assessment is exhibited in Tab. 4.1.

Table 4.1: Participant demographic information (mean ± SD); BMI = body mass index (weight / height²)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>N = 10</th>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>60.9 ± 8.6</td>
</tr>
<tr>
<td>BMI</td>
<td>32.1 ± 4.8</td>
</tr>
<tr>
<td>Diab Duration (yrs)</td>
<td>19.6 ± 14.1</td>
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<tr>
<td>M/F</td>
<td>7m / 3f</td>
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<tr>
<td>Diabetes Type</td>
<td>2 Type-1 / 8 Type-2</td>
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<tr>
<td>R Foot Length (cm)</td>
<td>26.6 ± 1.8</td>
</tr>
<tr>
<td>L Foot Length (cm)</td>
<td>26.4 ± 0.9</td>
</tr>
<tr>
<td>R Foot Width (cm)</td>
<td>10.2 ± 1</td>
</tr>
<tr>
<td>L Foot Width (cm)</td>
<td>10.4 ± 0.9</td>
</tr>
</tbody>
</table>

Measurement Equipment

In order to determine sensory threshold a 20-monofilament Semmes-Weinstein set was employed (Fig. 4.1; North Coast Medical Inc., U.S.A.). These filaments are ordered according to Semmes-Weinstein monofilament number, which can be determined from a logarithmic calculation based on the force required to cause the monofilament to buckle (Holewski et al., 1988; Laing, 1994; Nurse & Nigg, 1999; Saltzman et al., 2004). The filaments ranged in buckle-force requirement from 0.0045g to 447g.
Effect of the Intervention on Sensory Function

Figure 4.1: The 20-monofilament Semmes-Weinstein set (left), with the 1.65 (lightest), 5.07 and 6.65 (heaviest) monofilaments (right)

Experimental Protocol

Biomechanical assessments occurred at the same or similar (+/- one hour) time of day across all four assessments to minimise time-of-day effect. Sensory threshold testing was conducted in a quiet room with participants lying prone on a massage bench. Only the dominant limb was assessed (Nurse & Nigg, 1999, 2001). Limb dominance was determined by asking the participant which foot they would use to kick a soccer ball.

Foot sensitivity was assessed at four plantar foot locations, including the midpoint of the hallux, the midpoint of the 5th toe, the head of the 3rd metatarsal and the midpoint between the lateral and medial borders of the arch. The majority of test sites were therefore located in the forefoot area of the plantar surface of the foot (Boulton et al., 2008), and the heel was excluded from testing despite its common use in previous literature. The reasoning behind this selection was two-fold: firstly, as has been previously stated, peripheral neuropathy progresses from distal to proximal and therefore the detection of a loss of protective sensory threshold is more likely in these areas. Secondly, as previously mentioned discussions with clinical staff at Counties-Manukau District Health Board resulted in the discovery that Semmes-Weinstein monofilaments are only used on the forefoot and midfoot when conducting their clinical investigations, since callusing and thickening of the heel pad is
common. Sensory testing may falsely identify a loss in protective sensation in this area, when in fact it may be the thickness of the callus which prevents the monofilament from being sensed.

The protocol for testing foot sensitivity at a given location required the initial employment of the 4.56 monofilament. Ten touch trials were performed per filament, and filaments were applied perpendicular to the plantar surface (McPoil & Cornwall, 2006). Participants were asked if they could feel a touch trial, and a yes or no answer was given. The protocol required the application of three null stimuli at random intervals per monofilament test (Jain et al., 2008; Rosenbaum, et al., 2006), in order to avoid false-positive responses (Fig. 4.2; Appendix 5). If three failures occurred during a filament test, whether by failing to sense an applied filament (false-negative) or by sensing a null stimulus (false-positive), the filament was considered a failure.

Regarding the order of monofilament application during an assessment, the protocol followed a 4-2-1 pattern (Dyck, 1993; Nurse & Nigg, 1999; Praetorius et al., 2003; Rosenbaum, et al., 2006; Yarnitsky, 1998). Depending on whether or not the participant could sense the initial filament, the next filament to be used was either four filaments lighter or heavier. Once a filament was failed, two steps back were taken in terms of filament number, and then one step forward or back depending on the outcome of that test. The lightest filament successfully passed during the testing protocol was the sensory threshold of that tested location. When a participant was unable to sense the thickest monofilament – and therefore exhibited a complete absence of sensory function that can be detected using the Semmes-Weinstein monofilament test – the maximum possible sensory threshold value of 6.65 was entered for further data analysis and this occurrence was noted for future interpretation (Corriveau, Prince, et al., 2000).
**Effect of the Intervention on Sensory Function**

**Figure 4.2:** A typical 4-2-1 testing protocol for an individual foot site, where grey areas indicate an instance of null-stimuli

<p>| | | | | |</p>
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<tr>
<th></th>
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<tr>
<td>4.56</td>
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**Data Analysis**

Data analysis was conducted using Microsoft Excel (Microsoft Corp., U.S.A.). As well as assessing the individual sensory threshold at each tested site, sensory threshold at all four sites were averaged to give an average foot sensory threshold value. These five values were expressed in terms of the Semmes-Weinstein monofilament number (Jeng, et al., 2000; McPoil & Cornwall, 2006).

**Statistical Analysis**

Statistical analysis was conducted in SPSS v16.0 (SPSS Inc., U.S.A.) and Microsoft Excel. Due to the small sample size, non-parametric statistical analysis in the form of the Wilcoxon signed ranks test was performed to check for significant differences between assessments (Corriveau, Prince, et al., 2000).

Significance testing was conducted between subsequent assessments. An intervention effect was defined as a significant change between the pre-2 and post-1 assessments where no such change occurred between pre-1 and pre-2. For all tests the level of significance was set at $p < 0.05$. 

72
Results

Sensory threshold results

Sensory threshold results revealed a lack of group homogeneity in terms of sensory function, as exhibited by the large range observed for each foot region and assessment (Tab. 4.2). In addition, high inter-participant variability was observed in terms of response to the intervention, as exhibited by high standard deviations for the average change results. Despite this variability, statistically significant improvements were observed at three of the four tested foot sites as well as for the average foot sensory threshold. No significant changes were observed between either the two pre-intervention or two post-intervention assessments. Sensory threshold was highest at the 3rd metatarsal head and lowest at the 5th toe and midfoot across assessments.

Table 4.2: Sensory threshold results

<table>
<thead>
<tr>
<th>Day</th>
<th>Hallux</th>
<th>Avg (SW)</th>
<th>Range (SW)</th>
<th>Avg Δ (SW)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-1</td>
<td>5.56 ± 0.89</td>
<td>4.31 - 6.65</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>5.58 ± 0.92</td>
<td>4.08 - 6.65</td>
<td>0.02 ± 0.57</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>5.06 ± 1.00</td>
<td>3.84 - 6.65</td>
<td>-0.52 ± 0.42</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>5.33 ± 1.12</td>
<td>4.08 - 6.65</td>
<td>0.09 ± 0.30</td>
<td>0.47</td>
</tr>
<tr>
<td></td>
<td>5th Toe</td>
<td>Pre-1</td>
<td>5.18 ± 1.07</td>
<td>3.61 - 6.65</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pre-2</td>
<td>5.09 ± 1.14</td>
<td>3.61 - 6.65</td>
<td>-0.09 ± 0.45</td>
</tr>
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<td></td>
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<td>5.02 ± 1.13</td>
<td>3.61 - 6.65</td>
<td>-0.07 ± 0.83</td>
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<td>3.22 - 6.65</td>
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<td>3rd Met</td>
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<td>4.56 - 6.65</td>
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<td>5.41 ± 1.21</td>
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<td></td>
<td>Midfoot</td>
<td>Pre-1</td>
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<td>4.08 - 6.65</td>
<td>-0.06 ± 0.31</td>
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<td>4.82 ± 0.94</td>
<td>3.61 - 6.65</td>
<td>-0.34 ± 0.25</td>
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<td>4.82 ± 1.01</td>
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<td>Foot Avg</td>
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<td>-0.08 ± 0.30</td>
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<td>3.75 - 6.65</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Post-2</td>
<td>5.14 ± 1.12</td>
<td>3.63 - 6.65</td>
<td>0.02 ± 2.06</td>
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Effect of the Intervention on Sensory Function

Discussion

Addressing the hypotheses

It was hypothesised that sensory threshold at all measured plantar sites would decrease, a hypothesis that was proven largely correct. There was a lack of group homogeneity in terms of both initial sensory threshold and response to the intervention. However, statistically significant reductions in sensory threshold were observed following the intervention at three of the four plantar sites, as well as for the average foot sensory threshold. The regions at which improvements were observed were the hallux, 3\textsuperscript{rd} metatarsal head and midfoot. No improvements were observed at the 5\textsuperscript{th} toe.

It was hypothesised that improvements in sensory threshold would be short-term and return to baseline levels by the 2\textsuperscript{nd} post-intervention assessment. This hypothesis was proven incorrect, since no significant changes were observed between post-intervention assessments. A trend toward a return to baseline was exhibited at the hallux, but this was not significant.

Improvements in sensory function

Regarding the lack of group homogeneity in terms of sensory function, it can be observed in Tab. 4.2 that sensory threshold results ranged from low values that could have been found in a healthy individual (Jeng, et al., 2000) through to high values that suggest a considerable absence of sensory function. The observation of these low, seemingly non-neuropathic values is a reflection on the inclusion criteria for the study, whereby a participant only needed to exhibit a sensory threshold of greater than 5.07 at one of the tested foot regions. For example, a participant who exhibited a sensory threshold value of 3.61 for the 5\textsuperscript{th} toe may have exhibited a threshold of 5.18 for the hallux, and so on.

The variability observed in terms of average change following the intervention can be explained by three factors. Firstly, there was a lack of any change in sensory function in the two participants who suffered from the most severe sensory loss, each of whom exhibited either a complete absence of measureable sensory function – i.e. an inability to sense the thickest Semmes-Weinstein monofilament – or were only able to sense the thickest filaments. Secondly, of those foot regions where statistically significant improvements were observed,
not all participants without severe sensory loss showed improvements. Thirdly, where post-intervention improvements in sensory threshold were observed, these improvements differed in magnitude between participants. Other than the lack of improvement observed in the participants with the most severe sensory loss, there was no clear pattern regarding which participants responded most favourably to the intervention since these magnitudes varied between foot regions.

Despite the aforementioned variability, a significant improvement in sensory threshold was observed at three of the four tested foot sites as well as for the average foot sensory threshold. The discovery of improved sensory threshold in the current study is unique, since it is the first instance in which a group of neuropathic individuals have shown quantifiable improvements in sensory function following a low-impact exercise intervention. While these improvements were limited to participants who did not exhibit severe sensory loss, and the potential for high statistical power was limited by the small sample size of the current study – a limitation discussed in detail in Chapter 10 – cautious further discussion regarding the meaning of these findings is warranted.

The improvements in sensory function, although unique in terms of the type of exercise used to achieve them, are not without precedent in the exercise intervention literature. Previous research has also shown improvements in peripheral neural function following an exercise intervention in diabetic populations (Balducci, et al., 2006; Morrison, et al., 2010) as well as individuals who have suffered a stroke (Lynch, et al., 2007). In addition, the paper by Fisher et al. (2007) showed improvements in peripheral nerve conduction velocities in a small neuropathic diabetic population following an aerobic training programme. However, in contrast to the latter study the current intervention was low-impact in nature and held minimal risk of complication. The results of the current study clearly show that it is not necessary to place these participants at increased risk of a serious negative event in order to observe improvements in peripheral sensory function.

As mentioned in the literature review, the creation of new peripheral neural tissue as a result of an exercise intervention has been shown in animal studies (L. M. Doyle & Roberts, 2006). However, it is unlikely that the improvements in sensory function exhibited in the current study were due to dermal tissue neurogenesis. Rather, it is likely that improvements were the result of increases in function of pre-existing sensory nerves. There are two principle reasons for this supposition which will now be discussed.
Effect of the Intervention on Sensory Function

Firstly, the exercise intervention consisted of 24 exercise sessions of approximately 30 minutes duration. While this intervention – and the fact that it was 100% supervised – compares favourably to previous exercise interventions in diabetic populations, it is unlikely that a total of approximately 12 hours of exercise could cause the generation of new neural tissue. In the case of the axonal sprouting exhibited in the eel study (L. M. Doyle & Roberts, 2006), the intervention stimulus was continuous over 20 days and therefore a total of 480 hours of exercise intervention was delivered. For the current application this would require a 40-hour per week exercise intervention over 12 weeks, which aside from logistical considerations would be likely to cause more adverse clinical complications than it solved.

Secondly, examination of individual responses to the intervention revealed that the two participants who exhibited the most severe sensory loss showed no improvement following the intervention at any foot region. These participants clearly demonstrated advanced sensory neuropathy, and it is likely that their lack of improvement was the result of an absence of living sensory nerves in the plantar dermal tissue. This finding is congruent to the proposal by previous authors (Allet, et al., 2010b; Coppini et al., 2006; Yasuda, et al., 2007) that even improvements to cardiovascular risk factors and glycaemic control cannot halt the progression of sensory loss when neuropathic symptoms are already well established in individuals with diabetes. Perhaps there is an afferent sensory necrosis ‘cut-off’ point, beyond which it is not possible to improve sensory function without comprehensive neurogenesis. This adds to the argument against neurogenesis being the causative factor behind the observed improvements in sensory function in the current study; if it were possible to create new nerves after a 12-week exercise intervention then it would be more likely that the participants with severe sensory loss would have shown some improvement. Instead, significant reductions in sensory threshold were only observed in participants who showed some but not severe sensory loss. Therefore, the improvements in sensory threshold following the exercise intervention could be the result of improved function of pre-existing living nerves. This leads to a discussion on the cause of such an improvement in sensory neural function.

Living nerves rely on adequate blood supply for the proteins which comprise their structure and the energy required to propagate neural signals. A disruption to this supply is therefore detrimental to neural function. In diabetics, there can be several causes of such a disruption. Vascular flow can be reduced due to associated cardiovascular complications,
including the ‘shunting’ of blood from arteries straight to veins, bypassing the peripheral microcapillary network (Cameron et al., 2001). If starved of necessary protein and energy supplies for too long, the nerve will cease to function properly and eventually die.

However, it is possible to improve peripheral vascular function with the implementation of an exercise intervention. Supervised exercise interventions have been shown to be effective at improving claudication, peripheral vascular dilation and other clinically-relevant outcome measures in patients with peripheral vascular disease (Payvandi et al., 2009; Shalhoub, et al., 2009). Exercise has been linked to the stimulation of endothelium-dependent vasodilation in diabetic populations (Fuchsjager-Mayrl et al., 2002). In most cases, these exercise interventions were largely cardiovascular in nature and not specific to the periphery, while the exercises employed in the current intervention were specific to the lower limb with most exercises primarily requiring the use of the ankle joint. This was because it was the original premise of the intervention that the peripheral neuromuscular complications of diabetic neuropathy could be addressed at the site of their occurrence, i.e. the lower limb. By training the musculature around the ankle joint, it is possible that this caused not only an improvement in blood flow to the periphery but also of venous return, assisting in the removal of the by-products of glycation which can accumulate on nerve endings and cause disruptions to neural function (Horowitz, 2006; Sima, 2003). Both occurrences would serve to improve sensory function. However, it should be noted that any discussion about the link between improvements in vascular flow and improvements in sensory function are speculation that should be substantiated with quantitative measurement – an issue which will now be discussed.

Vascular flowmetry – the missing link?

As discussed, it is possible that the improvements in sensory function observed following the intervention were the result of improvements in vascular flow to peripheral neural tissue. However, this supposition cannot be quantitatively supported. While the measurement of peripheral vascular flow was considered at the onset of the current study, this idea was abandoned when an appropriate and realistic measurement technique could not be found. Peripheral vascular function is commonly measured with blood pressure cuffs positioned at the ankle and/or toes (Sahli et al., 2005); however this solely measures arterial
dilation at the periphery and was therefore not a fine enough tool for the current application. Another technique considered was Doppler analysis, which is used to examine peripheral microcapillarisation. However, as a result of a discussion at the onset of the current study with a clinician experienced in these techniques, it was determined that the inherent variability associated with the Doppler technique under consideration made its use as a pre-post measurement device undesirable. Upon the observation that significant improvements in sensory function had been found following the current intervention, further investigation into these techniques has been undertaken with a view toward future research directions. It was discovered that advances in laser Doppler flowmetry have been considerable. This technique provides a non-invasive means of determining dermal microcirculation (Quattrini, Harris, et al., 2007), an outcome measure sorely missed in the current study as a potential explanatory factor for the observed sensory improvements. It is therefore of considerable interest for future research to focus on the causal mechanisms behind the observed improvements in sensory neural function. Such research should employ advanced, reliable techniques for the measurement of peripheral vascular flow such as laser Doppler flowmetry.

It is also of interest to consider which types of nerves may have undergone improvements in function as a result of the intervention. It is known that the small afferent fibres, such as C and A-delta, are initially affected in peripheral neuropathy, followed by nerves of a larger fibre diameter which are linked to loss of sensation and proprioception (Yagihashi, et al., 2007; Ziegler, 2008). Therefore any improvement in sensory function following the intervention must, by definition, be the result of improvements in the function of these larger fibres, which include A-alpha and A-beta (Tavee & Zhou, 2009). However this supposition relies on the assumption that the Semmes-Weinstein monofilament test stimulates only the larger diameter nerves and not small, unmyelinated nerves. Future research should employ imaging techniques that allow for the assessment of peripheral neural function and/or growth, as well as the identification of different nerves by diameter analysis. Such analyses could include biopsies to determine the density of intraepidermal nerve fibres (Loseth et al., 2010; Tavee & Zhou, 2009); however in a pre-post clinical trial such as the current study this would only allow for the determination of neurogenesis and not afferent function of pre-existing nerves. Nerve conduction velocity analysis allows for the measurement of large nerve fibre function (Yasuda, et al., 2007), and can assess either motor or sensory nerve conduction. However it is often difficult to assess sensory nerve conduction
velocity in neuropathic diabetics who may have already lost sensory function (Kramer, et al., 2005).

**Limitations**

Because of the strict inclusion/exclusion criteria employed for the current study, sample size was significantly lower than desired. Sample size is a limiting factor in the current study since it decreases the power of the observation of changes in sensory threshold as a result of the intervention. Therefore we cannot be certain whether the neuropathic population in the current study is representative of the wider neuropathic population; we can only suggest that sensory function can be improved in individuals who fit the inclusion criteria for the current study but do not suffer from severe sensory loss.

Glycaemic control can affect neuropathic symptoms (Ziegler et al., 1991). A limitation of the current study was the lack of collection of blood glucose as a variable. While not a primary outcome measure, there was an intention at the onset of this study to collect this information and ethical approval was sought and granted for the collection of blood records from Diagnostic Medlab laboratory services. However, this idea was eventually discarded when it was discovered that contrary to advice from clinicians most diabetics encountered during the screening process did not undergo frequent fasting blood glucose assessments, and that there would be a high degree of difficulty in coordinating the collection of blood through Diagnostic Medlab in a reasonably synchronous fashion with the collection of biomechanical data at the Biomechanics Lab. When this problem was discovered, efforts were made to establish a protocol and secure equipment and expertise so that blood could be collected at the same location and time as the biomechanical data collection; however these factors proved difficult to coordinate and given the fact that no hypotheses of interest had been made regarding the effect of the intervention on blood glucose it was decided to discard this approach. At the current juncture, when explanatory factors regarding changes in sensory threshold are being sought, perhaps the additional information provided by blood glucose analysis would be helpful. However, changes in glycaemic control could not have been solely caused by an exercise intervention which did not significantly stress the cardiovascular system, nor have any consequence on BMI, which remained unchanged in all participants across the study period. This absence of change is unsurprising, since the American College
of Sports Medicine position paper on strategies for effective weight loss states that a combination of improved dietary intake and cardiovascular exercise is required to cause changes in body weight (Jakicic et al., 2001), neither of which were addressed by the current intervention. These additional, uncontrolled factors such as quality of nutrition are much more likely to predict glycaemic control than 12 hours of lower limb balance and low-impact strength training. Nevertheless it is acknowledged that glycaemic control can be a contributing factor to sensory function, and therefore its lack of availability as an outcome measure is a limitation of the current study.

The Semmes-Weinstein monofilament test has been shown to be a valid method of measuring sensory neuropathy, as well as a good predictor of the likelihood of ulceration and amputation (Perkins & Bril, 2003). It is also relatively inexpensive, simple and accurate (S. Lee et al., 2003). However, the Semmes-Weinstein method has a few key drawbacks which may influence sensitivity threshold data obtained from participants. Booth and Young (2000), when investigating differences in the 5.07 monofilament between manufacturers, found that the monofilaments can differ in their actual force level by more than 10%. They also found that the nylon monofilament becomes less rigid with each application, and can be rendered useless after 10 participants in one day and needs a 1-day recovery period in order to return to its original viscoelastic state. The effect of this on the results of this study cannot be quantified; however no such viscoelastic problem should be encountered in the current study since no more than two participants were ever recorded in one day.

It can be argued that the Semmes-Weinstein monofilament test relies too heavily on self-report to be adequately used as a pre-post measurement device. In clinical settings this is a valid concern; patients are usually asked whether they can feel a filament at a given foot region and their response is assumed to be accurate. For a number of psychosocial reasons a patient could theoretically not tell the truth and insist that a monofilament can be felt, when in fact it cannot. However, the protocol used for the current study employed ten touch-trials with three null-stimuli for each monofilament tested (Jain, et al., 2008; Rosenbaum, et al., 2006), meaning that if an individual was saying they could feel the null-stimuli they would fail that monofilament. Participants were never allowed to see the protocol sheet being used, and therefore were blinded to the occurrence of these null-stimuli.

The only foot region which exhibited a trend toward a return to baseline sensory threshold at the 2nd post-intervention follow-up was the hallux, while all other foot regions
remained at the improved levels observed immediately following the intervention. The current intervention study was designed to follow an A-B-A format, whereby A refers to baseline, B to the intervention, and the subsequent A to a return to baseline. Following the completion of the intervention and first post-intervention assessment, participants were instructed to return their activity levels to those practised during the four week period between pre-intervention assessments. When asked at the 2nd post-intervention assessment if they had done this, all participants answered affirmatively. However it was impossible to control whether or not participants followed this request. We can therefore not be certain that a true A-B-A format was adhered to for this study due to uncontrollable human factors.

All participants reported favourable personal outcomes immediately following the intervention, with several stating that they wanted to continue an exercise programme to ensure that they built on these outcomes. Upon retrospect it is possible that it was clinically unethical to disallow any other activity other than that conducted prior to the onset of the intervention, since for the participants who had been formerly sedentary this would be tantamount to a regression in potentially positive health outcomes. Nevertheless the purpose of the current study was to determine whether the neuromuscular complications of diabetic neuropathy could be improved with a specific type of exercise intervention, and part of this purpose required the removal of the intervention to determine its long-term efficacy. While the request to return to baseline activity levels can be considered a clinical limitation of the current study, this was done to adhere as closely as possible to the aforementioned A-B-A format. Future studies with larger sample sizes could possibly circumvent this limitation by allowing participants to engage in whatever physical activity they desire following the intervention, and then measure this activity. Upon conclusion of the follow-up assessment participants in such a study could be grouped according to post-intervention activity levels.

Conclusions

The findings of the current study suggest that it is possible, via a supervised exercise intervention which focuses on improving balance and lower limb strength, to improve sensory function in neuropathic diabetics who do not already have well-established severe sensory loss, have no cardiovascular disease, no current or healing ulcer, no rheumatic or arthritic
sensory function is a highly desirable clinical outcome. By improving sensory function, a diabetic patient is more likely to be able to sense potentially harmful loading and frictional force, thereby reducing the likelihood that they will sustain a plantar ulcer. The next chapter will investigate the effect of the exercise intervention on postural stability.
Chapter Five

Effect of the Intervention on Postural Stability
Effect of the Intervention on Postural Stability

Introduction

Overview

In the previous chapter, it was discovered that the intervention appeared to cause a significant improvement in sensory threshold for most foot regions in those participants who did not suffer from severe sensory loss. In the current chapter, the effect of the intervention on the maintenance of postural stability will be investigated.

Postural stability is severely reduced in neuropathic diabetic populations (Kim & Robinson, 2006). As discussed in Chapter 2, this postural stability dysfunction is caused by the diminished sensorimotor function common in neuropathic patients (Dickstein et al., 2001; Goldberg et al., 2008). As a result of this diminished capability, the risk of neuropathic diabetics sustaining a fall is greatly increased (Boucher, et al., 1995; Kanade et al., 2008).

A common means of determining postural stability is the measurement of postural sway during quiet standing, via the calculation of centre of pressure (CoP) and/or centre of mass (CoM). The CoP is the point of ground reaction force application (Brenda et al., 1994; R. J. Doyle et al., 2007), and is measured in the transverse plane in both the anterior-posterior (AP) and medio-lateral (ML) directions. The CoM is defined as the point at which whole body mass is theoretically concentrated, and any external forces applied to this point can cause translation but not rotation (Brenda, et al., 1994). Using these measures, several studies have shown that neuropathic populations exhibit increased postural sway (Boucher, et al., 1995; Corriveau, Prince, et al., 2000; Kanade, et al., 2008; Lafond, Corriveau, et al., 2004). Boucher et al. (1995) discovered that neuropathic participants exhibited similar or worse standing postural sway with their eyes open than non-neuropathic participants who had their eyes closed. Other previous research has shown that increases in postural sway are significantly correlated with severity of neuropathy (Bergin et al., 1995; Boucher, et al., 1995).

Assessment of postural sway

Calculation of CoP requires the use of one or two force plates (Boucher, et al., 1995; Centomo et al., 2007; Corriveau, Prince, et al., 2000; Kanade, et al., 2008; Lafond, et al.,
Effect of the Intervention on Postural Stability

2004). While calculation of the CoM has been conducted using non-kinematic methods (Lafond, Duarte, et al., 2004; Mesani et al., 2007), the implementation of a kinematic model on data collected using some form of motion capture device is most common (Chen & Chou, 2010; Corriveau et al., 2001; Hsue et al., 2009).

Assessments of postural sway are often conducted under varying environmental conditions, designed to disrupt postural stability. Postural sway studies will typically investigate the effect of varying visual conditions, i.e. eyes open versus eyes closed (Boucher, et al., 1995; Lafond, et al., 2004; Le Clair & Riach, 1996; Nardone et al., 2000), and may also investigate the effect of varying surface conditions, usually via the use of soft foam (Bergin, et al., 1995; Fujimoto et al., 2009; Horlings et al., 2008; Vuillerme et al., 2005). These varying conditions are designed to systematically remove the balance ‘assets’ available to an individual. By asking them to close their eyes, visual feedback is removed; by additionally placing soft foam under their feet, the texture of the foam reduces somatosensory cues and the base of support becomes an unstable surface. As these balance assets are systematically removed, postural sway can be expected to increase (Bergin, et al., 1995).

Relevant outcome measures

The measurement of parameters which relate to the distance the CoP trajectory moves during standing are the most common means of CoP analysis (R. J. Doyle, et al., 2007; Prieto et al., 1996; Salavati et al., 2009). The measurement of the average distance that the CoP trajectory is separated from its mean position enables the determination of the degree of postural steadiness, while mean velocity gives information on the regulatory activity required to achieve this steadiness (Prieto, et al., 1996). The calculation of total displacement gives information about the quantity of CoP movement in a given direction during a measurement (Deffeyes et al., 2009).

The calculation of the area about which the CoP trajectory moves is another commonly-used means of CoP analysis (R. J. Doyle, et al., 2007; Prieto, et al., 1996). These techniques fit a geometric shape – i.e. a circle or an ellipse – to CoP movement during a given measurement, using distance measures as radii, and then the area of the given shape is calculated. It is common to incorporate a confidence interval component to the calculation, to
ensure that the shape fitted to the trajectory is less likely to be skewed by outliers and therefore is representative of the trial (R. J. Doyle, et al., 2007). Measurement of CoP ellipse area over a given period of time is a useful indicator of ability to stand quietly (Gerbino et al., 2007). It has been contended that the calculation of circle area is not functionally relevant, since the ML component of the CoP will generally deviate less than its AP counterpart during quiet standing (Sparto & Redfern, 2001). Therefore the fitting of ellipsoids to CoP data has become more common in recent studies, since the narrowness of the width of an ellipse relative to its length can be considered more relevant for this type of analysis.

The movement of the CoP and CoM trajectories during quiet standing are thought to be closely related (Brenda, et al., 1994), with the CoP varying with the CoM in order to maintain the position of the latter within the base of support (Corriveau, Hebert, et al., 2000). The outcome measure CoP - CoM, which is found by subtracting the global position of the CoM in a given transverse direction by its CoP counterpart (Hsue, et al., 2009) is known to be closely related to acceleration of the CoM (Winter, 1995), and a large CoP - CoM distance is related to postural impairment (Termoz et al., 2008). Corriveau et al. (2000) contended that regardless of whether the CoP is ahead, behind, left or right of the CoM, it is the quantity of separation between these variables – i.e. the CoP - CoM value – that causes CoM instability.

It has been suggested that a deficiency in one of the three balance assets available to an individual – somatosensory, vestibular and visual – will be compensated for by an increase in dependence on the other remaining assets (Fujimoto, et al., 2009). Neuropathic diabetic patients whose peripheral somatosensory assets have been compromised will theoretically rely more heavily on vestibular and visual cues for maintaining balance. Calculation of the Romberg ratio is a common means of determining the effect of the loss of visual cues on postural sway during quiet standing (Prieto, et al., 1996), and is found by dividing the ‘no vision’ condition by its normal vision counterpart for a given CoP outcome measure (Bergin, et al., 1995). It has been suggested that this ratio is able to establish the magnitude of an individual’s dependence on their vision for maintaining upright balance (Fujimoto, et al., 2009).

Similar to the Romberg ratio, the calculation of a ‘foam ratio’ has been used to investigate the effect of reductions in somatosensory input on postural stability, and is found by dividing a given foam surface variable by its standard surface counterpart (Fujimoto, et al., 2009). The calculation of this variable allows for the determination of a given participant or
Effect of the Intervention on Postural Stability

population groups’ dependence on somatosensory information in order to maintain upright balance (Fujimoto et al., 2010).

Previous research has shown that during quiet standing, ankle musculature controls AP CoP movement while the hip ab/adductors control ML CoP movement (Winter et al., 1996). In order to examine this, cross correlation analysis can be employed (Masani et al., 2003; Termoz, et al., 2008), which assesses the correlation between two time series – in this case, CoP in a given direction and a given relevant joint moment – and returns a correlation coefficient between -1 (perfect negative relationship) and +1 (perfect positive relationship). Additionally, this type of analysis allows for the assessment of lag between the two signals in order to determine whether one is following the other or vice versa (Winter et al., 2003; Winter et al., 1998). This analysis has previously shown differences in mechanisms for maintaining upright balance in normal, elderly and some pathological populations (Gunther et al., 2009; Masani, et al., 2003; Termoz, et al., 2008), however it remains unknown what effect diabetic neuropathy has on this relationship. Logically, a reduction in ankle motor function could cause an alteration in this mechanism whereby control of postural stability is kept more central, i.e. at the hip. This would result in a reduction in the role of the ankle relative to the hip in maintaining upright balance in these populations; however since this is yet to be quantified, this is only speculative.

Improving postural stability in pathological populations

The employment of balance and lower limb-focussed strength training programmes is common in populations with some lower limb neuromuscular pathology. Lynch et al. (2007) showed improvements in multiple clinically-relevant balance tasks following a physical training intervention in patients immediately following a stroke. Lee and Lin (2008) showed improvements in postural stability in patients with unilateral functional ankle instability following a 12-week training programme using an ankle training device. Eils and Rosenbaum (2001) showed improvements in joint proprioception and postural stability in patients with chronic ankle instability following a six-week training programme which focussed on balance and low-impact lower limb strengthening exercises, not dissimilar to the intervention employed in the current study. Since many of the peripheral symptoms of neuropathy are shared with those of ankle instability – such as increased motor latency in response to
Effect of the Intervention on Postural Stability

perturbation (Di Nardo, et al., 1999; Konradsen & Ravn, 1991) – it is possible that an exercise intervention that has been observed to cause improvements in postural stability in populations with ankle instability may be equally successful in neuropathic populations.

Allet et al. (2010a; 2010b) recently showed an improvement in postural stability in a neuropathic population following a training programme which comprised of multiple stations, each of which required participants to complete gait- and balance-specific tasks, such as stair climbing, wobble board balancing and sit-to-stand transitions. The postural stability measures which showed improvements included clinical measures such as time taken to walk across a narrow beam, as well as a balance index recorded on a stabilometric system. Likewise, Richardson et al. (2001), when conducting a low-impact lower limb balance and strength training programme in a neuropathic population, showed improvements in clinical measures of balance such as functional reach and tandem stance time. More recently, Morrison et al. (2010) showed a reduction in fall risk as measured using a clinical index in diabetic patients following a six-week low-impact balance and strength training programme.

These investigations show that it is possible to improve at least the clinical measures of postural stability in neuropathic populations. However it is unknown whether such functional improvements may be the result of repetition and skill improvement, or are the result of an improvement in the neuromuscular mechanisms of balance maintenance. The clinically-relevant outcomes measured by Allet et al. (2010a; 2010b), Richardson et al. (2001) and Morrison et al. (2010) provide strong clinical support for the integration of such exercise programmes in populations with some gait and balance pathology, but offer little in the way of explanation of the mechanisms behind any exhibited improvements.

Therefore the purpose of this component of the current study was to investigate the effect of the exercise intervention (Chapter 3) on postural stability in a neuropathic diabetic population, measured using methodologies which allow for elaboration on the mechanisms behind balance maintenance. If, as a result of the intervention, these postural stability measures significantly improve, this is indicative of an improvement in neuromuscular control of postural stability and therefore a reduction in the likelihood of fall occurrence.
Effect of the Intervention on Postural Stability

Postural stability hypotheses

It was hypothesised that postural instability caused by peripheral motor and somatosensory dysfunction in the current neuropathic diabetic population would be improved as a result of the intervention. These improvements would manifest as reductions in the quantity of CoP movement, as well as alterations to the mechanisms of balance maintenance including increases in the role of the ankle due to the ankle-specific nature of the exercise intervention.

In summary, it was hypothesised that, as a result of the intervention:

- The quantity of movement of the CoP, as measured by the distance to mean, displacement, velocity and ellipse area variables, will decrease, indicating an improvement in the quantity of movement required to maintain postural stability;
- The separation between the CoP and CoM, as measured by the CoP - CoM variable, will decrease, indicating an improvement in postural stability;
- The cross-correlation strength between ankle moments and relevant CoP measures will increase and the latency between these measures will decrease, indicating an improvement in the role of the ankle in maintaining postural stability;
- The cross-correlation strength between hip moments and relevant CoP measures will decrease or stay the same and the latency between these measures will increase or stay the same, indicating a reduction in the role of the hip relative to the ankle in maintaining postural stability;
- Changes in postural stability will return to pre-intervention levels in the long-term follow up assessment, indicating that improvements were short-term due to the A-B-A format of the intervention.
Effect of the Intervention on Postural Stability

Methodology

Participants

Ten participants underwent kinetic assessment of balance, eight of whom additionally underwent kinematic assessment. Assessments were conducted at 0 weeks (pre-1), 4 weeks (pre-2), 16 weeks (post-1) and 28 weeks (post-2). As mentioned in Chapter 4, in the interim between post-1 and post-2 one participant developed a small ulcer under their right hallux and one participant underwent bariatric surgery. These participants were consequently excluded from the second follow-up assessment. Participant demographic information is exhibited in Chapter 4.

Measurement Equipment

In order to calculate CoP, ground reaction force data were collected during standing balance trials using two Bertec strain gauge-type force plates (Bertec Corp., U.S.A.), each measuring 0.6m x 0.4m. Each plate was covered with a 0.007m polyurethane flooring cover and was flush with the ground. Ground reaction force data were collected at a frequency of 1000Hz which is more than adequate for such an assessment (Anker et al., 2008; Centomo, et al., 2007; Corriveau, Prince, et al., 2000; Lafond, et al., 2004). In studies using similar equipment, the accuracy of CoP measurement has been reported as 0.002m (Corriveau, Prince, et al., 2000; Lafond, et al., 2004). Force data were collected using Vicon Workstation software (Vicon Motion Systems Inc., U.K.) and expressed in a global coordinate system, the origin of which was set during system calibration.

Three-dimensional kinematic data were collected during standing balance trials using retroreflective markers and an eight-camera Vicon MX motion capture system (Vicon Motion Systems Inc., U.K.) at a sampling frequency of 100Hz. A number of 9mm markers were attached to the skin, as well as marker ‘triads’, which are inflexible plates with three 25mm markers affixed at set distances from each other. Skin markers were attached using hypoallergenic wig tape, and secured using hypoallergenic Transpore medical tape (3M Health Care, U.S.A.). Marker triads were attached using Velcro straps and secured using Transpore medical tape.
Effect of the Intervention on Postural Stability

Experimental Protocol

(a) Conditions

Biomechanical assessments for each participant occurred at the same or similar time of day (+/- one hour) across all four assessments to minimise time-of-day effect. Postural stability was assessed during quiet standing under four different conditions (Bergin, et al., 1995; Fujimoto, et al., 2009). The four conditions were a variation of two visual and two surface conditions (Fig. 5.1); the visual conditions were eyes open and eyes closed, and the surface conditions were standing on standard polyurethane flooring as well as standing on soft foam (Comffit, Australia). CoP parameters were assessed in two directions in the transverse plane, being anteroposterior (AP) and mediolateral (ML).

For the foam conditions, two equally-sized pieces of foam (0.4m L x 0.25m W x 0.06m D) were placed in line with the medial border of each force plate, to ensure that the foam did not overlap between them. No previous research encountered during the current study which utilised foam during postural sway investigations made any mention of compensation within CoP calculations for deformation of the foam. However it was not considered methodologically sound to assume a standard thickness of the foam during trials, since some deformation due to body weight – and its distribution across the surface – will alter this thickness. Therefore an analysis of this deformation was conducted for each participant. Left heel marker height was measured across two trials for each participant – one from the standard surface-eyes open condition and one from the foam surface-eyes closed condition. The height of the marker was averaged over the entire trial for a given condition, and the relative difference in marker height was calculated between conditions. This value was then assumed to be the change in height offset, and was incorporated into subsequent CoP calculations for each participant. In order to determine foam deformation for the two participants who did not undergo kinematic assessment, foam height offset was plotted against both body mass and BMI for the participants that did undergo this analysis. A trend line was plotted and height offset for the two participants determined graphically for both body mass and BMI, which were then averaged to give the height offset used in subsequent calculations for these participants. As a matter of interest, a negative linear relationship existed between foam height and both body mass and BMI.
Figure 5.1: Four conditions for standing balance trials

(a) Kinetic data collection

Force data were collected with a foot on each force plate, separated by a set distance. In order to ensure this separation, a wooden block with a width of 0.143m was placed evenly between the two force plates, and participants were asked to place the medial borders of their forefoot and heel against this block. Therefore foot position on the force plates was standardised prior to each trial (Chiari et al., 2002), and the long axis of the foot was approximately aligned with the AP axis of the force plate.
(c) Kinematic data collection

The kinematic model employed in the current study was a modified version of the Cleveland Clinic model, adapted for the current study using the Vicon modelling software BodyBuilder (Vicon Motion Systems Inc., U.K.). The Cleveland Clinic model has been used in previous movement analysis research, particularly in groups with upper or lower limb pathology (Hsue, et al., 2009; Mackey et al., 2008; Noonan et al., 2003; Sutherland, 2002). A detailed explanation of this model and its modifications is provided in Appendix 1.

The kinematic model required the use of 39 retroreflective markers (‘markers’), 35 of which were left on during standing balance trials (dynamic marker set) and four used only during static trials (static marker set). Marker placement was always conducted by the same tester who had six years of experience with clinical and research motion capture marker placement prior to study onset. Additional markers used during the static trial were placed on the lateral and medial femoral condyles and used to define the knee joint centre (Fig. 5.2). The static trial involved the participant standing with their arms raised to the side to avoid hip and thigh markers being obscured from camera view. Following this static trial, the additional static knee markers were removed prior to the onset of standing balance trials. The position of these additional static markers was then recreated virtually by markers from the dynamic marker set (Tab. 5.1).

The dynamic marker set was comprised of 35 markers placed both directly on the skin and as part of marker triads. During dynamic trials, the neck, trunk, pelvis, hip and ankle joint centre positions were calculated based on dynamic markers, while the knee joint centre positions were calculated based on the recreated virtual markers. Based on these markers and joint centres a multi-segment ‘skeleton’ was created, comprised of arm, trunk, pelvis, thigh, shank and foot segments. Fig. 5.2 illustrates the placement of the static and dynamic markers, as well as the resultant joint centre positions with lines connecting them, as seen in Vicon Workstation. Tab. 5.1 lists all markers and their anatomical positions.
Effect of the Intervention on Postural Stability

Figure 5.2: Marker placement for modified Cleveland Clinic model in frontal plane (left), with perspective view (right) of lower limb.
Table 5.1: List of static, dynamic and virtual markers and their anatomical placement, where ASIS = Anterior superior iliac spine and Pelvis JC* is the pelvis segment origin

<table>
<thead>
<tr>
<th>Marker</th>
<th>Anatomical Placement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Static Markers</strong></td>
<td></td>
</tr>
<tr>
<td>Knee - Lateral</td>
<td>Lateral head of femoral condyle</td>
</tr>
<tr>
<td>Knee - Medial</td>
<td>Medial head of femoral condyle</td>
</tr>
<tr>
<td><strong>Dynamic Markers</strong></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>Midpoint between distal heads of radius and ulnar</td>
</tr>
<tr>
<td>Elbow</td>
<td>Lateral head of humeral condyle</td>
</tr>
<tr>
<td>Upper Arm</td>
<td>Lateral and posterior aspect of upper arm</td>
</tr>
<tr>
<td>Left Shoulder</td>
<td>Left acromion process</td>
</tr>
<tr>
<td>Right Shoulder</td>
<td>Right acromion process</td>
</tr>
<tr>
<td>Sacrum</td>
<td>Midpoint between left and right posterior superior iliac spine</td>
</tr>
<tr>
<td>Left ASIS</td>
<td>Anterior-superior crest of left iliac spine</td>
</tr>
<tr>
<td>Right ASIS</td>
<td>Anterior-superior crest of right iliac spine</td>
</tr>
<tr>
<td>Thigh Triad - Top</td>
<td>Top marker of triad attached laterally to thigh</td>
</tr>
<tr>
<td>Thigh Triad - Front</td>
<td>Front marker of triad attached laterally to thigh</td>
</tr>
<tr>
<td>Thigh Triad - Back</td>
<td>Back marker of triad attached laterally to thigh</td>
</tr>
<tr>
<td>Shank Triad - Top</td>
<td>Top marker of triad attached laterally to shank</td>
</tr>
<tr>
<td>Shank Triad - Front</td>
<td>Front marker of triad attached laterally to shank</td>
</tr>
<tr>
<td>Shank Triad - Back</td>
<td>Back marker of triad attached laterally to shank</td>
</tr>
<tr>
<td>Ankle - Lateral</td>
<td>Lateral head of malleolus</td>
</tr>
<tr>
<td>Ankle - Medial</td>
<td>Medial head of malleolus</td>
</tr>
<tr>
<td>Heel</td>
<td>Calcaneus, horizontally in line with 3rd metatarsal head marker</td>
</tr>
<tr>
<td>1st Met Head</td>
<td>Distal head of 1st metatarsal</td>
</tr>
<tr>
<td>3rd Met Head</td>
<td>Distal head of 3rd metatarsal</td>
</tr>
<tr>
<td>5th Met Head</td>
<td>Distal head of 5th metatarsal</td>
</tr>
<tr>
<td><strong>Virtual Markers</strong></td>
<td></td>
</tr>
<tr>
<td>Neck JC</td>
<td>Midpoint between Left Shoulder and Right Shoulder</td>
</tr>
<tr>
<td>Trunk JC</td>
<td>Midpoint between Pelvis and Sacrum</td>
</tr>
<tr>
<td>Pelvis JC*</td>
<td>Midpoint between Left ASIS and Right ASIS</td>
</tr>
<tr>
<td>Hip JC</td>
<td>Fitted based on pelvis, ASIS and anthropometric variables</td>
</tr>
<tr>
<td>Knee - Lateral</td>
<td>Recreated in dynamic trials based on Thigh Triad markers</td>
</tr>
<tr>
<td>Knee - Medial</td>
<td>Recreated in dynamic trials based on Thigh Triad markers</td>
</tr>
<tr>
<td>Knee JC</td>
<td>Midpoint of Knee - Lateral and Knee - Medial markers</td>
</tr>
<tr>
<td>Ankle - Lateral</td>
<td>Recreated in dynamic trials based on Shank Triad markers</td>
</tr>
<tr>
<td>Ankle - Medial</td>
<td>Recreated in dynamic trials based on Shank Triad markers</td>
</tr>
<tr>
<td>Ankle JC</td>
<td>Midpoint of Ankle - Lateral and Ankle - Medial markers</td>
</tr>
</tbody>
</table>
An additional measurement between ASIS marker placement and approximate ASIS location in the sagittal plane was made for two participants who both had large protruding abdomens which prevented the direct attachment of markers at these sites. ASIS position was then altered by this distance in the sagittal plane during subsequent analysis.

(e) Standing balance trials

Visual and somatosensory conditions were randomly allocated. Once positioned on the force plates, participants were asked to look directly ahead at a poster placed at eye-level on a wall 5.2m in front of them. Participants were given instructions regarding what was expected of them prior to each trial. For example, if the trial required the participant to stand quietly on a standard surface with their eyes closed, the instruction given would be to “keep your arms at your sides, look straight ahead at the poster – and now close your eyes”. A delay of ~3-5 seconds was added between the time that the instruction was given and the moment that data collection began to ensure adequate familiarisation with the trial condition.

Three trials were collected for each condition (Salavati, et al., 2009), since the collection of three trials has been shown to have high test-retest reliability (Manor, Doherty, et al., 2008). Reliability of CoP measures increases as data collection time increases (Carpenter et al., 2001; Le Clair & Riach, 1996). Standing balance trials lasted for 20s. One of the participants was unable to complete a full 20s trial for the FSEC condition during either of the pre-intervention assessments and only once during the 1st post-intervention assessment. Trial length in these cases was therefore dictated by how long this participant could maintain the required position without opening their eyes or stepping off the foam, a method employed in previous research measuring postural stability in patients with severe balance dysfunction (Fujimoto, et al., 2009). A rest period of 30 seconds was observed between trials and conditions. For the foam surface conditions, the position of the patient was reset following the rest period to negate any fatigue effect caused by the patient remaining on the unstable surface between trials (Saha et al., 2007).
Effect of the Intervention on Postural Stability

Kinetic Data Analysis

(a) Data filtering

Force data were analysed using a custom-written Matlab script (v7.4, The Mathworks Inc., U.S.A.). A residual analysis (Winter, 2005) was conducted to establish the appropriate cut-off frequency for the 4th-order Butterworth filter. The residual analysis compared the effect of filtering frequencies from 1-15Hz on two markers – a stable marker (sacrum) and high-velocity marker (3rd metatarsal) – as well as the xyz force components of the ground reaction force beneath the dominant limb of a randomly-selected participant. To ensure that the residual analysis was representative of the multiple conditions under which standing balance trials were collected, analysis was conducted for both the SSEC and FSEC conditions. Based on this analysis, a cut-off of 8Hz was selected for ground reaction force data (Salavati, et al., 2009).

(b) Calculation of kinetic outcome measures

Once raw force data were filtered, CoP trajectories were then calculated in both AP and ML directions for both plates. Additionally, a net CoP trajectory was calculated in both the AP and ML directions by determining the instantaneous average of the relevant CoP trajectories from each plate:

\[ \text{CoPNet}_{AP} = \frac{L\text{CoP}_{AP} + R\text{CoP}_{AP}}{2} \]

where \( L\text{CoP}_{AP} \) is the CoP position in the AP direction beneath the left limb, and \( R\text{CoP}_{AP} \) is the CoP position in the AP direction beneath the right limb.

Based on the calculated position of the AP and ML trajectories a number of outcome measures were derived, including distance, area, and non-linear measures (Tab. 5.2). In order to normalise CoP outcome measures between participants, distance and area measures were expressed as a percentage of foot length (Nardone et al., 2007; Wang & Lin, 2008).
Distance to the mean was calculated as the root mean square value of the distance between the instantaneous CoP position and average CoP position over a given trial. The total displacement of the CoP during a trial was calculated as the sum of the differences between consecutive CoP data points. Following the calculation of the displacement, it was possible to calculate the average velocity of the CoP during a given trial by dividing the displacement by the length of the trial in seconds. Ellipse area was calculated using the AP distance to the mean as the major radii and the ML distance to the mean as the minor radii and incorporating 95% of the data points (R. J. Doyle, et al., 2007; Prieto, et al., 1996). A detailed explanation of all CoP and outcome measure calculations is presented in the appendices (Appendix 2), while a brief explanation is offered in Tab. 5.2.
Table 5.2: Outcome measures and the formula(e) required for their calculation. The AP direction is used as an example, since formulae for the ML direction are generally the same. See Appendix 2 for detailed formulae explanation

<table>
<thead>
<tr>
<th>Measure</th>
<th>Formula(e)</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance to mean</td>
<td>( \text{CoPNet}<em>{\text{AP dist}} = \sqrt{\text{CoPNet}</em>{\text{AP}}^2} )</td>
<td>(R. J. Doyle, et al., 2007; Prieto, et al., 1996)</td>
</tr>
<tr>
<td>Total displacement</td>
<td>( \text{CoPNet}<em>{\text{AP disp}} = \sum \text{CoPNet}</em>{\text{AP}}[n+1] - \text{CoPNet}_{\text{AP}}[n] )</td>
<td>(Prieto, et al., 1996)</td>
</tr>
<tr>
<td>Average velocity</td>
<td>( \text{CoPNet}<em>{\text{AP vel}} = \frac{\text{CoPNet}</em>{\text{AP disp}}}{\text{Trial Length}} )</td>
<td>(Prieto, et al., 1996)</td>
</tr>
<tr>
<td>Area of ellipse</td>
<td>( \text{Area} = \pi a b \equiv 2\pi[F_{0.05}[2n-2] \sqrt{\text{CoPNet}<em>{\text{AP dist}}^2 \text{CoPNet}</em>{\text{ML dist}}^2 - \text{CoPNet}_{\text{APML dist}}^2} )</td>
<td>(R. J. Doyle, et al., 2007; Prieto, et al., 1996)</td>
</tr>
<tr>
<td>Romberg or foam ratio</td>
<td>( \text{Romberg Ratio} = \frac{\text{Eyes Closed}}{\text{Eyes Open}} )  ( \text{or Foam Ratio} = \frac{\text{Foam Surface}}{\text{Standard Surface}} )</td>
<td>(Fujimoto, et al., 2009)</td>
</tr>
<tr>
<td>CoP - CoM</td>
<td>( \text{CoP}<em>{\text{AP}}\text{CoM}</em>{\text{AP}}\text{Dist}<em>{\text{RMS}} = \sqrt{\text{CoP}</em>{\text{AP}}\text{CoM}_{\text{AP}}\text{Dist}^2} )</td>
<td>(Hsue, et al., 2009)</td>
</tr>
<tr>
<td>Cross-correlation</td>
<td>( C = \frac{(x_t - \bar{x})(y_t + lag - \bar{y})}{\sqrt{(x_t - \bar{x})^2 (y_t - \bar{y})^2}} )</td>
<td>(Li &amp; Caldwell, 1999; Termoz, et al., 2008; Winter, et al., 1996)</td>
</tr>
</tbody>
</table>
Kinematic Data Analysis

(a) Data filtering

Marker trajectories were digitised using Vicon Workstation software. As mentioned, a residual analysis of foot and hip markers was conducted in order to establish appropriate cut-off frequencies for low-pass filtering of marker trajectories (Winter, 2005). Based on this analysis, trajectory data were filtered using a low-pass 4\textsuperscript{th}-order Butterworth dual-pass filter at a frequency of 6Hz (Hsue, et al., 2009).

(b) Local coordinate system definition

Based on the dynamic and virtual markers previously described in this chapter, trunk, pelvis, thigh, shank and foot segments were created with each segment having at least three markers attached to it. Local coordinate systems were created for each segment, the axes of which were defined by the positions of dynamic and virtual markers. These axes were used to define movement directions for each segment. Table 5.3 lists each segment, the markers used to define it and the movement directions, while a detailed explanation of all calculations can be found in Appendix 1 for the sake of brevity.
Effect of the Intervention on Postural Stability

Table 5.3: List of segments with the markers and joint centres used to define them, as well as their relevant movements (F/E = flexion/extension; Abd/Add = abduction/adduction; I/E = internal/external rotation)

<table>
<thead>
<tr>
<th>Segment</th>
<th>Markers</th>
<th>Movement Directions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trunk</td>
<td>Neck JC</td>
<td>Trunk F/E</td>
</tr>
<tr>
<td></td>
<td>Left Shoulder</td>
<td>Trunk Abd/Abb</td>
</tr>
<tr>
<td></td>
<td>Right Shoulder</td>
<td>Trunk I/E</td>
</tr>
<tr>
<td></td>
<td>Trunk JC</td>
<td></td>
</tr>
<tr>
<td>Pelvis</td>
<td>Left ASIS</td>
<td>Pelvic F/E</td>
</tr>
<tr>
<td></td>
<td>Right ASIS</td>
<td>Pelvic Abd/Add</td>
</tr>
<tr>
<td></td>
<td>Sacrum</td>
<td>Pelvic I/E</td>
</tr>
<tr>
<td></td>
<td>Pelvis JC</td>
<td></td>
</tr>
<tr>
<td>Thigh</td>
<td>Hip JC</td>
<td>Hip F/E</td>
</tr>
<tr>
<td></td>
<td>Knee – Lateral</td>
<td>Hip Abd/Add</td>
</tr>
<tr>
<td></td>
<td>Knee – Medial</td>
<td>Hip I/E</td>
</tr>
<tr>
<td></td>
<td>Knee JC</td>
<td></td>
</tr>
<tr>
<td>Shank</td>
<td>Knee JC</td>
<td>Knee F/E</td>
</tr>
<tr>
<td></td>
<td>Ankle – Lateral</td>
<td>Knee Abd/Add</td>
</tr>
<tr>
<td></td>
<td>Ankle – Medial</td>
<td>Knee I/E</td>
</tr>
<tr>
<td></td>
<td>Ankle JC</td>
<td></td>
</tr>
<tr>
<td>Foot</td>
<td>Knee JC</td>
<td>Ankle F/E</td>
</tr>
<tr>
<td></td>
<td>Ankle JC</td>
<td>Ankle Abd/Add</td>
</tr>
<tr>
<td></td>
<td>Heel</td>
<td>Ankle I/E</td>
</tr>
<tr>
<td></td>
<td>Ankle – Lateral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ankle – Medial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1st Met Head</td>
<td></td>
</tr>
</tbody>
</table>

(c) Joint angles

Joint angles were calculated within the Vicon model based on the local coordinate system axes outlined above. Angles were expressed in degrees (°), and movement direction was relative to the neutral position of the joint, where neutral = 0°. One exception to this rule was the ankle dorsiflexion/plantarflexion (F/E) angle, for which the neutral position of the joint was approximately 90°. A detailed description of each joint angle calculation is provided in Appendix 1.
(d) **Joint moments**

In order to calculate joint moments, the inverse dynamic method was employed. Kinetic data from the two force plates was used to represent ground reaction force acting on the lower limb. Segment mass and moment of inertia parameters were also incorporated into calculations, while kinematic data were used to describe the position of the segment centre of mass and joint centres in order to calculate joint reaction forces (Chandler et al., 1975; Clauser et al., 1969; Dapena, 1978; Dempster, 1955). Based on these reaction forces, joint moments were calculated. These calculations are further detailed in Appendix 1.

(e) **Relationship between centre of mass and centre of pressure**

The global position of the whole body CoM was determined by multiplying the positions of segmental centres of mass by their respective ratio of segment mass to total body mass, and then summing all these individual segment calculations. Therefore the position of the whole body centre of mass was a weighted sum of the centres of mass of all other segments (Eames et al., 1999). Appendix 1 describes the calculation of segmental and whole body centres of mass in detail.

In order to directly compare CoP and CoM positions, CoP data were re-sampled to 100Hz using a custom-written Matlab script. Following re-sampling, whole body CoM trajectories in the x (AP) and y (ML) directions were subtracted from their CoP counterparts and the root mean square of the resultant time series was calculated in order to determine the CoP - CoM variable (Hsue, et al., 2009; Tab. 5.2).

(f) **Cross-correlation analysis**

Cross-correlation analysis was performed using a custom-written Matlab script. This determined the cross-correlation coefficient between two chosen time series of the same length relative to their respective means across a pre-defined number of lags. For the current study, cross-correlation coefficients were determined between the CoP and other calculated outcome measures over the course of a trial, with a separate coefficient calculated for each lag from -100 to +100 frames (-1 second to +1 second) including zero. The maximum and
Effect of the Intervention on Postural Stability

minimum cross-correlation coefficients were determined, as were the lags at which these maxima and minima occurred. The cross-correlation coefficients, or \( r \) values, ranged between -1 (perfect negative correlation) to 1 (perfect positive correlation). Lags were output in terms of number of frames and then subsequently converted to time in seconds.

Cross-correlation analyses were conducted between several related variables, including net CoP and whole body CoM as well as individual CoP trajectories and their relevant joint moments. For example, cross-correlation coefficients were calculated between net CoP in the AP direction and the F/E moment at the ankle joint.

**Statistical Analysis**

The first and last 0.5s of all calculated data were removed from analysis to avoid any ramping effect due to data filtering or re-sampling. Distance, velocity and non-linear results were averaged and standard deviations calculated for each condition using Microsoft Excel. Statistical analysis was conducted in SPSS v16.0 (SPSS Inc., U.S.A.), Microsoft Excel and Matlab. Due to the small sample size, non-parametric statistical analysis in the form of the Wilcoxon signed-ranks test was performed to check for significant differences between assessments (Corriveau, Prince, et al., 2000). Cross-correlation coefficients were calculated between CoP and related kinematic and kinetic time series data.

Significance testing was conducted between subsequent assessments. An intervention effect was defined as a significant change between the pre-2 and post-1 assessments where no such change occurred between pre-1 and pre-2. For all tests the level of significance was set at \( p < 0.05 \).
Results

CoP distance and area results

No clear intervention effect was observed for any of the CoP distance or area measures. In the few instances where a significant difference did exist between 2\textsuperscript{nd} pre-intervention and 1\textsuperscript{st} post-intervention assessments, this was undermined by high variability between baseline assessments. A reduction in CoP distance to the mean in the FS condition was observed between the two post-intervention assessments for both the AP ($p = 0.02$) and ML ($p = 0.03$) directions, as well as the ML direction for the FSEC condition ($p = 0.03$). The standard surface conditions exhibited the smallest values across assessments while the foam conditions exhibited the largest, congruent with expectations. Distances were 10-15 times larger in the AP direction than the ML direction (Tab. 5.4).

<table>
<thead>
<tr>
<th>Day</th>
<th>AP Direction</th>
<th>ML Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avg (%FL)</td>
<td>Avg Δ</td>
</tr>
<tr>
<td>SS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>2.1 ± 0.7</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>1.8 ± 0.5</td>
<td>-0.3 ± 0.3</td>
</tr>
<tr>
<td>Post-1</td>
<td>2.0 ± 0.5</td>
<td>0.2 ± 0.5</td>
</tr>
<tr>
<td>Post-2</td>
<td>2.3 ± 0.5</td>
<td>0.1 ± 0.7</td>
</tr>
<tr>
<td>SSEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>3.0 ± 1.8</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>2.8 ± 1.2</td>
<td>-0.2 ± 2.2</td>
</tr>
<tr>
<td>Post-1</td>
<td>2.7 ± 0.9</td>
<td>-0.1 ± 1.2</td>
</tr>
<tr>
<td>Post-2</td>
<td>2.7 ± 0.8</td>
<td>-0.1 ± 1.0</td>
</tr>
<tr>
<td>FS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>3.9 ± 1.3</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>3.8 ± 1.3</td>
<td>-0.1 ± 0.7</td>
</tr>
<tr>
<td>Post-1</td>
<td>3.7 ± 0.5</td>
<td>-0.1 ± 1.0</td>
</tr>
<tr>
<td>Post-2</td>
<td>3.2 ± 0.4</td>
<td>-0.4 ± 0.3</td>
</tr>
<tr>
<td>FSEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>6.3 ± 1.9</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>6.1 ± 1.5</td>
<td>-0.2 ± 1.3</td>
</tr>
<tr>
<td>Post-1</td>
<td>6.2 ± 1.4</td>
<td>0.2 ± 1.2</td>
</tr>
<tr>
<td>Post-2</td>
<td>5.6 ± 0.9</td>
<td>-0.2 ± 1.0</td>
</tr>
</tbody>
</table>
High inter-participant variability was observed for most displacement measures. Significant differences were found between the 2nd pre-intervention and 1st post-intervention assessments for the FS ($p = 0.01$) and FSEC ($p = 0.01$) conditions; however this difference is not a significant intervention effect due to high variability between the 1st and 2nd pre-intervention assessments. The standard surface conditions exhibited the smallest values across assessments while the foam conditions exhibited the largest. Displacements were 5-10 times larger in the AP direction than the ML direction (Tab. 5.5).

### Table 5.5: CoP displacement for AP and ML directions

<table>
<thead>
<tr>
<th></th>
<th>AP Direction</th>
<th>ML Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>Avg (%FL)</td>
<td>Avg Δ</td>
</tr>
<tr>
<td>SS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>111.8 ± 72.8</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>107.0 ± 72.5</td>
<td>-4.8 ± 12.7</td>
</tr>
<tr>
<td>Post-1</td>
<td>116.2 ± 67.1</td>
<td>9.2 ± 24.6</td>
</tr>
<tr>
<td>Post-2</td>
<td>112.4 ± 58.0</td>
<td>6.8 ± 32.3</td>
</tr>
<tr>
<td>SSEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>182.0 ± 116.4</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>186.9 ± 123.2</td>
<td>4.9 ± 47.3</td>
</tr>
<tr>
<td>Post-1</td>
<td>194.7 ± 141.7</td>
<td>7.8 ± 33.8</td>
</tr>
<tr>
<td>Post-2</td>
<td>164.8 ± 78.6</td>
<td>-16.0 ± 79.7</td>
</tr>
<tr>
<td>FS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>278.1 ± 214.7</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>267.7 ± 217.5</td>
<td>-10.4 ± 29.5</td>
</tr>
<tr>
<td>Post-1</td>
<td>260.7 ± 191.3</td>
<td>-7.0 ± 53.8</td>
</tr>
<tr>
<td>Post-2</td>
<td>209.7 ± 79.7</td>
<td>-21.8 ± 36.0</td>
</tr>
<tr>
<td>FSEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>423.4 ± 256.2</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>406.6 ± 190.1</td>
<td>-16.8 ± 115.0</td>
</tr>
<tr>
<td>Post-1</td>
<td>476.0 ± 279.1</td>
<td>69.5 ± 201.1</td>
</tr>
<tr>
<td>Post-2</td>
<td>440.3 ± 259.0</td>
<td>-13.4 ± 53.1</td>
</tr>
</tbody>
</table>
Regarding the velocity of the CoP, as expected the same trends and significant differences were observed as for CoP displacement. The standard surface conditions exhibited the slowest velocity across assessments while the foam conditions exhibited the largest. Velocities were 5-10 times faster in the AP direction than the ML direction (Tab. 5.6).

Table 5.6: Velocity of CoP for AP and ML directions

<table>
<thead>
<tr>
<th></th>
<th>AP Direction</th>
<th></th>
<th></th>
<th>ML Direction</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day</td>
<td>Avg (% FL/s)</td>
<td>Avg Δ</td>
<td>p</td>
<td>Avg (% FL/s)</td>
<td>Avg Δ</td>
</tr>
<tr>
<td><strong>SS</strong></td>
<td>Pre-1</td>
<td>5.6 ± 3.6</td>
<td>-</td>
<td>-</td>
<td>1.0 ± 0.2</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>5.4 ± 3.6</td>
<td>-0.2 ± 0.6</td>
<td>0.24</td>
<td>0.9 ± 0.2</td>
<td>-0.1 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>5.8 ± 3.4</td>
<td>0.5 ± 1.2</td>
<td>0.28</td>
<td>1.0 ± 0.2</td>
<td>0.1 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>5.6 ± 2.9</td>
<td>-0.1 ± 1.9</td>
<td>0.89</td>
<td>1.1 ± 0.1</td>
<td>0.0 ± 0.3</td>
</tr>
<tr>
<td><strong>SSEC</strong></td>
<td>Pre-1</td>
<td>9.1 ± 5.8</td>
<td>-</td>
<td>-</td>
<td>1.1 ± 0.3</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>9.3 ± 6.2</td>
<td>0.2 ± 2.4</td>
<td>0.80</td>
<td>1.1 ± 0.3</td>
<td>0.0 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>9.7 ± 7.1</td>
<td>0.4 ± 1.7</td>
<td>0.20</td>
<td>1.2 ± 0.5</td>
<td>0.1 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>8.2 ± 3.9</td>
<td>-0.8 ± 4.0</td>
<td>0.58</td>
<td>1.2 ± 0.3</td>
<td>-0.2 ± 0.5</td>
</tr>
<tr>
<td><strong>FS</strong></td>
<td>Pre-1</td>
<td>13.9 ± 10.7</td>
<td>-</td>
<td>-</td>
<td>1.7 ± 0.8</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>13.4 ± 10.9</td>
<td>-0.5 ± 1.5</td>
<td>0.28</td>
<td>1.5 ± 0.7</td>
<td>-0.2 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>13.0 ± 9.6</td>
<td>-0.3 ± 2.7</td>
<td>0.51</td>
<td>1.8 ± 0.7</td>
<td>0.3 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>10.5 ± 4.0</td>
<td>-1.1 ± 1.8</td>
<td>0.21</td>
<td>1.5 ± 0.5</td>
<td>-0.4 ± 0.2</td>
</tr>
<tr>
<td><strong>FSEC</strong></td>
<td>Pre-1</td>
<td>21.2 ± 12.8</td>
<td>-</td>
<td>-</td>
<td>2.3 ± 1.3</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>23.8 ± 14.0</td>
<td>-0.8 ± 5.8</td>
<td>0.39</td>
<td>2.0 ± 0.7</td>
<td>-0.3 ± 0.7</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>22.0 ± 12.9</td>
<td>3.5 ± 10.1</td>
<td>0.51</td>
<td>2.5 ± 1.3</td>
<td>0.5 ± 0.7</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>22.0 ± 12.9</td>
<td>-0.7 ± 2.7</td>
<td>0.58</td>
<td>2.4 ± 1.4</td>
<td>-0.5 ± 0.1</td>
</tr>
</tbody>
</table>
Effect of the Intervention on Postural Stability

Regarding the ellipse area, high variability was observed between the 1st and 2nd pre-intervention and 1st and 2nd post-intervention sessions for the foam conditions. A reduction in ellipse area between the post-intervention assessments was observed for the SS ($p = 0.01$), FS ($p = 0.03$) and FSEC ($p = 0.05$) conditions (Tab. 5.7).

Table 5.7: CoP ellipse area

<table>
<thead>
<tr>
<th></th>
<th>Ellipse Area</th>
<th>Day</th>
<th>Avg (% FL²)</th>
<th>Avg Δ</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SS</strong></td>
<td></td>
<td>Pre-1</td>
<td>4.7 ± 3.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pre-2</td>
<td>3.1 ± 1.8</td>
<td>-1.6 ± 2.1</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-1</td>
<td>3.9 ± 2.0</td>
<td>0.8 ± 1.3</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-2</td>
<td>5.5 ± 3.4</td>
<td>0.5 ± 2.4</td>
<td>0.753</td>
</tr>
<tr>
<td><strong>SSEC</strong></td>
<td></td>
<td>Pre-1</td>
<td>9.3 ± 9.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pre-2</td>
<td>9.0 ± 8.2</td>
<td>-0.3 ± 13.0</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-1</td>
<td>6.3 ± 5.1</td>
<td>-2.7 ± 8.0</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-2</td>
<td>8.3 ± 4.2</td>
<td>0.6 ± 7.1</td>
<td>0.917</td>
</tr>
<tr>
<td><strong>FS</strong></td>
<td></td>
<td>Pre-1</td>
<td>22.7 ± 22.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pre-2</td>
<td>17.6 ± 10.7</td>
<td>-5.1 ± 14.3</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-1</td>
<td>17.4 ± 10.0</td>
<td>-0.1 ± 7.1</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-2</td>
<td>11.5 ± 5.8</td>
<td>-10.6 ± 7.9</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td><strong>FSEC</strong></td>
<td></td>
<td>Pre-1</td>
<td>58.6 ± 51.4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pre-2</td>
<td>36.3 ± 20.0</td>
<td>-22.4 ± 33.0</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-1</td>
<td>38.0 ± 15.9</td>
<td>1.8 ± 16.4</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post-2</td>
<td>28.9 ± 15.6</td>
<td>-11.4 ± 9.0</td>
<td><strong>0.05</strong></td>
</tr>
</tbody>
</table>
Effect of the Intervention on Postural Stability

Romberg and foam ratio results

No intervention effect was observed for Romberg ratio for either the standard surface or foam surface conditions. Non-significant increases in Romberg ratio were observed for the distance to mean \( (p = 0.12) \), displacement \( (p = 0.16) \) and velocity \( (p = 0.16) \) measures in the foam conditions. High variability was observed between the two pre-intervention assessments for the standard surface but not the foam surface conditions. Romberg ratios tended to be larger for a given variable in the AP direction. Romberg ratio results are exhibited in Appendix 3 for brevity. No intervention effect was observed for foam ratio for either the eyes open or eyes closed conditions. Foam ratios were similar in size for both AP and ML directions. Foam ratio results are also exhibited in Appendix 3 for brevity.

CoP - CoM results

No intervention effect was found for the CoP - CoM variable in either the AP or ML directions. A significant difference was observed between the two pre-intervention assessments for the FSEC condition in the ML direction \( (p = 0.05) \). CoP - CoM distance appeared to increase between the two post-intervention assessments for most conditions, accompanied with an increase in inter-participant variability. While the FSEC condition appeared to exhibit the greatest average separation, the distance between the CoP and CoM remained relatively similar regardless of condition. The CoP - CoM distance was similar in the AP and ML directions (Tab. 5.8).
### Table 5.8: Root mean square of CoP - CoM

<table>
<thead>
<tr>
<th></th>
<th>AP Direction</th>
<th></th>
<th>ML Direction</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day</td>
<td>Avg (%FL)</td>
<td>Avg Δ</td>
<td>p</td>
</tr>
<tr>
<td><strong>SS</strong></td>
<td>Pre-1</td>
<td>1.6 ± 1.6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>1.0 ± 0.5</td>
<td>-0.6 ± 1.5</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>1.1 ± 0.7</td>
<td>0.1 ± 0.6</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>1.5 ± 1.6</td>
<td>0.2 ± 1.5</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td><strong>SSEC</strong></td>
<td>Pre-1</td>
<td>1.5 ± 1.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>1.2 ± 0.4</td>
<td>-0.3 ± 1.2</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>1.2 ± 0.7</td>
<td>0.1 ± 0.6</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>1.6 ± 1.4</td>
<td>0.2 ± 1.4</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td><strong>FS</strong></td>
<td>Pre-1</td>
<td>1.7 ± 1.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>1.3 ± 0.5</td>
<td>-0.4 ± 1.1</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>1.3 ± 0.7</td>
<td>0.0 ± 0.5</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>1.9 ± 1.7</td>
<td>0.5 ± 1.7</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td><strong>FSEC</strong></td>
<td>Pre-1</td>
<td>2.0 ± 1.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>1.7 ± 0.4</td>
<td>-0.3 ± 1.0</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>1.7 ± 0.7</td>
<td>0.1 ± 0.5</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>2.5 ± 2.0</td>
<td>0.7 ± 2.0</td>
<td><strong>0.03</strong></td>
</tr>
</tbody>
</table>
Cross-correlation results

There were few instances of significant differences that would have indicated an intervention effect for the cross-correlation and lag variables. An increase in correlation strength for the SSEC condition between ankle I/E moment and ML CoP was exhibited for the non-dominant limb following the intervention \((r = 0.48\) to \(r = 0.66, p = 0.04\)), which exhibited a trend back to baseline at the 2\textsuperscript{nd} post-intervention assessment \((r = 0.55, p = 0.60)\). Cross-correlation and lag results are exhibited in Appendix 3 for brevity.

Cross-correlation analysis revealed high correlations between AP CoP and the ankle F/E moment for both limbs and all conditions, with similar although slightly lower correlation strengths exhibited with the knee F/E moment (Fig. 5.3). In both cases, correlation strength was highest in the standard surface conditions with a visible drop in correlation strength for the foam conditions. The hip F/E moment exhibited moderate correlation strength with AP CoP across conditions. Average lag at maximum correlation strength ranged from 10-30ms between ankle F/E moment and AP CoP movement for all conditions, with a slight increase in lag time for the foam conditions. Average lags between AP CoP and both knee and hip F/E moments were inconsistent between session, condition and limb.

\textbf{Figure 5.3:} Cross-correlation coefficient \((r)\) results between AP CoP movement and ankle, knee and hip F/E moments during the SS condition for the dominant limb

![Cross-correlation coefficient results](image-url)
Effect of the Intervention on Postural Stability

The strongest cross-correlation for the ML direction was observed in the relationship between ML CoP and ankle I/E moment, while the hip rotation moment was also moderately correlated with ML CoP movement and the hip ab/adduction moment was weakly correlated (Fig. 5.4). Average lag at maximum correlation strength between these moments and the ML CoP trajectory were inconsistent between session, condition and limb.

Figure 5.4: Cross-correlation coefficient ($r$) results between ML CoP movement and ankle I/E, hip Ab/Ad and hip rotation moments during the SS condition for the dominant limb. Ankle values have been normalised to positive for graphical purposes.
Discussion

Addressing the hypotheses

The hypothesis that the quantity of movement of the CoP, as measured by the distance to mean, displacement, velocity and ellipse area variables, would decrease following the intervention was proven incorrect. The hypothesis that the separation between the CoP and CoM, as measured by the CoP - CoM variable, would decrease as a result of the intervention was also proven incorrect.

Furthermore, it was hypothesised that the cross-correlation strength between ankle moments and relevant CoP measures would increase and the latency between these measures would decrease as a result of the intervention. This hypothesis was proven largely incorrect; some non-significant increases in the correlation between ML CoP movement and ankle I/E moment were found, but no other consistent trends were discovered from cross-correlation or latency analysis.

It was hypothesised that cross-correlation strength between hip moments and relevant CoP measures would decrease or stay the same and the latency between these measures would increase or stay the same. This hypothesis was proven correct by default, since relevant cross-correlation coefficients and latency measures did not significantly change. However this hypothesis was based on the premise that the role of the ankle in maintaining postural stability would increase and the hip would remain the same, indicating a reduction in the role of the hip relative to the ankle in maintaining postural stability due to improvements in ankle function. Since the previous hypothesis regarding the role of the ankle was proven largely incorrect, the hypothesis regarding the relative role of the hip becomes redundant.

It was hypothesised that changes in postural stability would be short-term, a hypothesis based on the premise that multiple postural stability improvements would be found as a result of the intervention. This hypothesis is also redundant, since no significant changes in postural stability were exhibited as a result of the intervention.
Effect of the Intervention on Postural Stability

CoP distance and area measures

The CoP distance and area results of the current group were higher than those previously reported in healthy populations (R. J. Doyle, et al., 2007; Prieto, et al., 1996), which suggests that the current group of participants did exhibit dysfunctional postural stability prior to the onset of the intervention. The lack of any consistent and significant intervention effect found in the CoP distance and area measures may be explained by the observation that methodologically the outcome measures are not those that can be altered by such an intervention. In a randomised controlled trial with a similar goal to the current study, Allet et al. (2010a; 2010b) took a group of neuropathic diabetic patients through an intervention which consisted of gait, balance and lower limb-focussed strengthening exercises similar to those employed in the current study. However the outcome measures chosen for that study could be considered largely clinical; the measurement of postural stability included time to walk across a narrow beam, as well as a balance index derived from a stabilometric device which measures the angle of deviation away from neutral while participants stand on a deviating platform. The authors of this study found some improvement in these measures following their intervention (Fig. 5.6).

Figure 5.6: Time to cross a beam (left) and balance index (right) results from Allet et al. (2010b), Fig. 2, p463. BA = baseline, PI = post-intervention, FU = follow-up

Perhaps the postural stability outcome measures employed in the current study were not those that can be altered in a neuropathic population with a balance and low-impact strength training intervention, and more clinically-relevant measures should have been assessed. There are a number of studies which have investigated such measures in
neuropathic diabetics, using tests such as up-and-go (Goldberg, et al., 2008; Manor, Doherty, et al., 2008) and the Berg balance scale (Matjacic & Zupan, 2006). However it was decided at the beginning of the study that since improvements in the CoP outcome measures that were eventually employed had been exhibited in populations with other forms of peripheral sensorimotor dysfunction, it stood to reason that it was possible that similar improvements would be exhibited by a neuropathic diabetic group.

Also, as stated in the introduction it was the intention of the current study to explain the mechanisms behind improvements in motor function as a result of a low-impact exercise intervention, since the research by Allet et al. (2010a; 2010b) lacked the sophistication of outcome measures to do so. This purpose was unable to be expanded on due to the lack of change in postural stability exhibited by the current group of participants as a result of the intervention.

Romberg and foam ratios

In contrast to the CoP distance and area measures, the Romberg ratio results of the current group of participants were more similar to that previously reported in healthy controls than neuropathic populations (Bergin, et al., 1995). This suggests that the absence of change post-intervention was due to a lack of pre-intervention pathology for this measure. Also, the absence of any clear intervention effect on these results suggests that the role of vision in maintaining postural stability did not change as a result of the study. This finding could be explained by the fact that the intervention did not incorporate any exercises which would necessarily have improved this relationship. If an extra component was introduced to the training programme – for example the removal of vision during balance board exercises – perhaps a shift in Romberg ratio would have been expected.

In a study investigating postural control strategies from a bioengineering perspective, Sabatini (2000) used Romberg ratio analysis to organise clusters of data to examine the effect of vision on balance. A similar data treatment method was attempted for the current study; however no clear pattern occurred within the data set which allowed for the grouping of participants based on their Romberg ratio for a given variable.
Effect of the Intervention on Postural Stability

The calculation of the foam ratio determined the effect of the intervention on the dependence of the neuropathic participants on somatosensory information in order to maintain postural stability. Since this relationship did not show any significant intervention effect, it can be assumed that this dependence remained unaltered. The foam ratio values exhibited for velocity (and therefore displacement) were comparable with those previously found in patients with vestibulopathy, and slightly higher than healthy controls (Fujimoto, et al., 2010), therefore suggesting that the current group of participants did exhibit some logical pathology in terms of dependence on somatosensory feedback. Unfortunately this was not improved by the intervention, and this absence of change may therefore reflect an inability of the intervention to cause improvements in motor function.

CoP - CoM

No intervention effect was observed for CoP - CoM, including the cross-correlation between these two time series. This effectively means that there was no reduction in the distance between the CoP and CoM, which would be indicative of an improvement in CoM stability (Corriveau, Hebert, et al., 2000). Interestingly, the CoP - CoM results exhibited by the neuropathic population in the current study were similar to those exhibited in a previous study by a healthy control group (Corriveau et al., 2004), suggesting that perhaps the reason no improvements were exhibited for this measure following the intervention was that the separation between the CoP and CoM was not pathological prior to the onset of the intervention.

Role of the hip versus ankle in the maintenance of postural stability

It was hypothesised that, as a result of the intervention being ankle-specific in terms of exercise modality, there would be a shift in correlation strength between the centre of pressure position and moments at the hip and ankle, whereby correlation strength would decrease at the hip and correspondingly increase at the ankle. Ancillary to this, it was hypothesised that there would be a reduction in the latency between centre of pressure movement and the ankle moment response (or vice-versa), and a corresponding increase of the same latency at the hip. Regarding the first part of this hypothesis, the correlation
Effect of the Intervention on Postural Stability

between CoP movement in the AP direction and the ankle F/E moment did not change significantly as a result of the intervention. However it should be noted that the correlation between these variables was already considerable across all conditions prior to the onset of the intervention; $r$ values $>0.96$ were exhibited for the standard surface conditions, and although the correlation decreased for the foam conditions $r$ values were still $>0.8$. Any improvement in the latter values following the intervention – i.e. an increase towards the correlations exhibited in the standard surface conditions – did not materialise. The strong correlation between ankle F/E moment and AP CoP movement is congruent with previous findings in other populations (Winter, et al., 1996).

The correlation between the knee joint F/E moment and the A/P CoP movement also showed considerable strength regardless of day and condition. Similarly to the ankle joint, no evidence of an intervention effect on this relationship was exhibited. Never attaining the correlation strength exhibited at the ankle or knee joints, the relationship between AP CoP movement and hip F/E moment also exhibited no intervention effect.

In contrast to the findings of previous authors (Winter, et al., 1996), who found that ML postural stability was maintained by the hip ab/adductors, the strongest correlations with ML CoP movements in the current study were found with the ankle I/E moments (Fig. 5.4). Weak correlations – and no intervention effects – were observed between ML CoP movement and ankle ab/adduction for all conditions. Only weak ($<0.5$) correlations were found between ML CoP movement and both rotational and ab/adduction moments at the hip, with the latter showing the weakest correlation strength. These results suggest that while the ankle I/E moments played the major role in the compensatory postural position changes required to maintain ML balance, hip ab/adductors and rotators also regulated these changes. Following the intervention a slightly higher correlation between ML CoP movement and the ankle I/E moment was observed in the standard surface conditions, with $r$ values shifting from $<0.7$ to $>0.7$ in most cases. Furthermore, since the correlation between ML CoP movement and ankle I/E moment appears to have increased as a result of the intervention, it can be tentatively suggested that the hypothesis that the role of the ankle in maintaining ML stability was enhanced by the intervention. However this intervention effect only reached statistical significance in one instance, namely the non-dominant limb during the SSEC condition ($p = 0.04$), and is therefore too weak an effect from which to draw any general conclusions. It should also be noted that this dubious post-intervention change was not observed for the foam
conditions, where the correlation between ML CoP movement and ankle I/E moment remained <0.7. These theoretical suppositions regarding the maintenance of ML stability should be accompanied with the observation that due to a much larger base of support the ML movement of the CoP was vastly smaller than its AP counterpart, as were the related joint moments. Therefore the role of these moments in balance maintenance during these trials was important but always secondary to those maintaining AP stability.

Bergin et al. (1995) found a significant correlation between severity of neuropathy as measured with vibration perception tests and increases in postural sway, but no correlation between muscular strength and postural sway. Based on these findings, the authors contended that the instability exhibited by neuropathic patients was caused by reductions in proprioception rather than muscle function (Bergin, et al., 1995). Bloem et al. (2002) contended that hip proprioception is the key factor in the maintenance of postural stability. Their research investigated the effect of total peripheral proprioceptive loss – found in patients with ganglionopathies – on the maintenance of postural stability following an external perturbation. The authors suggested that almost all balance corrections necessary for the maintenance of postural stability are generated by hip and trunk proprioceptors – that corrective responses to perturbations of balance by the lower limb are not generated by peripheral sensory proprioception, but rather dictated from a different region. It is likely that the truth resides somewhere in the middle; that it is the combination of all proprioceptive inputs upon which appropriate balance corrections are based. However this is a potentially enlightening theory that may explain the lack of improvement in the role of the ankle in the maintenance of postural stability following the intervention, particularly in the foam conditions in which proprioceptive loss was compounded. If, as suggested by Bloem et al. (2002), the hip has the major role in the maintenance of postural stability, any improvements in lower limb proprioceptive function following the intervention (Chapter 4) would be unlikely to manifest as any improvement in postural stability.

Perhaps this is a reflection upon a larger issue. The main philosophy of the design of the exercise intervention was to focus directly on the symptoms of the disease in question, namely loss of sensorimotor function at the periphery. By designing a training programme which focussed directly on the lower limb, it was theorised that these symptoms could be addressed at the location at which they present. This was proven to be successful in improving sensory threshold; however, the results presented in the current chapter suggest
that this localised approach is not as effective at improving postural stability. Perhaps a more systemic approach, encompassing whole-body exercises would be more effective at causing greater improvement in this area.

Variability

Large within-group variability was exhibited for a number of the postural stability outcome measures. This is obvious from the large standard deviations exhibited in variables such as CoP displacement and CoP ellipse area (Tabs. 5.5 and 5.7), and suggests that the group lacked homogeneity in terms of quality of postural stability. While within-group variability was found to be very low when examining the cross-correlation between two highly-correlated time series – such as CoP in the AP direction versus F/E moment at the ankle joint – within-group variability tended to be high when the two correlated time series had only a moderate or weak strength of correlation.

The variability exhibited for some outcome measures can be partially explained by inter-participant variability in quality of postural stability; however the statistical techniques employed to ascertain whether the effect of the intervention was significant only examined the intra-participant effect and how that relates to the rest of the group. Therefore, the lack of a clear group effect on most of the postural stability variables is most simply explained by the observation that each of the participants responded differently to the intervention, or most commonly exhibited a null response. Also, intra-participant responses were unpredictable; just because a participant improved in one outcome measure did not necessarily translate into improvements across several related variables. It seems that while changes were observed in some variables for some participants, the determination of a clear pattern from these results was not possible.

For example, it was not necessarily the case that a high level of balance dysfunction in a given participant translated into an increased likelihood of exhibiting improvements. Upon examination of the individual responses to the intervention, it was discovered that those that exhibited the greatest postural sway for a given distance measure were no more likely to exhibit changes than those participants with the smallest postural sway. While this finding is not contrary to any of the initial hypotheses – when it was naively assumed that the
attainment of a highly homogenous group was possible – it does seem counterintuitive. Common sense may lead one to believe that those who are the most unskilled at a task will show the most relative improvement following an intervention when compared to those who are already somewhat adequate at its performance, particularly when the intervention is the same for everyone as it was in the current study.

Another factor which makes the determination of clear intervention effects difficult is the high within-session variability observed for some outcome measures between the first and second pre-intervention assessments. It is possible that some of this variability is due to methodological error; however, it should be emphasised that all methodologies chosen for the assessment of postural stability in the current study were shown to be highly repeatable by previous researchers, and that the current author had multiple years’ experience conducting each aspect of the study. It is possible that the neuropathic population examined in the current study may exhibit some variability in some postural stability measures when assessments are separated by a duration of one month. It can be speculated that this variability is caused by an inherent variability of the disease itself; that the symptoms of diabetic peripheral neuropathy which affect postural stability may not present themselves equally from month-to-month or even day-to-day. This theory is supported by statements made by several participants at a number of instances during the intervention period, who complained that their neuropathic symptoms, including sense of balance, were particularly severe that day or vice-versa.

Limitations

The sampling duration for standing balance trials in the current study was 20 seconds. This sampling duration can be considered a limitation, since Carpenter et al. (2001) recommend sampling frequencies of 60 seconds and above. Their reasoning for this recommendation was that sampling frequencies lower than this time frame may not allow for the collection of low-frequency oscillations in the CoP but only higher frequency components, a suggestion also made by Winter et al. (1998). However, Carpenter et al. (2001) do state that while their recommendations would be beneficial to trial validity, the individual researcher needs to ‘weigh-up’ the limitations of their own participant population and decide upon an appropriate sampling frequency. Unlike their research, the participant
population of the current study had varying levels of sensory loss, meaning that most participants found certain conditions of the postural stability test difficult to complete. While no serious falls occurred during testing, there were a few instances where trials needed to be reset due to participants needing to step off the foam, or open their eyes, or a combination of both. One patient had such severe postural stability dysfunction that they were unable to complete the FSEC condition during any of the pre-intervention assessments. The incompletion of standing balance trials is to be expected when investigating postural stability in populations that may suffer from severe balance dysfunction (Black et al., 1982; Fujimoto, et al., 2009). Therefore there is no doubt that a sampling duration of longer than 20 seconds would have been problematic if employed in the current study. While it is possible that most would have been able to complete the conditions eventually, it is likely that the number of trial resets due to participant failure during the difficult surface and visual conditions would have greatly increased. Such an increase would not only further extend the already time-consuming biomechanical assessment sessions, but more importantly fatigue effects may have occurred. However, it is accepted that since previous research has shown a beneficial effect to trial validity when sampling durations are in excess of 60 seconds (Carpenter, et al., 2001), the sampling duration of 20 seconds employed in the current study may be a limitation – but one which was largely unavoidable.

There is an assumption when investigating postural stability under foam surface conditions that the centre of pressure being measured is indicative of the position of the centre of pressure at the foot-ground interface. However, what is actually being measured is the position of the centre of pressure at the foam-ground interface, not the foot-ground (or foot-foam) interface. Therefore, as with all studies that measure centre of pressure during foam surface conditions using force plates, there is inherent error in this measure because of this necessary assumption. The effects of this error cannot be quantified via outcome measures employed in the current study – but given the test-retest design of the study this limitation should not have any significant effect on postural stability results.

Following drop-outs, only 10 participants – 8 of whom underwent both kinematic and kinetic analysis – completed the exercise intervention. As stated in Chapter 4, this small sample size is a limitation that reduces the power of the supposition that the experimental hypotheses were proven incorrect since no significant intervention effect was exhibited by the current neuropathic group.
As previously discussed, high variability existed between the pre-intervention assessments for several postural stability outcome measures. Although it was contended that this may be due to the natural variability of the disease itself, another explanation could be that participants underwent some form of learning effect. While it can be argued that such a learning effect was possible, it is theorised that since pre-intervention assessments were separated by one month any such effect should have been minimised. Nevertheless, the fact that participants had no experience in undergoing postural sway assessment prior to the 1\textsuperscript{st} pre-intervention assessment, and then had this previous experience for the 2\textsuperscript{nd} pre-intervention assessment, is acknowledged as an unavoidable limitation.

**Conclusions**

The lack of any definitive improvements in postural stability suggests that, at least for the current group of neuropathic diabetics, the assessed measures of postural stability cannot be improved with the volume and intensity of balance and lower limb-focussed strength training employed by the current intervention. High variability existed within the current group of participants for some of the postural stability measures. Perhaps if a larger sample size had been acquired, a stratification of participants into groups according to dysfunction of postural stability could have been conducted. This would allow for a more robust investigation of the effect of severity of balance dysfunction on adaptation following the intervention.

While the intervention did not alter the mechanisms of motor function required during the maintenance of postural stability, it is possible that the mechanisms of larger dynamic movements could have been affected. The next experimental component will investigate the effect of the exercise intervention on gait.
Chapter Six

Effect of the Intervention on Gait
Introduction

Overview

In the previous chapter, it was discovered that the intervention had no significant effect on postural stability, despite evidence that some instability existed prior to the implementation of the intervention. In the current chapter, the effect of the intervention on the kinematic and kinetic aspects of gait will be investigated.

Human gait is a cyclical motor task that requires fine control over the timing and amplitude of the movement of multiple joints. These movements rely on sensory feedback, particularly joint proprioception, which as previously discussed is impaired in neuropathic populations. Individuals with diabetic peripheral neuropathy may exhibit altered gait mechanics which places this population at an increased risk of falling (Akashi et al., 2008; Allet, et al., 2010a; Dingwell et al., 2000; Meier et al., 2001). In fact, diabetics with peripheral neuropathy are approximately fifteen times more likely to sustain an injury during gait than diabetics without peripheral neuropathy (P.R. Cavanagh, Derr, et al., 1992).

The gait of neuropathic diabetics has been referred to as conservative (Courtemanche et al., 1996), a phrase which insinuates avoidance of risk of injury. It can be hypothesised that individuals with neuropathic symptoms may, without awareness, alter their gait patterns in a manner which places them at less risk of falling. One way this is accomplished is by reducing walking speed, in order to allow them more time to react to unexpected obstacles or perturbations. Manor et al. (2008) examined the effect of walking speed on variables related to gait stability in neuropathic diabetics, and stated that the faster the walking speed, the greater the degree of instability exhibited.

Assessment of gait

Gait can be assessed with a variety of different equipment and methodologies. Sophistication of measurements can range from the collection of three-dimensional kinematic and kinetic data using motion capture systems and force plates, through to the measurement of temporal spatial parameters which may only require a stopwatch or other readily-available
Effect of the Intervention on Gait

equipment. The latter is appropriate for use in clinical settings, where outcome measures are generally related to gross gait function such as walking speed and stride length. However, in order to understand the mechanisms behind pathological gait, a comprehensive analysis of gait kinematics and kinetics is necessary (Sutherland, 2002).

*Relevant outcome measures*

Because of their simplicity and availability, temporal spatial parameters are the most commonly-described outcome measures in the neuropathic gait literature. This may also be due to the immediate relevance in terms of quality of life of measures such as how quickly a patient can move or how many steps they can take in a minute (Allet, et al., 2010a; Allet, et al., 2010b), as opposed to the in-depth investigation of the kinematic and kinetic qualities of gait which offer more information on the mechanisms behind such gross measures of motor function.

Regarding these temporal spatial measures, previous studies revealed a reduction in walking speed in neuropathic populations compared to healthy controls (Courtemanche, et al., 1996; Kanade et al., 2006; Katoulis et al., 1997; Yavuzer et al., 2006) as well as non-neuropathic diabetics (Paul et al., 2009). Furthermore, it has been demonstrated that this population exhibits a reduced cadence compared to healthy controls (Allet et al., 2009; Allet et al., 2008; Menz et al., 2004). Previous researchers have also shown an alteration in the amplitude of distance covered by each gait cycle in neuropathic diabetics (Courtemanche, et al., 1996; Yavuzer, et al., 2006), and it has been suggested that this reduction in stride length is part of a strategy to reduce plantar loading (Rao et al., 2006).

Neuropathic diabetics also spend less time in the single-support phase of gait than healthy controls (Courtemanche, et al., 1996), and have been shown to spend longer in the double-support phase than non-neuropathic diabetics (Paul, et al., 2009). The concept that a population with peripheral neuromuscular dysfunction would reduce time spent in single-support is unsurprising, when we consider the inherent improvement in dynamic stability achieved by having two feet on the ground instead of one. Related to this, the measurement of the distance between the centre of pressure (CoP) as measured by a force platform and whole body centre of mass (CoM) can offer information regarding the quality of dynamic
Effect of the Intervention on Gait

stability exhibited during gait (Hsue, et al., 2009). However although researchers have used this measure when investigating standing balance in neuropathic diabetics (Corriveau, Prince, et al., 2000), it is yet to be used to investigate dynamic balance during gait in this population.

The description of the range of movement of a given relevant joint during gait can offer information on the quality of function of that joint. Previous research has found significant reductions in joint range of motion as a result of diabetic neuropathy, particularly at the ankle (Mueller et al., 1994; Rao, et al., 2006; Sacco et al., 2009; Sawacha et al., 2009; Turner et al., 2007) which is likely to be caused by increased joint stiffness in these populations (D. S. Williams et al., 2007). A key factor may also be disturbances to the neural innervations of the muscles which control gait, and reductions in afferent feedback from the periphery. This notion is supported by previous researchers, who suggested that neuropathic diabetics may not receive sufficient critical information for a complete and precise control over the timing of gait events (Dingwell et al., 1999; Gates & Dingwell, 2007).

The description of joint moments and powers during gait provides information on joint strength and function during a dynamic task. Previous research has shown reduced peak plantarflexor moment and power production during gait in neuropathic populations compared to healthy controls (Mueller, et al., 1994; Yavuzer, et al., 2006). It has been suggested that the cause of this ankle dysfunction is reductions in joint mobility and strength (Mueller, et al., 1994). It has also been shown that the properties of the muscle and tendon tissue which assist in adequate ankle function are altered in diabetic populations. Andreassen et al. (2009) found using MRI techniques that as neuropathy progresses, lower limb muscle becomes more atrophied, beginning at the feet and progressing proximally. Cronin et al. (2010) showed a significant reduction in change in Achilles tendon length during gait in a diabetic population compared to healthy controls, suggesting that this was tantamount to a reduction in the efficiency of diabetic gait.

Gait analysis is a widely used clinical tool, particularly as a pre-post marker of the effectiveness of a given intervention. Since the interpretation of given gait measures may be a critical determinant of efficacy of treatment modality, there must be some indication given of confidence in the data and its variability (McGinley et al., 2009). In the current study, understanding this variability is critical in order to ensure that small changes following the intervention are not necessarily interpreted as strong intervention effects, but are always viewed alongside their corresponding variability (Schwartz et al., 2004).
The understanding of the variability of neuropathic gait is still in its relative infancy. While some authors contend that neuropathic patients do not exhibit any greater variability than healthy controls (Cavanagh et al., 1993; Dingwell and Cavanagh, 2001), others have suggested that this pathological population show trends towards increases in gait variability which, while not statistically significant, may be clinically significant (Allet, et al., 2009; Dingwell, et al., 1999). However it has been shown that any increase in gait variability is likely to be the result of a reduction in walking speed as opposed to any pathological reason (Dingwell & Cavanagh, 2001). Therefore it can be suggested that any increases in walking speed following an intervention may be accompanied by a commensurate improvement in gait variability.

The calculation of a coefficient of variation – which is essentially the ratio between the variability of a measure of interest and its average (Benedetti et al., 1998) – is a commonly-utilised means of calculating intra-individual variability for given gait measures (Allet, et al., 2009; Dingwell, et al., 1999; Petrovsky et al., 2005). Expressed as a percentage, this variable offers an immediate understanding of the consistency of a given measure.

### Improving gait in pathological populations

Recent research has shown that it is possible to improve clinically-relevant measures of gait in neuropathic diabetic populations with an exercise intervention. Li and Manor (2010) demonstrated improvements in distance walked over a set time period following an intervention which consisted of 24 weeks of Tai Chi exercises in a neuropathic population. Allet et al. (2010a) reported an increase in walking speed and cadence in a neuropathic diabetic group following a similar intervention to that employed in the current study. The improvement of gait measures with an exercise intervention has also been shown in other populations suffering from neuromuscular dysfunction; Lynch et al. (2007) revealed an improved walking distance over a set time period in stroke patients following an exercise intervention involving balance and lower limb strength training, as well as cardiovascular exercises, for one hour per week over a two week period. Hartmann et al. (2010) showed significant improvements in walking speed and step length in a healthy elderly population following a 12 week intervention which consisted of a combination of aerobic and strength training. However since the measures of gait improvement in the above studies were
temporal spatial in nature, no further understanding of the mechanism behind the changes exhibited could be offered. Perhaps the improvements exhibited by some were a result of gait task repetition in a population that had been previously sedentary, or a Hawthorne effect since the participants were aware they were in an intervention study.

In a study that exhibited a reduction in peak ankle plantarflexor moments and powers during gait in a neuropathic population compared to healthy controls, the authors suggested that an exercise intervention which focussed on balance and strengthening exercises could have a positive effect on neuropathic gait (Yavuzer, et al., 2006). Since it is the lower limb that is primarily affected by the neuromuscular complications of diabetic neuropathy, it stands to reason that an exercise intervention that focuses on improving ankle joint strength and function may improve the propulsive capability of this joint during gait.

Therefore the purpose of the current experiment was to investigate the effect of the intervention (Chapter 3) on neuropathic gait, measured using methodologies which allow for elaboration on the mechanisms behind any temporal spatial improvements. If, as a result of the intervention, these gait measures significantly improve, this would be indicative of an improvement in dynamic function of the lower limb.

**Gait hypotheses**

It was hypothesised that gait abnormalities caused by peripheral motor and sensory dysfunction in the current neuropathic diabetic population would be improved as a result of the intervention. These improvements would manifest as an increase in the common measures of gait efficiency such as walking speed, a reduction in gait variability, an improvement in ankle function and an increase in stability during gait.

In summary, it was hypothesised that, as a result of the intervention:

- Walking speed, stride length and cadence will increase, indicating a gross functional improvement in gait;
- Time spent in double-support will decrease while time spent in single-support will increase, indicating an improvement in single limb dynamic stability during gait;
Effect of the Intervention on Gait

- The distance between the centre of pressure and centre of mass will decrease, also indicating an improvement in dynamic stability;
- Ankle joint range of movement over a gait cycle will increase, indicating an improvement in ankle joint mobility during gait;
- Knee and hip joint range of movement over a gait cycle will decrease or remain the same, indicating an increase in the role of the ankle relative to the hip and knee;
- Peak ankle plantarflexion moment and power generation will increase, indicating an improvement in the propulsive capability of the ankle joint;
- Peak hip joint moments and powers will decrease or remain the same, indicating an increase in the role of the ankle relative to the hip and knee;
- CoV values for given gait measures will decrease, indicating a reduction in gait variability;
- Changes in gait will return to pre-intervention levels in the long-term follow up assessment, indicating that improvements were short-term due to the A-B-A format of the intervention.
Methodology

Participants

Eight participants underwent full-body kinematic and kinetic gait analysis at 0 weeks (pre-1), 4 weeks (pre-2), 16 weeks (post-1) and 28 weeks (post-2). As mentioned in Chapter 4, in the interim between post-1 and post-2 one participant developed a small ulcer under their right hallux and one participant underwent bariatric surgery. These participants were consequently excluded from the second follow-up assessment. Participant demographic information collected at the 1st pre-intervention assessment is exhibited in Tab. 6.1.

Table 6.1: Participant demographic information

<table>
<thead>
<tr>
<th></th>
<th>( N = 8 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>61.8 ± 8.9</td>
</tr>
<tr>
<td>( BMI )</td>
<td>32.1 ± 5.3</td>
</tr>
<tr>
<td>( Diab Duration (yrs) )</td>
<td>19.1 ± 15.6</td>
</tr>
<tr>
<td>( M/F )</td>
<td>5m / 3f</td>
</tr>
<tr>
<td>( Diabetes Type )</td>
<td>1 Type-1 / 7 Type-2</td>
</tr>
<tr>
<td>( R Foot Length (cm) )</td>
<td>26.3 ± 1.6</td>
</tr>
<tr>
<td>( L Foot Length (cm) )</td>
<td>26.1 ± 1.7</td>
</tr>
<tr>
<td>( R Foot Width (cm) )</td>
<td>9.9 ± 0.6</td>
</tr>
<tr>
<td>( L Foot Width (cm) )</td>
<td>10 ± 0.6</td>
</tr>
</tbody>
</table>

Measurement Equipment

Kinematic and kinetic data were collected using the same experimental setup described in Chapter 5, including the kinematic model.

Experimental Protocol

Biomechanical assessments occurred at the same or similar (+/- one hour) time of day across all four assessments to minimise time-of-day effect. Participants walked at a self-
selected pace along a 10 m walkway (Fig. 6.1) and were given adequate time to familiarise themselves fully with the environment and their task prior to data collection. Force plates were aligned so that ground reaction forces could be collected on up to three consecutive steps in one gait trial. Following familiarisation a minimum of six trials were collected, comprised of at least three force plate contacts per limb. Trials were rejected if a participant did not strike a force platform or visibly altered their gait pattern to aim for such a strike.

Figure 6.1: Walkway and force platform setup for collection of gait trials

Data Analysis

As for the assessment of postural stability, a residual analysis (Winter, 2005) was conducted on gait data to establish the appropriate cut-off frequency for the 4th-order Butterworth filter. The residual analysis compared the effect of filtering frequencies from 1-15Hz on two markers – a stable marker (sacrum) and high-velocity marker (3rd metatarsal) – as well as the xyz ground reaction force components during stance phase. This was conducted for a single gait trial from a randomly selected patient. Based on this analysis, a
cut-off frequency of 8Hz was selected for the raw marker data and 10Hz selected for force plate data.

Local coordinate systems were defined as described in Chapter 5, as were joint angles and moments. Joint powers were also calculated, based on the relevant joint moment and its angular velocity. Angular velocity was calculated 0.04s about each frame of data for use in this calculation (Vicon, 2002). The resultant joint power was then divided by body mass in order to normalise the data to Watts per kilogram, or W/kg. A detailed description of all kinematic and kinetic calculations can be found in Appendices 1.

Marker trajectories were digitised and gait events (foot contact, toe-off) labelled using Vicon Workstation software. Following the execution of the modified Cleveland Clinic model described in Chapter 5 (and Appendix 1), data were normalised to 100% of gait cycle using Vicon Polygon, with 1 frame of data describing 1%. This enabled the averaging of time series data and therefore the pooling of gait trials.

Once in this format, gait data were analysed using a custom-written Matlab script and Microsoft Excel. Hip, knee and ankle data were assigned to either dominant or non-dominant limbs (Chapter 4) prior to further analysis. In terms of joint angle, the ranges of movement of the trunk, pelvis, hip, knee and ankle were calculated about their three rotational axes across the entire gait cycle (Pohl et al., 2007). Peak joint moments at the hip were calculated for internal/external (I/E) rotation, abduction/adduction (Ab/Ad), and flexion/extension (F/E); peak joint moments at the knee were calculated for Ab/Ad and F/E; while peak joint moments at the ankle were calculated for inversion/eversion, Ab/Ad and plantarflexion/dorsiflexion. Peak joint absorption and generation powers were calculated in the sagittal plane for the hip, knee and ankle joint. The timing at which peak moments and powers occurred was also calculated and expressed as a percentage of stance phase.

As described in Chapter 5, the position of the whole body centre of mass was determined as a weighted sum of the centres of mass of all other segments (Eames, et al., 1999). To determine the CoP - CoM variable, whole-body CoM trajectories in the anteroposterior (AP) and mediolateral (ML) directions were subtracted from their CoP counterparts and the root mean square of the resultant time series was calculated (Hsue, et al., 2009). The range of CoP - CoM over the course of a given stance phase was also determined.
To determine gait variability, coefficients of variation (CoV) between strides were calculated for all variables for each participant and then averaged over all participants (Allet, et al., 2009; Dingwell, et al., 1999; Petrovsky, et al., 2005). CoV values were calculated by dividing the standard deviation by the mean and expressing this as a percentage:

\[ CoV_x = \frac{SD_x}{Mean_x} * 100 \]

where \( x \) is a given variable, e.g. sensory threshold at the hallux. Standard deviations were also calculated for each averaged variable as part of the normal descriptive analysis, and presented alongside their respective averages.

Statistical Analysis

Statistical analysis was conducted in SPSS v16.0 (SPSS Inc., U.S.A.), Microsoft Excel and Matlab. Due to the small sample size, non-parametric statistical analysis in the form of the Wilcoxon signed-ranks test was performed to check for significant differences between assessments for all variables (Gok et al., 2003). Change in variability between assessments was also investigated using the Wilcoxon signed-ranks test.

Significance testing was conducted between subsequent assessments. For all significance tests the level of significance was set at \( p < 0.05 \). A significant intervention effect was defined as a significant change between the pre-2 and post-1 assessments where no such change occurred between pre-1 and pre-2.
Results

Temporal-spatial results

No significant intervention effect was observed for any of the temporal-spatial parameters of gait. Some changes were observed between the two pre-intervention assessments. Low temporal-spatial variability was observed, with CoV values $<5\%$ in most cases. No significant changes in variability consistent with an intervention effect were observed (Tab. 6.2).
### Effect of the Intervention on Gait

**Table 6.2: Temporal-spatial results**

<table>
<thead>
<tr>
<th>Day</th>
<th>Cadence (steps/min)</th>
<th>Walking Speed (m/s)</th>
<th>Stride Length (x foot length)</th>
<th>Single Support (% gait cycle)</th>
<th>Double Support (% gait cycle)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avg</td>
<td>Δ</td>
<td>p</td>
<td>Avg</td>
<td>Δ</td>
</tr>
<tr>
<td>Pre-1</td>
<td>102.2 ± 8.6</td>
<td>-</td>
<td>-</td>
<td>102.1 ± 8.1</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>107.6 ± 10.1</td>
<td>0.3</td>
<td>0.89</td>
<td>106.8 ± 10.7</td>
<td>-0.2</td>
</tr>
<tr>
<td>Post-1</td>
<td>109.1 ± 11.5</td>
<td>1.5</td>
<td>0.6</td>
<td>107.0 ± 8.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Post-2</td>
<td>109.1 ± 11.5</td>
<td>1.5</td>
<td>0.6</td>
<td>107.0 ± 8.9</td>
<td>0.2</td>
</tr>
</tbody>
</table>

**Notes:**
- Avg: Average value
- Δ: Change from baseline
- p: Statistical significance
- CoV (%): Coefficient of variation as a percentage

For walking speed, stride length, and single support, the table shows average values for each day, with changes from baseline and statistical significance. For double support, only the values for each day are provided, without changes or statistical significance.
Effect of the Intervention on Gait

Range of movement results

No significant intervention effect was observed for range of movement during gait at the trunk, pelvis, hip, knee or ankle. F/E range of movement at the knee and ankle exhibited the lowest variability (CoV ≤ 5%), while trunk range of movement in all planes exhibited the highest variability (CoV = 13-28%). A reduction in the variability of trunk obliquity range of movement was observed following the intervention (from 27% to 16%, \( p = 0.02 \)), but no other changes in variability were observed. Graphs of averaged joint angle across all assessments are shown in Figs. 6.2 – 6.3. The dominant limb is used as an example. Average toe-off across all trials and participants was calculated as occurring at 63 ± 1% of stance phase, and is marked accordingly. Range of movement tables including CoV values are presented in Appendix 4 for brevity.
Effect of the Intervention on Gait

Figure 6.2: Trunk, pelvis and hip joint angle during gait cycle. Units are degrees (°) and the vertical line denotes toe-off.
Effect of the Intervention on Gait

Figure 6.3: Knee and ankle joint angle during gait cycle. Units are degrees (°) and the vertical line denotes toe-off.
Moment and power results

There was no change in peak joint moments or the timing of their occurrence as a result of the intervention. Variability at the hip was low for hip extension (CoV ≤ 10%) and ankle plantarflexion (CoV ≤ 5%), moderate (CoV= 10-20%) for hip adduction and knee extension, and generally high (CoV >20%) for other measures. There was no clear intervention effect on variability for any measure.

No significant intervention effect was observed in terms of peak joint powers or the timing of their occurrence. Variability was moderate (CoV = 10-20%) for hip, knee and ankle generation powers, but high (CoV > 20%) for absorption powers. There was no clear intervention effect on variability for any measure. Graphs of joint moments and powers across all assessments are shown in Figs. 6.4 – 6.5. The dominant limb is used as an example. Joint moment and power tables including their respective timing and CoV values are presented in Appendix 4 for brevity.
Figure 6.4: Joint moments during gait cycle. Units are Nm/kg and the vertical line denotes toe-off.
Effect of the Intervention on Gait

Figure 6.5: Joint powers during gait cycle. Units are Watts/kg and the vertical line denotes toe-off.
CoP - CoM results

The root mean square of the CoP - CoM distance in the ML direction increased significantly \((p = 0.04)\) for the dominant limb but not for the non-dominant limb \((p = 0.26)\) following the intervention. However the variability exhibited for this measure between the two pre-intervention sessions means this is not a clear intervention effect (Tab. 6.3). Variability was low \((\text{CoV} \leq 5\%)\) in most instances for the AP direction, but moderate \((\text{CoV} = 10\text{-}20\%)\) to high \((\text{CoV} >20\%)\) for ML measures. There was no clear intervention effect on variability for any measure. CoP - CoM results are shown in Tab. 6.3.
Table 6.3: CoP - CoM results for the AP and ML directions during gait

<table>
<thead>
<tr>
<th>Day</th>
<th>AP RMS</th>
<th></th>
<th></th>
<th>Non-Dominant Limb</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>158 ± 17</td>
<td>-</td>
<td>2.6 ± 2.0</td>
<td>158 ± 17</td>
<td>-</td>
<td>3.9 ± 2.5</td>
</tr>
<tr>
<td>Pre-2</td>
<td>165 ± 21</td>
<td>7 ± 9</td>
<td>2.7 ± 1.4</td>
<td>191 ± 84</td>
<td>33 ± 75</td>
<td>14.4 ± 32.4</td>
</tr>
<tr>
<td>Post-1</td>
<td>158 ± 21</td>
<td>-7 ± 9</td>
<td>4.6 ± 3.2</td>
<td>158 ± 21</td>
<td>-32 ± 72</td>
<td>4.6 ± 3.5</td>
</tr>
<tr>
<td>Post-2</td>
<td>166 ± 18</td>
<td>2 ± 10</td>
<td>3.0 ± 1.6</td>
<td>243 ± 106</td>
<td>78 ± 119</td>
<td>33.5 ± 45.2</td>
</tr>
<tr>
<td></td>
<td>ML RMS</td>
<td>61 ± 10</td>
<td>11.2 ± 8.2</td>
<td>58 ± 10</td>
<td>-</td>
<td>25.5 ± 11.2</td>
</tr>
<tr>
<td>Pre-2</td>
<td>56 ± 11</td>
<td>-4 ± 13</td>
<td>19.8 ± 11.2</td>
<td>57 ± 7</td>
<td>-1 ± 10</td>
<td>18.5 ± 11.7</td>
</tr>
<tr>
<td>Post-1</td>
<td>67 ± 15</td>
<td>11 ± 9</td>
<td>13.3 ± 9.4</td>
<td>62 ± 14</td>
<td>5 ± 8</td>
<td>13.7 ± 10.3</td>
</tr>
<tr>
<td>Post-2</td>
<td>53 ± 7</td>
<td>-10 ± 9</td>
<td>14.1 ± 5.1</td>
<td>55 ± 7</td>
<td>-8 ± 12</td>
<td>15.5 ± 7.6</td>
</tr>
<tr>
<td></td>
<td>AP Range</td>
<td>531 ± 63</td>
<td>2.5 ± 2.8</td>
<td>525 ± 50</td>
<td>-</td>
<td>3.8 ± 2.1</td>
</tr>
<tr>
<td>Pre-2</td>
<td>553 ± 77</td>
<td>22 ± 33</td>
<td>2.9 ± 0.9</td>
<td>566 ± 99</td>
<td>41 ± 67</td>
<td>6.4 ± 10.8</td>
</tr>
<tr>
<td>Post-1</td>
<td>536 ± 73</td>
<td>-17 ± 35</td>
<td>4.9 ± 2.9</td>
<td>530 ± 72</td>
<td>-35 ± 54</td>
<td>4.4 ± 2.3</td>
</tr>
<tr>
<td>Post-2</td>
<td>558 ± 66</td>
<td>4 ± 32</td>
<td>2.9 ± 1.8</td>
<td>616 ± 45</td>
<td>66 ± 89</td>
<td>16.1 ± 14.3</td>
</tr>
<tr>
<td></td>
<td>ML Range</td>
<td>35 ± 21</td>
<td>28.4 ± 30.2</td>
<td>48 ± 20</td>
<td>-</td>
<td>52.0 ± 26.8</td>
</tr>
<tr>
<td>Pre-2</td>
<td>33 ± 12</td>
<td>-2 ± 25</td>
<td>43.6 ± 35.2</td>
<td>38 ± 16</td>
<td>-10 ± 24</td>
<td>41.4 ± 13.3</td>
</tr>
<tr>
<td>Post-1</td>
<td>30 ± 13</td>
<td>-4 ± 12</td>
<td>27.6 ± 23.6</td>
<td>36 ± 19</td>
<td>-2 ± 23</td>
<td>31.5 ± 10.8</td>
</tr>
<tr>
<td>Post-2</td>
<td>50 ± 44</td>
<td>22 ± 33</td>
<td>45.4 ± 25.9</td>
<td>83 ± 33</td>
<td>45 ± 43</td>
<td>87.4 ± 31.2</td>
</tr>
</tbody>
</table>

"Effect of the Intervention on Gait"
Discussion

Addressing the hypotheses

The hypothesis that walking speed, stride length and cadence would increase as a result of the intervention was proven incorrect. Furthermore, the hypotheses that time spent in double-support would decrease while time spent in single-support would increase was also proven incorrect. It was hypothesised that the distance between the centre of pressure and centre of mass would decrease as a result of the intervention, indicating an improvement in dynamic balance; again, this hypothesis was proven incorrect.

It was hypothesised that ankle joint range of movement would increase while knee and hip joint range of movement would decrease or remain the same, indicating an improvement in ankle joint function during gait and an increase in the role of the ankle relative to the hip and knee. These hypotheses were proven incorrect.

It was hypothesised that the propulsive capability of the ankle joint, as measured by moments and powers, would significantly increase as a result of the intervention, and that corresponding hip and knee joint measures would decrease or remain the same, again indicating an increase in the role of the ankle relative to the hip and knee. These hypotheses were proven largely incorrect, since whilst hip and knee joint moments and powers did remain the same, no significant increases in peak ankle joint moments or powers were observed.

It was hypothesised that CoV values for given gait measures would decrease, indicating a reduction in gait variability. While a significant reduction in the variability of trunk obliquity was observed, no other significant changes in terms of variability were observed following the intervention.

It was hypothesised that changes in gait would be short-term and return to baseline by the 2nd post-intervention assessment, a hypothesis based on the premise that multiple significant changes in gait would be observed. The reduction in variability of trunk obliquity exhibited a trend toward a return to baseline, but this was not statistically significant. No other changes in gait measures as a result of the intervention were observed, and therefore this hypothesis is largely redundant.
Effect of the Intervention on Gait

Temporal spatial measures

It is possible that the lack of temporal spatial changes following the intervention was the result of the current neuropathic participants not exhibiting significant pre-intervention gait dysfunction, and therefore not requiring significant improvement. Comparisons with the findings of previous neuropathic gait studies – whose participant population were of similar age and BMI – can be made.

The current group exhibited comparable results to that previously described in neuropathic populations for walking speed (Courtemanche, et al., 1996; Kanade, et al., 2006; Katoulis, et al., 1997; Paul, et al., 2009; Sawacha, et al., 2009) and stride length (Courtemanche, et al., 1996; Sawacha, et al., 2009). However the current group exhibited similar results to healthy controls in terms of cadence (Courtemanche, et al., 1996; Paul, et al., 2009; Yavuzer, et al., 2006) and time spent in single or double-support (Courtemanche, et al., 1996; Paul, et al., 2009). Therefore the participants in this study did show some dysfunction in terms of walking speed and stride length, but not in terms of cadence or time spent in single or double-support.

As discussed in the previous chapter regarding the lack of change in CoP distance measures during quiet standing, the lack of improvement in walking speed observed in the current experiment may have been the result of the modality of exercise administered. The intervention studies which have shown improvements in this measure in pathological populations (Allet, et al., 2010a; Hartmann, et al., 2010) consisted of gait-specific tasks, whilst the current intervention did not incorporate such dynamic whole-body movements. Perhaps the changes observed in those studies were the result of an improved gait performance due to its repetition over the course of the intervention, rather than necessarily reflecting any improvements in lower limb neuromuscular function.

Range of movement

There was no change in joint range of movement as a result of the intervention – in fact, there was remarkable consistency for most measures in terms of joint angle across all four assessments despite their occurrence over a seven-month period (Figs. 6.2 – 6.3). The pelvis, hip, knee and ankle joint mobility exhibited by the current group of neuropathic
**Effect of the Intervention on Gait**

diabetics was more similar to those exhibited by healthy controls than their neuropathic counterparts, in many cases actually exhibiting greater mobility than healthy controls (Rao, et al., 2006; Turner, et al., 2007; Yavuzer, et al., 2006). Therefore no pathological limitations of joint mobility existed in the current group of neuropathic diabetics. It stands to reason that since no pathology of dynamic joint mobility was observed prior to implementation of the intervention, improvements in these measures were not required for adequate gait function.

**Moment and power production**

The ankle moments and powers observed in the current study were not comparable to that reported in previous neuropathic diabetic groups; rather, they were more similar to healthy controls (Rao, et al., 2006; Yavuzer, et al., 2006). It was the same case for moments and powers at the hip and knee (Yavuzer, et al., 2006). Therefore, there were no clear indications of gait pathology in terms of lower limb joint moment or power production.

The design of the exercise intervention was heavily weighted towards improving ankle strength and function, via exercises that required fine control of ankle musculature to maintain upright balance under unstable conditions, as well as strengthening exercises over the ankle range of movement. It is reasonable to assume that the lack of change in ankle joint moment or power production was due to the fact that no pathological dysfunction existed for these measures prior to the delivery of the intervention. Despite this, we may still have expected some change in ankle joint dynamics – or at least an increase in the relative role of the ankle with respect to the hip and knee – as a result of this ankle-specific intervention. However, as stated in the introduction gait is a repetitive and finely-controlled motor task, one which requires synergistic activity between neural systems and motor actuators (Akashi, et al., 2008). Any changes in ankle strength and function as a result of the intervention may not have been of consequence with regard to the role of the ankle joint in maintaining normal, healthy gait.
Effect of the Intervention on Gait

**CoP - CoM**

The lack of any intervention effect on the CoP - CoM variable, in conjunction with the aforementioned lack of pathological dysfunction in terms of joint mobility and propulsive capability, suggests that the neuropathic participants of the current study were already able to maintain adequate dynamic balance and therefore needed no further improvement. This lack of pre-intervention pathology in terms of this measure is congruent with the findings of the previous chapter, where the CoP - CoM values exhibited by the current group of neuropathic diabetics under static conditions was more similar to healthy controls than pathological populations.

The maintenance of dynamic balance requires an individual to keep the movement of their CoM tightly coupled to the movement of their CoP, with a view to maintaining the CoM as central as possible within the base of support. Perhaps the achievement of this goal is the cause of the reduction in walking speed and stride length exhibited by the current group of participants; for example, a decrease in stride length would reduce the distance between the CoP and CoM in the AP direction, thereby theoretically improving dynamic balance. It is possible that in order to reduce risk of falling, the first priority of individuals with dysfunctional afferent feedback is the maintenance of dynamic balance, while walking velocity beyond a pace which is adequate for community ambulation is a secondary consideration.

**Gait variability**

The one significant improvement in gait variability following the intervention was not exhibited at the ankle, knee or hip, but rather at the trunk; variability of trunk obliquity was reduced from 27% to 16%. However it is highly unlikely that this was the result of the intervention, considering that no exercises should have caused any improvement in variability of trunk movement. Rather, it is likely that this was a random occurrence.

For most gait measures the current group of neuropathic diabetics exhibited low variability. For the hip joint and non-sagittal plane ankle and knee joint measures, only moderate variability was exhibited. While high variability was shown for some measures, these variables tended to be small in amplitude and therefore secondary in importance.
Effect of the Intervention on Gait

compared to other measures. The lack of change in variability of relevant measures following the intervention is likely to be the result of low levels of variability already existing prior to the delivery of the intervention.

While it is generally accepted that increased gait variability is a dysfunctional consequence of neuropathic gait (Dingwell & Cavanagh, 2001; Manor, Wolenski, et al., 2008), it has also been suggested that a reduction in gait variability is equivalent to a reduction in an individuals’ flexibility to adapt and respond to changing environmental stimuli (Austin, 2001). Based on this supposition, an increase in gait variability could have been considered a positive intervention effect; however neither a significant increase nor significant decrease in the variability of relevant gait measures was observed in the current study.

Limitations

Only eight of the ten participants who completed the exercise intervention underwent gait analysis. This was due to unforeseen technical complications which prevented the collection of kinematic data for both pre-intervention assessments for two of the participants. As stated in Chapters 4 and 5, this small sample size is a limitation that reduces the power of the supposition that the exercise intervention had no effect on the gait of the current group of neuropathic diabetics.

As previously stated, it is likely that the principal reason for the lack of change in gait measures following the intervention was the fact that no gait pathology was exhibited prior to its delivery. This is perhaps a reflection on the screening process adhered to for the current study, which excluded patients who were not able to walk unaided or who experienced pain during walking. By excluding these patients, it is possible that those who were included in the study were from a select group of neuropathic diabetics who did not experience severe gait pathology. This limits the applicability of the results of the current study to a wider neuropathic diabetic population. Perhaps if severe gait dysfunction had been shown prior to the intervention, a significant effect could have been shown; however this is entirely theoretical.

As can be seen in Fig. 6.3, the knee rotations exhibited in the current study showed considerable inter-individual variability. It was never intended to use knee rotation values as
Effect of the Intervention on Gait

as an outcome measure; rather, they are presented as a means of exhibiting the error encountered at this joint due to limitations in the kinematic model. The knee rotation axis was defined by the placement of static markers on the lateral and medial femoral condyles. The orientation of the knee rotation axis can vary depending on the placement of these markers; if one is placed too far anterior or posterior, the rotation axis will be shifted. The result of this error is not a change in knee rotation range of movement during gait, but rather a shift in the ‘neutral’ or starting position of this angle. The sensitivity of this axis of rotation to error has been reported in previous literature (Marin et al., 1999), and would only have been of concern for the current study if abnormalities were exhibited in the knee flexion/extension axis, which may have suggested erroneous cross-talk between these axes. However no such abnormalities were observed, and knee joint angle results were comparable to previous research in healthy populations.

As discussed, variability was low for all temporal spatial measures, as well as for most of the relevant joint mobility, moment and power measures. It is probable that the collection of a greater number of trials per session from which to calculate averages could have resulted in lower variability for those relevant measures that exhibited moderate to high CoV values, such as peak ankle eversion moment. However, considerations regarding the length of time a participant spent undergoing biomechanical assessment – which averaged two hours per session – dictated that in order to reduce the likelihood of any fatigue effect, it was necessary to collect the minimum number of successful trials required for each assessment component. While the collection of only six successful trials per session can be considered a limitation, it was one that was consciously acknowledged as necessary when considering the possible negative effects of an elongated testing session on participant fatigue.

Conclusions

The lack of any change in gait measures observed in the current intervention study is not necessarily a reflection on the efficacy of the intervention in improving dynamic function, but rather the result of a near-absence of gait pathology prior to intervention delivery. The current group of neuropathic diabetics, due to strict screening, may not have exhibited the typical gait patterns associated with diabetic neuropathy. However, perhaps the addition of
Effect of the Intervention on Gait

gait-specific exercises into the intervention could have elicited improvements in measures of walking speed and stride length, which were shown to be pathological in the current group of participants.

The next chapter will investigate the effect of the intervention on plantar loading and foot morphology. Since no relevant changes to gait were observed following the intervention, it is of interest to investigate whether plantar loading and foot morphology measures will also remain unaltered, particularly since these measures are related to foot morbidity.
Chapter Seven

Effect of the Intervention on Foot Morphology and Plantar Loading
Introduction

Overview

In previous chapters, it was discovered that although significant improvements in sensory function observed as a result of the intervention, dynamic function during standing balance and gait remained largely unaffected. While some dysfunction was exhibited by the current group of participants in terms of postural stability, by contrast the lack of change in gait was largely due to an absence of pre-intervention pathology in all measures except walking speed and stride length. The assessment of foot morphology and plantar loading during gait in the current chapter will offer further information regarding dynamic function of the lower limb, and whether the intervention significantly altered this function.

Plantar pressures are increased in the neuropathic diabetic foot compared to healthy populations (Bacarin, et al., 2009; Boulton, 2004; Bus, et al., 2005; P.R. Cavanagh, et al., 1998). These increases in peak plantar pressures are the result of a combination of morphological, muscular and sensory abnormalities (Boulton, 1992; Bus, et al., 2005; D'Ambrogi, et al., 2003; Duffin, et al., 2002; Fernando, et al., 1991). There is a high correlation between elevated plantar pressures and plantar ulceration (P.R. Cavanagh, et al., 1998; P.R. Cavanagh & Ulbrecht, 1994; Frykberg, et al., 1998; Mueller et al., 2008). The vast majority of diabetic foot complications that result in amputation begin with the formation of foot ulcers, which might be prevented by early detection with methods such as plantar pressure distribution measurements (P.R. Cavanagh et al., 2000).

Assessment of dynamic foot morphology and plantar loading

Dynamic foot morphology and plantar loading can be measured via pedobarographic techniques, which require the use of a pressure distribution system (P.R. Cavanagh & Ulbrecht, 1994; Gurney et al., 2009; Mittal et al., 2006; Nakhaee et al., 2008; Rosenbaum & Becker, 1997; Vincenzino et al., 2006). These systems can either be insole-based (P.R. Cavanagh, Hewitt, et al., 1992) or platform-based (Peters et al., 2002), the latter of which generally has a higher spatial resolution, meaning that it has a greater number of sensors per given unit of area.
At the onset of the current study, there was poor evidence found in the literature for between-session reliability of pressure distribution systems, and considering the multiple assessments required for the current study this was an issue which needed to be addressed. Therefore an investigation of between-day reliability was conducted for the most common plantar loading parameters across multiple days. Good reliability was exhibited for most parameters and foot regions, and it was concluded that this tool was therefore appropriate for use in the current study. This research was subsequently published in the peer-reviewed journal Gait and Posture (Gurney et al., 2008).

**Relevant outcome measures**

Several outcome measures derived from pedobarographic analysis have clinical relevance with respect to neuropathic populations. The neuropathic diabetic foot is highly at risk of developing abnormal foot morphology; the ‘clawing’ of the toes is common (Boulton, 1992), and may lead to potentially harmful increases in plantar pressure at the metatarsal heads (Bus, et al., 2005). Another morphological abnormality is the presentation of hallux valgus (Lavery et al., 1998; Thomson et al., 1991), a complication which arises in one-third of all diabetics (Bus, 2008) due to weakening of intrinsic foot musculature in the hallucis region (Kusumoto et al., 1996). The presence of hallux valgus can be detected by measuring hallux angle; a lateral hallux deviation of greater than 10° can be considered hallux valgus (Nerrozzi & Tentoni, 2008).

Diabetic patients, regardless of neuropathy status, may also exhibit significantly thicker plantar fascia tissue than non-diabetics, again potentially leading to increases in plantar pressure (D'Ambrogli, et al., 2003; Duffin, et al., 2002). With respect to this structural change, the combination of a flat foot and diabetic neuropathy has been linked with an increase in the likelihood of plantar ulcer occurrence (Sacco, et al., 2008). The investigation of midfoot morphology can be achieved by measuring sub-arch angle, which indicates arch height, and arch index, which indicates the ratio of midfoot area to total foot area excluding the toes.

High peak plantar pressures are closely related to risk of ulceration in neuropathic populations (P.R. Cavanagh, et al., 1998). As measured by a pressure distribution system,
peak pressure is the amount of force acting over a given area; in the case of a platform which has two sensors per cm², this pressure represents a given amount of force acting over 0.5 cm². This analysis provides critical information regarding the stress that small areas of the plantar surface are experiencing, and allows for the quantification of these stresses. Peak pressure measurements are therefore heavily dependent on underlying tissue stiffness; if the soft plantar tissue has low compliance, or if the soft tissue has been reduced in thickness, then bony prominences such as the metatarsal heads will cause elevated pressures at these sites.

On the other hand, the measurement of maximum force – and impulse, the product of force amplitude and duration – offers us more information about foot function. Rather than representing the amount of load occurring across small areas, maximum force offers information about loading across a given foot region, and is therefore less dependent on tissue stiffness and more dependent on gait mechanics.

The duration of time that given foot regions remain in contact with the ground can also offer insight into foot function. Rao et al. (2010) discovered significant increases in the percentage of stance phase spent loading the forefoot in neuropathic diabetic patients compared to healthy controls. If these results indicate some sort of plantar loading pathology, then it can be postulated that it is desirable to reduce the duration of forefoot loading in these populations.

Improving dynamic foot morphology and plantar loading in pathological populations

As pedobarographic analyses are proven to be robust and reliable measures, they are increasingly becoming a vital and widely-used clinical tool. The measurement of plantar loading is a common pre-post marker for the effect of orthopaedic interventions in many different pathological populations, where the goal is the reduction of potential tissue-damaging loads. Such interventions could include shoe orthotics for arthritis patients (Rao et al., 2009), surgical interventions on Charcot foot deformities (Najafi et al., 2010), or footwear designed to redistribute plantar loading in neuropathic diabetic patients (Bus, et al., 2009).

However comparatively few studies have investigated the effect of an exercise intervention on dynamic foot morphology or plantar loading. In a recent study by Monteiro et al. (2010), the authors took 60 post-menopausal women through an exercise intervention
while 61 matched post-menopausal women acted as controls. The intervention consisted of one year of tri-weekly supervised sessions, which were 60 minutes in duration and consisted of a mixture of cardiovascular and strength training exercises. Among other measures, the authors investigated the effect of the intervention on peak pressures at multiple foot regions, and found that these pressures were significantly lower following the intervention in the exercise group compared to the control group.

For the current study it was of considerable interest to investigate the effect of the exercise intervention on dynamic foot morphology and plantar loading. Based on the findings of previous chapters, which showed no change in balance or gait, changes in these foot measures seem unlikely; however it is possible that the specificity of the measurements in the current chapter may yet offer an opportunity for changes in dynamic lower limb function to be observed. Since increases in plantar loading have been shown in neuropathic populations compared to healthy controls (Bus, et al., 2005), it stands to reason that an improvement in sensory function could lead to improvements in plantar loading.

**Plantar loading and foot morphology hypotheses**

It was hypothesised that the measures of plantar loading and foot morphology affected by peripheral sensorimotor dysfunction in the current neuropathic population would be improved as a result of the intervention. These improvements would manifest as reductions in plantar loading beneath anatomical sites which frequently ulcerate, as well as alterations to foot morphology which will indicate a strengthening of intrinsic foot musculature and improved foot function during gait.

In summary, it was hypothesised that, as a result of the intervention:

- Sub-arch angle will increase and arch index will decrease, indicating a lifting of the arch due to the strengthening of intrinsic foot musculature;
- Hallux angle will decrease towards neutral, indicating an improved strength of intrinsic hallucis musculature;
- Peak pressure will decrease beneath the forefoot, indicating a reduction in the likelihood of forefoot ulceration occurrence;
Effect of the Intervention on Foot Morphology and Plantar Loading

- Maximum force and impulse will also decrease at the forefoot, indicating a reduction in loading and improved foot function;
- Contact time will decrease at the medial midfoot, indicating a lifting of the arch and therefore a reduction in plantar loading at this region; contact time will also decrease at the forefoot, indicating a reduction in the duration of loading at sites which typically ulcerate;
- Changes in foot function and morphology will return to pre-intervention levels in the long-term follow up assessment, indicating that improvements were short-term due to the A-B-A format of the intervention.
Methodology

Participants

Ten participants underwent dynamic foot morphology and plantar loading assessment at 0 weeks (pre-1), 4 weeks (pre-2), 16 weeks (post-1) and 28 weeks (post-2). As previously mentioned, in the interim between post-1 and post-2, one participant developed a small ulcer under their right hallux and one participant underwent bariatric surgery. These participants were consequently excluded from the second follow-up assessment. Participant demographic information is exhibited in Chapter 4.

Measurement Equipment

Plantar loading and dynamic foot morphology data were collected using a Novel EMED-AT capacitive pressure distribution platform (Novel GmbH, Munich, Germany; Fig. 7.1), which has a resolution of 2 sensors/cm² and a measurement area of 36 x 19cm. Data were collected at a frequency of 50Hz. The pressure platform was embedded flush with floor level within a 10m runway, comprised of temporary raised flooring.

Figure 7.1: Novel EMED-AT pressure distribution platform
Experimental Protocol

Assessments occurred at the same or similar (+/- one hour) time of day across all four assessments to minimise time-of-day effect. For walking trials, patients were instructed to walk at a self-selected speed (Bryant et al., 1999; Gurney, et al., 2008; Hayafune et al., 1999; Murphy et al., 2005; Rosenbaum, et al., 2006) and given adequate familiarisation time (Rosenbaum & Becker, 1997). A three-step approach was used, requiring the participant to strike the platform with their third step, to ensure that plantar loading data were collected mid-gait (Bus & De Lange, 2005). The participants were instructed to walk normally and not to attempt to aim for the platform, but instead walk towards a target at the end of the 10m runway.

The Novel EMED platform has been shown to be reliable when three to five trials are collected (Gurney, et al., 2008; Hughes et al., 1991; Vincenzino, et al., 2006), and therefore five trials were collected for the current study. Recent work presented by this author has shown that plantar loading asymmetries are common between limbs, and that these asymmetries may be exacerbated in neuropathic populations (Gurney & Kersting, 2008). Therefore both feet were investigated separately, but grouped into dominant and non-dominant limbs (Chapter 4).

Data Analysis

For the purposes of data analysis, the foot was divided into ten anatomical regions as shown in Fig. 7.2 (Gurney, et al., 2008; Rosenbaum, et al., 2006). Regions included the hallux (HA), second toe (T2), third to fifth toes (T3-5), medial forefoot (MF), central forefoot (CF), lateral forefoot (LF), medial midfoot (MM), lateral midfoot (ML), medial heel (HM) and lateral heel (HL). This compartmentalisation of the foot is referred to as a mask, and the mask used for the current study was the PRC mask (Eils et al., 2002; Gurney, et al., 2008).
Dynamic foot morphology measures included sub-arch angle, hallux angle and arch index (Gurney, et al., 2009). The geometric lines used to define these variables are also shown in Fig. 7.2. Sub-arch angle \((a)\) has its origin at the medial border of the narrowest point of the midfoot, with axes extending out to the medial borders of the forefoot and heel. Hallux angle \((b)\) is the lateral deviation of the hallux (D) from a tangential line connecting the medial heel with the medial forefoot \((B)\). Arch index is the ratio of midfoot area to total foot area, excluding the toes (Novel, 2003).

A number of plantar loading outcome measures were assessed. These included peak pressure (kiloPascals or kPa), maximum force (percentage body weight, or %BW), impulse (%BW.s) and contact time (% stance phase). Peak pressure was defined as the peak pressure exhibited at a given foot region over the course of a trial. Likewise, maximum force was defined as the maximum force exhibited at a given foot region over the course of a trial.
Effect of the Intervention on Foot Morphology and Plantar Loading

Impulse was defined as the mean impulse exhibited at a given foot region over the course of a trial, where impulse is the area beneath the vertical ground reaction force curve. Contact time was defined as the mean contact time exhibited at a given foot region over the course of a trial, measured as a percentage of stance phase; for example, a given forefoot region may exhibit some contact with the ground for 80% of stance phase.

Data were collected using Novel Emed software and then managed using Novel Database Medical software. Data were analysed using Novel Geometry and Novel Project software, and then exported for subsequent statistical analysis.

Statistical Analysis

Statistical analysis was conducted in SPSS v16.0 (SPSS Inc., U.S.A.) and Microsoft Excel. Due to the small sample size, non-parametric statistical analysis in the form of the Wilcoxon signed-ranks test (Bisiaux & Moretto, 2008; Eils, et al., 2002; Taylor et al., 2004) was performed to check for significant differences between assessments for all variables.

As in Chapter 6, intra-participant variability was calculated for each assessment and therefore was an indication of within-session gait variability. This variability was measured using a coefficient of variation (CoV) calculation, defined in Chapter 6. A CoV value was calculated for each outcome measure for each assessment, and then averaged across participants to give an indication of average variability for that assessment. Change in variability between assessments was investigated using a non-parametric Wilcoxon signed-ranks test.

Significance testing was conducted between subsequent assessments. For all significance tests the level of significance was set at $p < 0.05$. A significant intervention effect was defined as a significant change between the pre-2 and post-1 assessments where no such change occurred between pre-1 and pre-2.
Effect of the Intervention on Foot Morphology and Plantar Loading

Results

Foot morphology results

No intervention effect was observed for any investigated foot morphology measure. One participant exhibited a varus hallux angle (>13°), which was unaffected by the intervention. Three participants exhibited a valgus hallux angle (>10°), which was also unaffected by the intervention.

High inter-participant variability was observed for hallux angle, which was the result of most participants exhibiting hallux angles close to zero that varied by one or two degrees. Variability was low (3 – 12%) for all other foot morphology measures. Apart from a small change in sub-arch angle between post-intervention assessments, no significant changes in variability of foot morphology measures were observed between assessments (Tab. 7.1).
Effect of the Intervention on Foot Morphology and Plantar Loading

Table 7.1: Foot morphology results

<table>
<thead>
<tr>
<th></th>
<th>Day</th>
<th>Avg</th>
<th>Avg Δ</th>
<th>p</th>
<th>CoV (%)</th>
<th>p</th>
<th>Dominant Limb</th>
<th>Non-Dominant Limb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hallux Angle</strong> (°)</td>
<td>Pre-1</td>
<td>3 ± 14</td>
<td>-</td>
<td>-</td>
<td>29 ± 78</td>
<td>-</td>
<td>5 ± 9</td>
<td>178 ± 466</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>2 ± 13</td>
<td>0 ± 2</td>
<td>0.28</td>
<td>66 ± 132</td>
<td>0.51</td>
<td>5 ± 10</td>
<td>32 ± 98</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>1 ± 14</td>
<td>-1 ± 2</td>
<td>0.17</td>
<td>69 ± 121</td>
<td>0.88</td>
<td>5 ± 10</td>
<td>44 ± 43</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>1 ± 11</td>
<td>2 ± 4</td>
<td>0.07</td>
<td>22 ± 67</td>
<td>0.07</td>
<td>5 ± 10</td>
<td>39 ± 54</td>
</tr>
<tr>
<td><strong>Sub-Arch Angle</strong> (°)</td>
<td>Pre-1</td>
<td>102 ± 7</td>
<td>-</td>
<td>-</td>
<td>5 ± 3</td>
<td></td>
<td>101 ± 5</td>
<td>4 ± 2</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>101 ± 7</td>
<td>0 ± 6</td>
<td>0.44</td>
<td>5 ± 1</td>
<td>0.77</td>
<td>99 ± 5</td>
<td>5 ± 3</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>103 ± 6</td>
<td>2 ± 3</td>
<td>0.14</td>
<td>4 ± 2</td>
<td>0.51</td>
<td>98 ± 6</td>
<td>5 ± 3</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>102 ± 5</td>
<td>-1 ± 2</td>
<td>0.46</td>
<td>**8 ± 3 **</td>
<td><strong>0.03</strong></td>
<td>98 ± 8</td>
<td>1 ± 6</td>
</tr>
<tr>
<td><strong>Arch Index</strong></td>
<td>Pre-1</td>
<td>0.25 ± 0.06</td>
<td>-</td>
<td>-</td>
<td>6 ± 7</td>
<td></td>
<td>0.24 ± 0.06</td>
<td>10 ± 14</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>0.25 ± 0.06</td>
<td>0.00 ± 0.01</td>
<td>0.41</td>
<td>9 ± 7</td>
<td>0.17</td>
<td>0.24 ± 0.06</td>
<td>12 ± 15</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.24 ± 0.06</td>
<td>-0.01 ± 0.02</td>
<td>0.46</td>
<td>8 ± 11</td>
<td>0.39</td>
<td>0.24 ± 0.06</td>
<td>12 ± 15</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.24 ± 0.07</td>
<td>0.01 ± 0.02</td>
<td>0.34</td>
<td>7 ± 8</td>
<td>0.22</td>
<td>0.25 ± 0.05</td>
<td>6 ± 7</td>
</tr>
</tbody>
</table>

CoV (%): Dominant Limb Non-Dominant Limb Avg Avg Avg
Plantar loading results

No intervention effect was observed for peak pressure values. An increase in peak pressure was observed at the lateral forefoot of the dominant limb between the two pre-intervention assessments ($p = 0.022$). The highest pressures were observed beneath the forefoot, with the lowest occurring beneath the midfoot.

No intervention effect was observed for maximum force. The highest forces were observed at the lateral forefoot, with the lowest occurring at the 2$^{nd}$ and 3$^{rd}$-5$^{th}$ toe regions.

A reduction in impulse was observed following the intervention at the 3$^{rd}$-5$^{th}$ toes of both the dominant ($p = 0.007$) and non-dominant ($p = 0.047$) limbs; however impulse at this foot region is largely irrelevant due to its small size relative to other foot regions. No other intervention effects were exhibited for this variable. The highest impulse was observed at the lateral forefoot, with the lowest occurring at the 2$^{nd}$ and 3$^{rd}$-5$^{th}$ toe regions.

No intervention effect was observed for contact time. The longest contact times occurred at the forefoot regions, while the shortest occurred at the medial midfoot (Fig. 7.3).
Effect of the Intervention on Foot Morphology and Plantar Loading

Figure 7.3: Average values for plantar loading measures for all foot regions; the dominant limb is used as an example

**Peak Pressure**

- Hallux
- Toe 2
- Toes 3-5
- Lat Forefoot
- Cent Forefoot
- Med Forefoot
- Lat Midfoot
- Med Midfoot
- Lat Heel
- Med Heel

**Maximum Force**

- Hallux
- Toe 2
- Toes 3-5
- Lat Forefoot
- Cent Forefoot
- Med Forefoot
- Lat Midfoot
- Med Midfoot
- Lat Heel
- Med Heel

**Impulse**

- Hallux
- Toe 2
- Toes 3-5
- Lat Forefoot
- Cent Forefoot
- Med Forefoot
- Lat Midfoot
- Med Midfoot
- Lat Heel
- Med Heel

**Contact Time**

- Hallux
- Toe 2
- Toes 3-5
- Lat Forefoot
- Cent Forefoot
- Med Forefoot
- Lat Midfoot
- Med Midfoot
- Lat Heel
- Med Heel
Average within-session variability of peak pressure beneath the lateral heel of the non-dominant limb increased from 9% to 12% following the intervention ($p = 0.047$). The highest average variability was observed at the medial forefoot, with the lowest occurring at the central forefoot.

Within-session variability of maximum force beneath the medial midfoot of the non-dominant limb decreased from 37% to 27% following the intervention ($p = 0.017$); however it should be noted that this region was typically one of the least loaded during walking trials. The highest variability was observed at the midfoot regions, with the lowest occurring at the heel regions.

Significant reductions in the variability of impulse beneath the medial midfoot of the dominant (54% to 34%; $p = 0.013$) and non-dominant (47% to 30%; $p = 0.009$) limbs were observed following the intervention; however it should again be noted that this region was typically one of the least loaded during walking trials. The highest variability was observed at the midfoot regions, with the lowest occurring at the central forefoot.

No clear intervention effect on variability of contact time was observed. The highest variability was observed at the medial midfoot, with the lowest occurring at the lateral and central forefoot regions (Fig. 7.4).
Figure 7.4: Within-session variability results for plantar loading measures for all foot regions; the dominant limb is used as an example

**Peak Pressure**

**Maximum Force**

**Impulse**

**Contact Time**
Effect of the Intervention on Foot Morphology and Plantar Loading

High and low peak pressure sub-group results

Upon examination of the data set, it was discovered that five of the ten participants exhibited potentially clinically-relevant elevated peak plantar pressures at either the medial heel or one of the forefoot regions. It was therefore of interest to conduct a separate analysis in which participants were divided into high peak pressure and low peak pressure sub-groups, and a re-investigation of the effect of the intervention on all measures was conducted on these separate groups. Participants were stratified into groups either above or below a 650kPa threshold, a value based on previous research on thresholds for preventing plantar ulceration (P.R. Cavanagh & Ulbrecht, 1994; Owings et al., 2009).

No intervention effects were observed for either the low or high peak pressure groups for any foot morphology measure. For peak pressure, no intervention effect was observed in the low pressure group, but for the high pressure group a decrease in peak pressure beneath the dominant lateral forefoot was observed following the intervention ($p = 0.043$; Fig. 7.5). For maximum force and impulse, no consistent intervention effect was found for either the low or high pressure groups. A significant increase in contact time at the hallux of the dominant limb for the low pressure group was observed following the intervention ($p = 0.043$). This was not found for the high pressure group, who did not exhibit any intervention effect for this parameter.

Figure 7.5: Peak pressure beneath the dominant lateral forefoot (* denotes $p < 0.05$)
Effect of the Intervention on Foot Morphology and Plantar Loading

Discussion

Addressing the hypotheses

It was hypothesised that sub-arch angle would increase while arch index decreased, indicating a lifting of the arch during gait. These hypotheses proved incorrect. It was hypothesised that hallux angle would decrease toward neutral, indicating a strengthening of intrinsic foot musculature, which also proved incorrect.

It was hypothesised that peak pressure would decrease beneath the forefoot, indicating a reduction in the likelihood of ulceration at this region. While this hypothesis was proven incorrect for the group as a whole, it was discovered that peak pressure beneath the lateral forefoot of those participants who exhibited clinically-relevant high peak pressures was reduced following the intervention, while no change was exhibited in those participants who exhibited relatively low peak pressures. No other changes were found within these separated groups for any other measure or region.

It was hypothesised that maximum force and impulse would also decrease at the forefoot, indicating a reduction in loading and improvement in foot function. A reduction in impulse was observed following the intervention at the 3rd-5th toes of both limbs, and variability of impulse at the medial midfoot was found to significantly decrease following the intervention for both limbs. However these findings are clinically irrelevant due to the small impulse size at these regions relative to other regions. No other intervention effects were observed, and therefore this hypothesis was largely proven incorrect.

The hypothesis that contact time would decrease at the medial midfoot, indicating a lifting of the arch and therefore reduction in plantar loading at this region, proved incorrect. This is not unexpected considering the lack of any intervention effect on arch morphology as mentioned above.

It was hypothesised that changes in foot morphology and function as a result of the intervention would be short-term, and return to baseline at the 2nd post-intervention assessment. The largely irrelevant improvement observed at the 3rd-5th toes and medial midfoot for the impulse measure exhibited a trend to return to baseline for the 2nd post-intervention assessment, but this change was not significant. In the case of the reduction in
Effect of the Intervention on Foot Morphology and Plantar Loading

peak pressure beneath the lateral forefoot in the participants who exhibited clinically-relevant high peak pressures, this reduction was maintained at the 2nd post-intervention assessment, and therefore did not follow the hypothesised pattern.

Foot morphology

The lack of any significant changes in dynamic foot morphology suggests that the exercise intervention did not make any functional improvements in the intrinsic foot musculature which control hallux and midfoot activity during gait. Unlike the previous chapter, the lack of change at the hallux cannot be solely attributed to a lack of pathology; three participants exhibited significant hallux valgus while one participant exhibited significant hallux varus, none of whom showed any change as a result of the intervention. However, while the hallux deviations exhibited by some participants could be considered valgus or varus in nature, none of the participants had severe hallux deformity that might require surgical intervention. It can therefore be concluded that the intervention employed in the current study is not effective at altering dynamic function of the hallux in populations with moderate hallux valgus.

At the midfoot, dynamic arch index and sub-arch angle results were comparable to those exhibited by elite athletes in our previous research (Gurney, et al., 2009). Arch index values were slightly greater – indicating a flatter arch – in the current population than those reported in a non-diabetic population (Bosch et al., 2009); however in that study participants were not drawn from the same population as the current study, and the aforementioned research published by the current author found that ethnicity can affect arch index. We may therefore conclude that the characteristics of dynamic midfoot morphology exhibited by the current participants were not pathological in nature but comparable to other healthy participants drawn from the same population. This may explain why no changes in these measures were observed as a result of the intervention.
Effect of the Intervention on Foot Morphology and Plantar Loading

Plantar loading

The measurement of peak pressures beneath the plantar surface of the foot offers both the clinician and the researcher the opportunity to view the interface between foot and ground in a way that few other measures can. We are able to observe first-hand the regionalised loading of the foot, which is of considerable interest since it is this localised loading that causes the ulcerations that we are ultimately attempting to avoid in these neuropathic populations. Similar to the postural stability findings, the lack of any significant group effect with regard to peak pressure was a reflection on the variability exhibited in this measure by participants across the group; however, in contrast to the postural stability findings, it was possible to stratify participants according to peak pressure results. While half of the participants exhibited clinically-relevant high peak pressures greater than 650kPa, the other participants exhibited low peak pressures that were of less concern regarding potential tissue damage. When participants were grouped according to high and low peak pressure, only one improvement in peak loading was observed – namely the reduction at the lateral forefoot in the high-pressure group which was sustained through to the 2nd post-intervention assessment. This can hardly be referred to as a significant indication that the intervention was effective at reducing high peak loading beneath plantar sites which typically ulcerate. The fact that this reduction was not observed at any other plantar region, combined with a sample size of only five high-pressure participants, suggests that these changes are more likely to have occurred randomly.

The fact that peak plantar pressure did not significantly change as a result of the intervention may still be a clinically-relevant finding. When designing the current intervention, it was a priority that the exercise modalities chosen would not repetitively load the plantar surface, since this would not be desirable in a population at risk of plantar wound development. The exercises chosen were therefore low-impact in nature, none of which required repetitive loading and unloading of the plantar surface – as would be the case in an intervention which employed treadmill walking, for example. Such repetitive loading could have caused callous formation which may have led to ulceration (Zinman, et al., 2004), and it is this concern that makes the design of an exercise intervention in neuropathic populations difficult. Therefore it is a positive result of the current study that the intervention was able to significantly improve sensory function in most participants using exercises that did not stress the plantar surface and lead to increases in peak plantar pressure. In short, the fact that peak
Effect of the Intervention on Foot Morphology and Plantar Loading

pressures did not increase as a result of the intervention suggests that the exercises employed are appropriate for use in neuropathic populations at risk of wound development.

While the measurement of peak pressure gives information on the loading of small plantar surface areas, the maximum force measure allows the observation of gross loading at a particular foot region. While these loadings are not as closely related to risk of ulceration, they do offer extra insight into foot function which cannot be observed in the peak pressure measure. If an individual alters their gait, these alterations may not change peak pressure since this measure is more dependent on tissue stiffness, but they will alter the way the foot is loaded and changes will be observed in the maximum force variable. Therefore the lack of any change in maximum force as a result of the intervention is a reflection on the fact that no significant alterations to gait were observed, a finding congruent with those detailed in Chapter 6. The changes observed in impulse were clinically irrelevant, since they occurred at foot regions which exhibit low impulse and therefore their contribution to foot function is largely inconsequential.

Similar to the force measures, the lack of any change in contact time is also an indication that gait – and more specifically the roll-over process of the foot during stance phase – remained unchanged following the intervention. Regarding the previous findings by Rao et al. (2010), in which neuropathic diabetics were found to spend a significantly greater percentage of stance phase loading the forefoot compared to healthy controls (89% vs. 83%), the results of the current population were more comparable to their neuropathic group, perhaps indicating some pathology in the current group. However the masking technique used in their study to divide the foot into different regions is not automatically comparable to the current study, since their forefoot was considered as one region as opposed to the division of the forefoot into three regions. The results of the current study show that there was a difference in the duration of stance phase spent loading each forefoot region, whereby the lateral forefoot was loaded ~89% of stance phase, the central forefoot ~86% and the lateral forefoot ~82%. This indicates that different forefoot regions were loaded for slightly different durations, and without further information regarding which specific forefoot region the data from Rao et al. (2010) represents it is not possible to make definitive comments regarding the existence of a forefoot contact time pathology in the current group of participants. Since no pathology was exhibited for the previous measures related to foot function, it stands to reason that the contact time results observed in the current study are most probably non-pathological.
Case study: the participant that ulcerated post-intervention

As stated in the methodology, one participant sustained a small ulcer beneath their non-dominant hallux in between the 1\textsuperscript{st} and 2\textsuperscript{nd} post-intervention assessments. Since the relationship between peak pressure and ulceration has been discussed in this chapter, it was considered of interest to present hallux peak pressure data for this participant for the first three assessments. These are exhibited in Fig. 7.7.

Figure 7.7: Peak pressure beneath the non-dominant hallux of the participant that sustained an ulcer post-intervention, plotted alongside the group average for this region

It can be clearly observed that the participant that sustained an ulcer did not exhibit high peak pressures prior to the interim period between the post-intervention assessments. Since all participants were checked for foot wounds and heavy callusing prior to each assessment – and at multiple points throughout the intervention period – it can be concluded that the ulcer was most likely sustained several weeks after the 2\textsuperscript{nd} post-intervention assessment. The participant was unaware of the wound, and it was first discovered by the current author when they presented for their 2\textsuperscript{nd} post intervention assessment. The wound was still fresh and without infection, again leading to the supposition that it had been recently
sustained. The patient was immediately released from their 2nd post-intervention assessment prior to any data collection and contact was made with clinical staff at CMDHB to ensure the wound was adequately addressed. Since the participant was unaware that they had sustained a wound until it was discovered by the current author, no further information regarding the mechanics of ulcer occurrence were available. Since the wound occurred following the completion of the intervention, combined with the fact that the participant exhibited healthy plantar tissue at all regions prior to the interim between post-intervention assessments, it can be safely concluded that the intervention itself did not cause the formation of the ulcer.

It is an interesting finding that the participant did not exhibit any high peak pressures beneath the hallux prior to the interim between post-intervention assessments, and yet sustained an ulcer at this site sometime during that period. Without a complete understanding of how the ulcer in question developed, we cannot be certain whether it was caused by peak pressures occurring repetitively beneath this site, pressures that we can assume the participant was unaware of since they were also unaware that an ulcer had developed until it was shown to them by the current author. At the very least the comment can be made that if the ulcer was sustained in this manner, then it is possible that clinically-relevant increases in peak pressure can be sustained over a relatively short period of time, and therefore frequent podiatric checks – i.e. separated by less than 12 weeks, as is currently the case for diabetics under chronic care management within CMDHB – of callous development, possibly combined with pedobarographic quantification of peak plantar loading, are recommended for neuropathic patients. It should be noted that the wound could also have been sustained from a sudden trauma to the hallux; however when queried, the participant reported no such trauma occurrence.

Limitations

When it was observed that it was possible to stratify participants into high and low peak pressure groups, a cut-off peak pressure value of 650kPa was employed. The selection of this value was based on both the clinical experience of the current author and peak pressure values exhibited in previous literature. Recent work by Owings et al. (2009), investigating peak plantar pressures beneath previous ulcer sites that have remained healed, suggested a target threshold of 556kPa above which ulceration occurrence may increase. Since no
participants in the current study had any recent or present ulceration, a higher threshold was set for the stratification of participants into the high and low peak pressure groups (>650kPa). Anecdotally, there was a reasonably clear separation of participants between the two groups, whereby no participants in the low-pressure group exhibited peak pressures beyond 500-600kPa for a given foot region. However, the separation of participants into essentially high- and low-risk groups based on some threshold value may not adequately represent actual ulceration risk. Cavanagh and Ulbrecht (1994) stated that they had observed ulceration occurrence in participants that had exhibited peak pressures below 500kPa, which suggests that even relatively low peak pressures can cause tissue damage under certain circumstances. Therefore the separation of high and low peak pressure groups based on a set threshold may be clinically erroneous, in spite of efforts to make this threshold as relevant as possible.

Dynamic pedobarographic data collection was not conducted synchronously with the gait analysis detailed in Chapter 6, therefore preventing the calculation of joint moments and powers at the same time as the foot morphology and plantar loading measures. The reason for this is the necessity for the Emed pressure distribution platform to be flush with the ground, which required the use of temporary portable flooring since it was not possible to embed the platform in line with the other force plates. Therefore a limitation of the current experiment was the unavailability of any comparison between plantar loading measures and joint mechanics; however, this sort of analysis was beyond the scope of the current study and a comprehensive gait analysis has already been described in Chapter 6.

Conclusions

The change in lateral forefoot peak pressure exhibited by the high pressure group following participant stratification is not likely to be a reflection upon the efficacy of the intervention at reducing peak pressures in high-risk populations; rather, it is more likely to be a random occurrence. Although peak pressures were not reduced as a result of the intervention, it is just as clinically-relevant that peak pressures did not increase when we consider the improvements in sensory function (Chapter 4) that were made without increasing risk of ulceration to our neuropathic diabetic group.
The next chapter will investigate the effect of the intervention on ankle muscle strength. Since the previous chapters have shown no significant changes in dynamic lower limb function, it is of interest to investigate whether any improvements in ankle muscle strength under isolated conditions were observed following the intervention.
Chapter Eight

Effect of the Intervention on Ankle Strength


**Introduction**

*Overview*

In previous chapters, it was shown that the intervention had a negligible effect on lower limb motor function, and it is of interest to investigate whether this is a reflection on a lack of change in absolute lower limb strength. In this chapter, an investigation of ankle strength under isolated conditions is presented.

Motor weakness is a critical symptom of diabetic neuropathy (Andersen, 1996). It has been shown that the strength of ankle musculature decreases at a rate of 3% per year in neuropathic diabetics but does not decline in diabetic patients with no neuropathy (Horowitz, 2006). Peripheral musculature becomes progressively weak and atrophied in neuropathic diabetics (Andersen, 1998; Andersen et al., 1997; Andreassen, et al., 2009), and ankle reflexes may regress or disappear (Horowitz, 2006; Ziegler, 2008). Muscle strength impairments at the ankle and knee are closely related to severity of neuropathy (Andersen, et al., 1998). Ankle joint plantar- and dorsiflexors play a critical role in the performance of functional activities such as gait (Suzuki et al., 2001). Therefore the assessment of ankle strength is of considerable interest in neuropathic populations who may exhibit dysfunction in this area.

*Assessment of ankle strength*

The measurement of lower limb strength is possible via the use of dynamometric techniques. Previous researchers have assessed lower limb strength in diabetic populations using isokinetic (Andersen, 1996; Andersen, et al., 1998; Andreassen, et al., 2006) as well as isometric (Andersen et al., 2005; Sakkas et al., 2006) methods. In a study examining the effect of glycaemic control on lower limb strength in Type-1 diabetics, Andersen et al. (2005) discovered that while significant decreases in isometric strength were observed during hyperglycaemia, no changes in isokinetic strength were found. This suggests that only isometric methods were sensitive enough to show differences in strength following the onset of hyperglycaemia.
Effect of the Intervention on Ankle Strength

Isometric strength can be measured using either hand-held dynamometers or fixed-position dynamometers. While the use of hand-held dynamometers is desirable in terms of portability and cost, this method has been shown to underestimate lower limb strength when compared to a fixed-position dynamometer (Allet, et al., 2010b; Martin et al., 2006), and therefore the use of the latter method is preferable.

Relevant outcome measures

Most studies which have investigated the effectiveness of resistance training in similar populations to the current study have assessed strength in knee and hip musculature (Chetlin et al., 2004; Levinger et al., 2007; Praet, et al., 2008). However, ankle dorsi- and plantarflexor strength was considered to be of most interest for the current application, for two key reasons. Firstly, since the current exercise intervention focussed on improving ankle strength and function it was theorised that it would be this musculature which would exhibit the most post-intervention adaptation. Secondly, as previously discussed it is the distal muscle groups which are most impaired by peripheral neuropathy (Andersen, 1996), and therefore it was of interest to investigate whether this impairment could be improved by the current exercise intervention.

Improving ankle muscle strength in pathological populations

There is some limited evidence that suggests that lower limb muscle strength can be improved in neuropathic populations via an exercise intervention. Praet et al. (2008) showed increases in the one-repetition-maximum strength of the knee flexors and extensors in neuropathic diabetic patients following a 10-week resistance training intervention. However as previously discussed the use of weight-bearing exercises is contraindicated in this population due to their increased risk of plantar ulceration and other complications (Zinman, et al., 2004). One of the lower limb exercises employed by the authors was a horizontal leg press, which would have placed high loads on the plantar surface of the foot and therefore placed their participants at increased risk of foot complications. No information regarding whether foot inspections were conducted to monitor any negative intervention effect on this tissue was provided.
Effect of the Intervention on Ankle Strength

Allet et al. (2010b) measured isometric ankle plantar- and dorsiflexor strength in a neuropathic diabetic group before and after a 12-week exercise intervention which was comprised of gait and balance exercises. They observed significant improvements in isometric plantarflexor but not dorsiflexor strength. However it should be noted that these authors used a hand-held isometric dynamometer, which they admit may have underestimated peak torque development as previously discussed (Martin, et al., 2006).

Regarding other populations, Hartmann et al. (2009) found significant improvements in isokinetic ankle plantarflexor force development in non-pathological elderly participants following a 12-week exercise intervention which involved a combination of cardiovascular and strength training. Their training group was further divided into two groups, one of whom received additional foot exercises similar to those employed in the current study; however no differences in improvement of ankle strength were observed between these two training groups. The authors admit that this lack of difference between groups may have been due to low compliance, since the additional foot exercises were completed by the participants at home, unsupervised. Unlike the current study, the authors could not be certain that the exercises had been completed by the participants, and therefore could not make any statements regarding the efficacy of the additional foot exercises.

For the current study it was of interest to determine the effect of the intervention on isolated ankle strength, since the exercises employed during the intervention were heavily ankle-centric. The measurement of ankle strength would therefore indicate whether the intervention stimulated increases in absolute strength, or whether the exercises were too low-intensity to cause any such adaptation. The results of this analysis could also assist in understanding the lack of change in motor function observed in the previous three chapters.

Ankle strength hypotheses

It was hypothesised that changes in ankle strength caused by peripheral motor dysfunction in the current neuropathic population would be improved as a result of the intervention. These improvements would manifest as increases in isometric dorsi- and plantarflexor strength as measured using a dynamometer.
Effect of the Intervention on Ankle Strength

In summary, it was hypothesised that, as a result of the intervention:

- Peak torque generated by the ankle dorsi- and plantarflexors, under isometric conditions, will increase;
- Changes in isometric ankle strength will return to pre-intervention levels in the long-term follow up assessment, indicating that improvements were short-term due to the A-B-A format of the intervention.
Methodology

Participants

Ten participants underwent isometric ankle strength assessment at 0 weeks (pre-1), 4 weeks (pre-2), 16 weeks (post-1) and 28 weeks (post-2). As previously mentioned, in the interim between post-1 and post-2 one participant developed a small ulcer under their right hallux and one participant underwent bariatric surgery. These participants were consequently excluded from the second follow-up assessment. Participant demographic information is exhibited in Chapter 4.

Measurement Equipment

Ankle dorsi- and plantarflexor isometric strength was assessed using a Biodex dynamometer, hereafter referred to as the Biodex (Biodex Medical Systems Inc., U.S.A.; Fig. 8.1). The Biodex allows for the measurement of strength of muscle groups about a given joint while controlling joint position (Tiffreau et al., 2007), and has been shown to be a highly reliable method of assessing strength in both healthy and neuropathic populations (Andersen, 1996; Aydog et al., 2004; Ortvqvist et al., 2007).

Figure 8.1: The Biodex isokinetic dynamometer
Effect of the Intervention on Ankle Strength

Experimental Protocol

The Biodex measured torques created about a central pivot point, which was positioned to coincide with the ankle joint in the transverse axis as determined by the position of the lateral malleolus (Andersen, 1996; Atkinson & Nevill, 1998; Aydog, et al., 2004; Holmback & Lexell, 2007). Care was taken in ensuring the correct placement of the ankle joint, since previous research has shown that deviations of 1.5cm can cause a 10% change in ankle peak torque measurements (Andersen, 1996).

The Biodex included a moving arm attached to a motor, with an adjustable chair in which the participant was braced (Fig. 8.1). Participants were seated and strapped into the chair via three seatbelt-type straps, two of which diagonally crossed the trunk and one which horizontally crossed the waist. Stabilisation of the trunk was critical since previous research has shown that torques produced during ankle strength testing are significantly higher if participants do not have their trunk strapped to the chair (Holmback et al., 1999). An extra padded arm was used to elevate the knee of the leg to be assessed (Aydog, et al., 2004; Holmback & Lexell, 2007), and a Velcro strap was applied to the thigh to stabilise the upper leg (Andersen, 1996). The thigh of the non-assessed leg was also strapped to the chair to prevent movement.

The moving arm of the motor has several attachments which can be fitted depending on the desired outcome measure; for the current application a steel foot plate was fitted, upon which the foot was braced by a heel cup and a Velcro strap with the ankle in a neutral position. The hip joint was positioned in approximately 85° of flexion (Tiffreau, et al., 2007). The knee joint was positioned in approximately 30° of flexion (Holmback & Lexell, 2007), assessed via the use of a goniometer. Participant position in the seat was standardised between testing sessions by replicating these joint positions in each subsequent session (Holmback & Lexell, 2007).

Biomechanical assessments occurred at the same or similar (+/- one hour) time of day across all four assessments to minimise time-of-day effect. The primary outcome measure of the muscle strength assessment was peak torque of the ankle plantar- and dorsiflexors during maximal isometric contractions, expressed in Newton-metres (Nm). While it has been found that learning effect is negligible when using the Biodex system (Ortqvist, et al., 2007), other authors have suggested that this effect should still be considered when designing testing
Effect of the Intervention on Ankle Strength

protocol. Aydog et al. (2004) found that intraclass correlation coefficient values between testing sessions on the same participants increased when the first trial was removed from analysis. Therefore a familiarisation period was implemented into the testing protocol of the current study, whereby the participant was explained exactly what was required of them and then asked to perform the given task once prior to data collection.

Three maximal contractions were then performed (Holmback & Lexell, 2007). Dorsiflexion movements were always first to be assessed, followed by the plantarflexion movements (Andersen, 1996). No verbal motivation was given during trials since the effect of varying this factor is not well understood and it is difficult to standardise between testing sessions (Holmback, et al., 1999). Participants were given a 30 second break between individual trials, and a two minute break between conditions to minimise the effect of fatigue (Holmback, et al., 1999).

In order to standardise the torque generated during assessments irrespective of the gravity effect, limb weight was acquired by the Biodex prior to assessments. This weight was then removed by the Biodex software from further torque calculations (Andersen, 1996; Aydog, et al., 2004).

Data Analysis

Peak isometric torque data were derived from the Biodex software and imported into Microsoft Excel. Prior to subsequent analysis, data were normalised to body weight and expressed as Nm/kg.

Statistical Analysis

Statistical analysis was conducted in SPSS v16.0 (SPSS Inc., U.S.A.) and Microsoft Excel. Due to the small sample size, non-parametric statistical analysis in the form of the Wilcoxon signed-ranks test was performed to check for significant differences between assessments for all variables.
Effect of the Intervention on Ankle Strength

Significance testing was conducted between subsequent assessments. For all significance tests the level of significance was set at $p < 0.05$. A significant intervention effect was defined as a significant change between the pre-2 and post-1 assessments where no such change occurred between pre-1 and pre-2.
Effect of the Intervention on Ankle Strength

Results

Peak isometric torque results

No intervention effect was observed for either plantarflexion ($p = 0.33$) or dorsiflexion ($p = 0.59$) peak isometric torque production. No significant change was detected between pre-intervention or post-intervention assessments. Plantarflexor torque development was more than twice that produced by the dorsiflexors (Tab. 8.1).

Table 8.1: Peak isometric torque results

<table>
<thead>
<tr>
<th>Day</th>
<th>Avg PF (Nm/kg)</th>
<th>Avg Δ PF (Nm/kg)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-1</td>
<td>0.64 ± 0.14</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>0.65 ± 0.13</td>
<td>0.02 ± 0.07</td>
<td>0.39</td>
</tr>
<tr>
<td>Post-1</td>
<td>0.68 ± 0.13</td>
<td>0.03 ± 0.07</td>
<td>0.33</td>
</tr>
<tr>
<td>Post-2</td>
<td>0.71 ± 0.12</td>
<td>-0.01 ± 0.05</td>
<td>1.00</td>
</tr>
<tr>
<td>Avg PF</td>
<td>0.65 ± 0.14</td>
<td>0.02 ± 0.07</td>
<td>0.39</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Day</th>
<th>Avg DF (Nm/kg)</th>
<th>Avg Δ DF (Nm/kg)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-1</td>
<td>0.31 ± 0.16</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>0.30 ± 0.14</td>
<td>-0.01 ± 0.13</td>
<td>0.77</td>
</tr>
<tr>
<td>Post-1</td>
<td>0.29 ± 0.16</td>
<td>-0.02 ± 0.16</td>
<td>0.59</td>
</tr>
<tr>
<td>Post-2</td>
<td>0.35 ± 0.16</td>
<td>0.02 ± 0.11</td>
<td>0.58</td>
</tr>
</tbody>
</table>
**Effect of the Intervention on Ankle Strength**

**Discussion**

*Addressing the hypotheses*

It was hypothesised that peak isometric torque generation at the ankle would increase following the intervention, a hypothesis that was proven incorrect. It was also hypothesised that any changes in peak isometric torque production would return to baseline at the 2nd post-intervention assessment, which due to the lack of any change became a redundant hypothesis.

*Lack of change in isometric ankle strength*

The lack of any intervention effect in peak isometric torque development at the ankle is congruent to the findings of the previous chapters, which showed no change in lower limb motor function. It can therefore be hypothesised that the lack of change in ankle function observed during the maintenance of postural stability (Chapter 5), as well as the lack of change in ankle moment and power production during gait (Chapter 6), may be a reflection on the absence of any improvement in absolute ankle strength; however as discussed in those chapters, other reasons such as a lack of pre-intervention ankle pathology are more probable explanatory factors. It should also be emphasised that the method of determining ankle strength in the current study offers only a limited understanding of the function of ankle musculature, a point which will be discussed in the limitations section of this chapter.

The lack of any change in isometric ankle strength must be a reflection on the low-intensity of the strength training component of the intervention. In order to increase the likelihood of observing an ankle strength adaptation, the current intervention would need to be changed to include a higher volume of more difficult resistance exercises. However this would need to be implemented without placing neuropathic participants at increased risk of previously-discussed autonomic and plantar surface complications. Perhaps the addition of an extra training session per week, whilst still retaining the same intensity and volume within each training session, could provide the opportunity to increase training stimulus by 33% without increasing the workload completed in one session. If the same protocol as used in the current study regarding individual supervision of each session was adhered to, such an increase in intervention volume would also represent a 33% increase in time resources and
associated fiscal costs. Also, the effect of such an increase on participant fatigue would need to be closely monitored to ensure that no negative complications arise as a result of the increased training stimulus.

It is also possible that the lack of any intervention effect could be due to a lack of ankle strength pathology prior to the onset of the intervention. Isometric plantar- and dorsiflexor strength were substantially greater in the current group than that exhibited in a previous study by elderly females with physical limitations (Suzuki, et al., 2001). However, the plantarflexor strength results of the current group were more similar to those previously reported in elderly female fallers and significantly lower than elderly female non-fallers (LaRoche et al., 2010). Peak isometric plantarflexor torque production by the current group of participants was also significantly lower than reported in young healthy populations (Arampatzis et al., 2008). All of these previous studies employed similar data collection methods to that used in the current study. The similarity between the current results and those observed by LaRoche et al. (2010) suggests that the plantarflexor ankle strength of the current group may have been pathological in nature; however the lack of any significant pathology in terms of ankle plantarflexor moment or power production during gait (Chapter 6) suggests that the existence of such a pathology is either doubtful or at the very least irrelevant to dynamic ankle joint function.

Limitations

The choice of an isometric method – as opposed to isokinetic – for determining ankle strength was made for an important reason. There was a desire when designing the methodology to ensure that all aspects of data collection were as low-impact as possible, particularly on the foot and cardiovascular system. In the case of the latter, this was a concern because of the possibility of any participants having underlying, undiagnosed autonomic cardiovascular disease. Regarding the foot, it was determined that isokinetic exercises would also cause an increase in loading of plantar tissue, and it was decided that isometric exercises would stress these areas less than isokinetic exercises. In retrospect, this reasoning may have been erroneous. It is acknowledged that an isokinetic methodology may have offered more information about dynamic function of the ankle joint, and in retrospect the decision not to use isokinetic methods may have been overly-protective of participant
safety. Therefore the absence of isokinetic data from the current study is a limitation, but one which was chosen based on careful consideration.

Only plantar- and dorsiflexor strength were included in the final methodology of the current study, and therefore these sagittal plane movement directions were used to represent strength at the ankle joint. However, when the study was being initially designed, inversion and eversion directions were also piloted. The Biodex was setup in the manner described in the Biodex manual (Biodex Medical Systems, 2007), which involves the employment of several lever arms and the tilting of the Biodex motor itself. The analysis of isometric inversion/eversion strength was eventually discarded for two reasons: firstly, it was decided that the manner in which the Biodex is setup to determine peak torque production in this direction is convoluted and not a true measurement of ankle inversion/eversion strength. Secondly, the time taken to reconstruct the Biodex between two setups, i.e. plantar/dorsiflexion to inversion/eversion, elongated the testing time by a considerable amount and therefore was not desirable when biomechanical assessments were already approximately two hours long and fatigue of the participants was of concern. Therefore while it is a limitation that isometric ankle strength was only measured in the sagittal plane, this limitation was largely unavoidable from both a pragmatic and quality of methodology perspective.

The calculation of rate of torque development was also considered to be a measure of interest for the current study. It was intended that this would be calculated for each trial based on torque traces, derived from the Biodex software. However it was discovered that due to technical limitations these traces could not be exported for further analysis in Microsoft Excel. This limitation could have been overcome via the use of a third-party data collection method, whereby instead of using the Biodex software itself, data is collected with another computer using third-party software. However at the onset of this study the current author was unaware of the possibility of using this method and had only received training in the use of the Biodex system with the Biodex software. The lack of any other outcome measures of interest that could have been calculated based on the isometric torque traces is therefore a limitation of the current study.
Effect of the Intervention on Ankle Strength

Conclusions

The most significant finding of the current chapter is that the exercise intervention, which was designed to improve lower limb sensorimotor function via an ankle-specific training programme, was unable to cause any significant improvement in isometric ankle strength. This is an unexpected finding, but one that can be understood when we consider the nature of the intervention. Clearly, the exercise intervention was not sufficiently challenging to the ankle musculature to cause any hypertrophy or change in strength. Considering the low-intensity nature of the exercises, combined with the fact that it is doubtful whether any dynamically-relevant ankle motor pathology was present in the current participants prior to the intervention, the absence of any change following the intervention is a sensible finding.

While no changes were found in terms of motor function as a result of the intervention, the significant improvements in sensory function combined with other non-quantifiable factors may have led to an improvement in the quality of life of the current group of neuropathic diabetics. Therefore the next chapter will investigate the effect of the intervention on health-related quality of life.
Chapter Nine

Effect of the Intervention on Quality of Life
Introduction

Overview

In the final experimental component of this thesis, the effect of the intervention on quality of life was investigated. It has been suggested that measurements of quality of life are as necessary as any quantitative analysis in the assessment of peripheral neuropathy (Yasuda, et al., 2007). The pain associated with diabetic neuropathy has a considerable impact on the quality of life of the patient (Ziegler, 2008). There is also good evidence for an association between diabetic neuropathy and psychological depression in diabetic patients (Vileikyte, et al., 2005; Yoshida et al., 2009). Painful diabetic neuropathy has been linked with great disturbances to normal sleep (Ziegler, 2008), another factor which may affect quality of life. Recently, Vedhara et al. (2010) showed a significant correlation between ulcer healing and both levels of depression and coping ability.

The loss of lower limb function associated with diabetic neuropathy can have a profound effect on quality of life (van Schie, 2008). In fact, severity of neuropathic symptoms is significantly correlated with quality of life scores. In a study by Currie et al., it was discovered that psychological constructs such as self-perceived physical function, social function (including the ability to maintain personal relationships), bodily pain, vitality and general mental health are significantly reduced in neuropathic diabetic populations, and these reductions linearly increase as symptom severity increases (2006). While negligible changes in motor function were observed as a result of the intervention, the significant improvement in sensory function is tantamount to an improvement in neuropathic symptoms and therefore may have resulted in improvements in health-related quality of life in the current group of neuropathic diabetics.

Assessment of quality of life

Quality of life can be assessed in diabetic populations using many self-reported questionnaires, and the choice of which to use is dependent on the research question being addressed. The SF-36 Health Survey is a commonly-employed and reliable questionnaire for assessing quality of life (QoL) in neuropathic diabetics (Cocito et al., 2006; Currie, et al.,
Effect of the Intervention on Quality of Life

2006; Nabuurs-Franssen et al., 2005; Ribu et al., 2006; Yasuda, et al., 2007), and for this reason was employed in the current study. The SF-36 is a short questionnaire comprised of 36 items, and measures such aspects of QoL as physical function, pain, vitality and mental health (Nabuurs-Franssen, et al., 2005).

Relevant outcome measures

The SF-36 measures eight different scores, each of which relates to different contributing factors in an individual’s sense of health-related quality of life. One of these measures is physical functioning, which relates to an individual’s self-perceived ability to perform certain physical activities. Questions related to this measure ask an individual to rank the types of activities that can be performed, in order to ascertain physical ability. Other questions are asked regarding the limitations an individual feels as a result of their physical health, which attempt to determine the extent of the detrimental effect of their health on physical ability. These measures are relevant to neuropathic populations since physical function is reduced in this population (Cimbiz & Cakir, 2005; Resnick et al., 2002).

Another area of quality of life investigated by the SF-36 is vitality, which relates to an individual’s level of stamina or fatigue. This measure is also of interest, since diabetes is known to significantly reduce feelings of vitality in diabetic populations (Gautam et al., 2009). The SF-36 also measures bodily pain, which is of most interest in neuropathic populations that are experiencing painful symptoms such as allodynia (Nelson & Little Jr, 2007; Rosenstock et al., 2004). While the current group of participants did not suffer from severe painful symptoms, the measurement of the effect of the intervention on perceptions of pain is still of much interest.

There are also questions in the SF-36 which relate how an individual copes in social situations, particularly in terms of the development and maintenance of relationships with others. Also measured is the perceived limitation on the performance of daily activities that an individual senses due to emotional problems. These factors are also of particular interest with respect to the current group of participants, since a reduction in ability to perform social roles and a link between reduced ability to perform daily tasks and depression has been found in neuropathic diabetics (Vileikyte et al., 2009). The SF-36 also measures general perceptions of physical and mental health, which are logically related to an individual’s sense
Effect of the Intervention on Quality of Life

of health and well-being and can be significantly affected by diabetic neuropathy (Yoshida, et al., 2009).

Improving quality of life in pathological populations

Exercise has been shown to improve quality of life in many pathological populations. Jeiger et al. (2009) showed improvements in all quality of life variables measured with the SF-36 in patients with coronary heart disease following a cardiovascular exercise intervention. Karapolat et al. (2007), conducting an eight-week exercise intervention employing stretching, strengthening and aerobic exercises in heart transplant patients, showed significant improvements in all SF-36 quality of life measures with the exception of vitality and social functioning following their intervention. Molsted et al. (2004) showed significant improvements in physical functioning score as measured with the SF-36 in dialysis patients following a five-month exercise intervention.

With regard to diabetic populations, Gonzalez Calvo et al. (2003) found significant improvements in all quality of life variables measured with the SF-36 following a 12-week cardiovascular exercise intervention in diabetic patients without neuropathy. While there has been some evidence of improvements in quality of life in neuropathic diabetic populations following phototherapy (Powell et al., 2006; Swislocki et al., 2010) or pharmaceutical (Casellini et al., 2007) interventions, there is limited understanding regarding the effect of an exercise intervention on quality of life in these populations. Of course, this is most likely linked with the fact that it is still uncommon to conduct exercise interventions in these populations due to the risk of negative side effects, as previously discussed. Therefore the purpose of the current experimental component was to investigate the effect of the intervention on health-related quality of life in the current group of neuropathic diabetics.

Quality of life hypotheses

It was hypothesised that changes in quality of life caused by peripheral sensorimotor dysfunction in the current neuropathic population would be improved as a result of the
intervention. These improvements would manifest as increases in quality of life scores as measured using the SF-36 questionnaire.

In summary, it was hypothesised that, as a result of the intervention:

• Health-related quality of life will improve as a result of the intervention, which will manifest as an improvement in the constructs of quality of life measured by the SF-36 questionnaire;

• Changes in quality of life will return to pre-intervention levels in the long-term follow up assessment, indicating that improvements were short-term due to the A-B-A format of the intervention.
**Methodology**

**Participants**

Ten participants underwent health-related quality of life assessment at 0 weeks (pre-1), 4 weeks (pre-2), 16 weeks (post-1) and 28 weeks (post-2). As previously mentioned, in the interim between post-1 and post-2, one participant developed a small ulcer under their right hallux and one participant underwent bariatric surgery. These participants were consequently excluded from the second follow-up assessment. Participant demographic information is exhibited in Chapter 4.

**Measurement Equipment**

The SF-36 Health Survey (QualityMetric Inc., U.S.A.) was employed to assess quality of life. This questionnaire consists of 36 items, each of which is related to a clinically-relevant area of health-related quality of life. The SF-36 has been proven to be a reliable and valid measure of quality of life in pathological populations (Garrat et al., 1993), and as mentioned is commonly employed in neuropathic diabetic populations (Cocito, et al., 2006; Nabuurs-Franssen, et al., 2005; Ribu, et al., 2006; Yasuda, et al., 2007).

Areas of quality of life measured include physical functioning, social functioning, vitality, bodily pain, sense of limitation due to physical health and emotional problems, perceptions of general health and general mental health. The method used to answer questions varies from dichotomous yes or no answers, through to selection on a scale of an answer that suits the participant most. An example of a question relating to physical functioning is shown in Fig. 9.1.
Effect of the Intervention on Quality of Life

**Figure 9.1: Typical questions from the SF-36 related to physical functioning**

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

<table>
<thead>
<tr>
<th>ACTIVITIES</th>
<th>Yes, Limited A Lot</th>
<th>Yes, Limited A Little</th>
<th>No, Not Limited At All</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**Experimental Protocol**

Assessments occurred at the same or similar (+/- one hour) time of day across all four assessments to minimise time-of-day effect. The SF-36 questionnaire was always the last assessment to occur during a given testing session. Participants were left alone in a quiet work space and were given as long as necessary to answer the questionnaire.

**Data Analysis**

Answers to the SF-36 items are numerical, making the quantification of these answers possible. Results were entered into a Microsoft Excel template file, which was then imported into QualityMetric Outcome Measures software for processing. This software calculates scores between 0 and 100 for the eight aforementioned quality of life parameters based on answers to the 36 items in the questionnaire, with 100 being the best possible outcome and 0 being the worst. As well as evaluating a score for each parameter, the Health Outcomes software tests for inconsistencies between answers for given measures and returns an error if these are found. An example of such an inconsistency would be if an individual answered question 3(a) in Fig. 9.1 with “3 – Not limited at all” and then proceeded to answer question 3(b) with “1 – Yes limited a lot”. Anecdotally no such inconsistencies were observed in any of the 10 participants of the current study.

Scores for each of the eight quality of life measures (Currie, et al., 2006) were exported from the Health Outcomes software for subsequent analysis in Microsoft Excel.
Statistical Analysis

Statistical analysis was conducted in SPSS v16.0 (SPSS Inc., U.S.A.) and Microsoft Excel. Due to the small sample size, non-parametric statistical analysis in the form of the Wilcoxon signed-ranks test (Van Ittersum et al., 2009) was performed to check for significant differences between assessments for all variables.

Significance testing was conducted between subsequent assessments. For all significance tests the level of significance was set at $p < 0.05$. A significant intervention effect was defined as a significant change between the pre-2 and post-1 assessments where no such change occurred between pre-1 and pre-2.
Results

**SF-36 quality of life results**

No intervention effect was observed for physical functioning, vitality, social functioning, limitations due to physical health, limitations due to emotional problems, perceptions of general health or general mental health. A non-significant trend towards an improvement in bodily pain score was observed following the intervention ($p = 0.09$; Fig. 9.2).

![Figure 9.2: SF-36 results for bodily pain](image)

Moderate to high inter-participant variability in quality of life scores were observed for most measures, with the highest occurring in the scores for limitations due to physical health and the lowest occurring in the scores for general mental health (Tab. 9.1).
Table 9.1: SF-36 quality of life results

<table>
<thead>
<tr>
<th></th>
<th>Avg</th>
<th>Avg Δ</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day</td>
<td>(SF-36 Score)</td>
<td>(SF-36 Score)</td>
</tr>
<tr>
<td><strong>Physical Functioning</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>73 ± 19</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>71 ± 18</td>
<td>-2 ± 9</td>
<td>0.50</td>
</tr>
<tr>
<td>Post-1</td>
<td>80 ± 17</td>
<td>9 ± 17</td>
<td>0.19</td>
</tr>
<tr>
<td>Post-2</td>
<td>73 ± 25</td>
<td>-7 ± 18</td>
<td>0.35</td>
</tr>
<tr>
<td><strong>Vitality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>57 ± 15</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>59 ± 17</td>
<td>2 ± 11</td>
<td>0.40</td>
</tr>
<tr>
<td>Post-1</td>
<td>63 ± 15</td>
<td>4 ± 8</td>
<td>0.19</td>
</tr>
<tr>
<td>Post-2</td>
<td>64 ± 15</td>
<td>4 ± 7</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>Bodily Pain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>56 ± 16</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pre-2</td>
<td>59 ± 20</td>
<td>3 ± 10</td>
<td>0.47</td>
</tr>
<tr>
<td>Post-1</td>
<td>71 ± 14</td>
<td>12 ± 20</td>
<td>0.09</td>
</tr>
<tr>
<td>Post-2</td>
<td>59 ± 24</td>
<td>-10 ± 19</td>
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<tr>
<td>Pre-1</td>
<td>71 ± 26</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Pre-2</td>
<td>81 ± 18</td>
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</tr>
<tr>
<td>Post-1</td>
<td>88 ± 13</td>
<td>6 ± 19</td>
<td>0.38</td>
</tr>
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<td>81 ± 12</td>
<td>-5 ± 18</td>
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<tr>
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<tr>
<td>Pre-2</td>
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<tr>
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<td>Pre-2</td>
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<td>Pre-1</td>
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<td>Pre-2</td>
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<td>-</td>
</tr>
<tr>
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<tr>
<td>Post-2</td>
<td>82 ± 15</td>
<td>4 ± 8</td>
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Effect of the Intervention on Quality of Life

Discussion

Addressing the hypotheses

It was hypothesised that the score for physical functioning would increase as a result of the intervention, indicating an improvement in performance of physical activities. This hypothesis was proven to be incorrect.

The hypothesis that the score for vitality would increase following the intervention, indicating increased levels of stamina and decreased levels of fatigue, was proven incorrect, as was the hypothesis that the score for social functioning would improve. There was a trend toward an improvement in bodily pain score following the intervention, but this change was not significant.

It was hypothesised that the scores for limitations due to both physical health and emotional problems would increase, indicating a reduction in the negative effect of these factors on the performance of daily activities. Both of these hypotheses proved incorrect. It was hypothesised that scores for general health perception and general mental health would improve as a result of the intervention, hypotheses that also proved incorrect.

Regarding the hypothesis that changes in quality of life would be short-term and return to baseline at the 2nd post-intervention assessment, the lack of any significant changes as a result of the intervention makes this hypothesis irrelevant.

Lack of significant improvement in quality of life

As indicated above, there were no observations of significant improvement in quality of life as a result of the intervention. However it is possible that, for most variables, this lack of improvement was the result of high perceptions of quality of life prior to the onset of the intervention. Currie et al. (2006) conducted a study investigating the correlation between quality of life measures and severity of neuropathic symptoms, ranking Type-1 and Type-2 diabetics according to whether or not they experience none, mild, moderate or severe symptoms. Compared to their data, the current group of participants firmly align with the
asymptomatic group in terms of physical and social functioning, vitality, limitations due to emotional problems and general mental health. The bodily pain scores of the current group were more similar to the mild symptom group of their study prior to the intervention, but improved to a level similar to their asymptomatic group following the intervention. The limitations due to physical health and perceptions of general health results of the current group were somewhere between the asymptomatic and mild symptom groups of their study; however comparisons are particularly difficult in these cases due to high inter-participant variability. The comparison between the current study and that performed by Currie et al. (2006) suggests that the participants in the current study enjoyed a quality of life similar to diabetics that have no neuropathic symptoms, in spite of the fact that all the participants in the current study were diagnosed as neuropathic.

Perhaps the exclusion criteria of the current study, designed to maintain as homogenous a group as possible, prevented the inclusion of participants that may have suffered from symptoms which have a more pronounced effect on quality of life, or at least the aspects of quality of life measured with the generic SF-36. If patients with cardiovascular disease, or even rheumatoid conditions such as gout, had been included, perhaps the baseline level of quality of life in the current study would not have been so high. This potentially could have led to an increased likelihood of observing some improvements following the intervention; however the resulting lack of group homogeneity would have reduced the validity of any statements regarding the efficacy of the intervention at improving purely neuropathic symptoms.

Another factor when we consider the relatively high pre-intervention quality of life levels is the conditions under which participants were recruited into the study. All participants were under no particular duress at the time of recruitment – meaning that the current study was not attempting to evaluate the effect of an intervention on an acute pathological population, such as stroke victims (Lynch, et al., 2007), but rather a chronic condition that some participants had lived with for decades. In addition, the lack of any significant change in sensory threshold between the two pre-intervention assessments suggests that their condition was generally stable. Therefore a 12-week exercise intervention that focuses only on the lower limb is unlikely to play as large a role in a neuropathic diabetics’ quality of life as their own personal mechanisms for coping with their chronic peripheral dysfunction, most probably learned over an extended period of time.
Effect of the Intervention on Quality of Life

Along a similar line of reasoning, perhaps the lack of significant improvement in quality of life measures beyond pre-intervention levels was also a reflection on the specific nature of the training programme. The exercises employed were all lower limb-specific, with a particular focus on the ankle and foot, and the reasoning behind this modality of exercise has already been discussed. Perhaps the intervention was not systemic enough – both physiologically and figuratively – to cause significant improvements in quality of life. If the exercises employed in the current study had been combined with a nutritional intervention, or an extra session was added per week where participants met with a clinical psychologist, perhaps a more significant improvement in quality of life measures could have been observed.

Limitations

The SF-36 is an effective tool for investigating generic quality of life in pathological populations. However it is this generic quality which is ultimately a limitation of this experimental component. When designing the current study, emphasis was firmly placed on the methodological design of the biomechanical assessments and resultant sensorimotor function outcome measures, since these were the variables that the current author had the most interest and experience in. Following discussions with advisors, it was decided to include a psychological profiling aspect to the study design, since it was hypothesised that the intervention could have a significant positive impact on holistic quality of life in a neuropathic population. Following a review of the relevant literature, the SF-36 was chosen as the measurement tool for this aspect of the study, since it had been used in previous neuropathic literature and also shown to be a valid and reliable measure in pathological populations. The efficacy of the SF-36 in determining quality of life is not disputed; however, in retrospect this tool was inadequate in determining the neuropathy-specific factors associated with perceptions of quality of life. The combination of the SF-36 with a symptom score (2006) or a falls efficacy scale (Allet, et al., 2010b) would have offered more information on these specific factors beyond the assessment of sensorimotor function already presented in this thesis.

Another consideration regarding the limitations of the SF-36 is that the SF-36 employed in the current study had a ‘standard recall period’ (Saris-Baglama et al., 2009).
This refers to the questions which ask participants to recall how their physical health has prevented them from accomplishing certain tasks over a certain period of time, with the standard recall period being four weeks. This is opposed to the ‘acute recall period’, which is one week. Therefore the answers given to these recall questions in the 1st post-intervention assessment should reflect upon the final four weeks of the exercise intervention. It is possible that the acute version of the SF-36 may have been more appropriate for use in the current study, since theoretically improvements made in the last four weeks of the intervention would not factor as strongly in answers to these questions as improvements made in the first eight weeks. However it can be argued that, in spite of being asked to recall the previous four weeks, participants were more likely to answer questions based on a brief period of time prior to the final assessment and so the effect of the four-week recall period may have been negligible.

Conclusions

The intervention had a negligible effect on most quality of life measures, possibly due to relatively high quality of life levels in the current participants prior to the intervention. The score for bodily pain showed a trend toward improvement following the intervention, but this was non-significant. Moderate to high inter-participant variability was observed for all measures.

This chapter concludes the experimental components of the current study. In the next chapter, the findings of all six experimental components will be combined to form general points of discussion, recommendations and thesis conclusions.
Chapter Ten

General Discussion, Recommendations and Conclusions
General Discussion

Introduction

The purpose of this final chapter is to amalgamate the conclusions of all six experimental components into a series of discussion points, comprising the key findings of the current study. Following this a series of recommendations for both clinical practitioners and researchers are presented, and finally general conclusions for the thesis are made.

Answering the hypotheses

In the introduction (Chapter 1) the general hypotheses of the current study were stated, and these can now be addressed. It was hypothesised that:

1. Peripheral sensory function, as measured with Semmes-Weinstein monofilaments, would significantly improve as a result of the intervention, and return to baseline at the follow-up assessment. This hypothesis was proven largely correct, since significant improvements in sensory function were observed at three of the four plantar sites tested. The hallux was the only site to exhibit a trend toward a return to baseline, and this was not statistically significant.

2. Postural stability, as measured by standing balance assessments, would significantly improve as a result of the intervention, and return to baseline at the follow-up assessment. This hypothesis was proven incorrect as no significant changes in balance performance were revealed.

3. Dynamic lower limb function, as measured by gait analysis, would significantly improve as a result of the intervention, and return to baseline at the follow-up assessment. This hypothesis was proven incorrect due to a lack of change in temporal spatial, kinematic or kinetic measures of gait.
4. Dynamic foot function, as measured by the foot morphology and plantar loading assessments, would significantly improve as a result of the intervention, and return to baseline at the follow-up assessment. Although some changes were observed in peak plantar loading at one foot region when participants were stratified according clinically-relevant high peak pressures, this hypothesis was proven largely incorrect since these changes were most likely random and no other significant improvements in foot morphology or loading characteristics were observed following the intervention.

5. Lower limb muscle strength, as measured by isometric ankle strength assessments, would significantly improve as a result of the intervention, and return to baseline at the follow-up assessment. This hypothesis was proven incorrect since ankle strength remained unchanged following the intervention.

6. Health-related quality of life, as measured with the SF-36 questionnaire, would significantly improve as a result of the intervention, and return to baseline at the follow-up assessment. This hypothesis was proven incorrect since no significant group improvements were found.

Summary of findings

As a result of the exercise intervention, sensory threshold improved significantly at three of the four plantar regions assessed plus the average for the foot. A lack of group homogeneity existed in terms of range of sensory loss. Participants who exhibited the most severe sensory loss showed no improvement following the intervention, and the magnitude of change varied in those participants that did show improvement.

The intervention had no significant effect on CoP movement during standing balance assessments under differing visual and surface conditions. The lack of improvement in postural stability may be the result of the high inter- and intra-individual variability, whereby some participants exhibited postural stability dysfunction for some measures and others did not. It may also be a reflection on an inability of the intervention in its current form to cause any adaptations to balance performance.
The intervention had no significant effect on relevant temporal spatial, kinematic or kinetic aspects of gait. Walking speed and stride length results were comparative with those reported in previous neuropathic gait research (Courtemanche, et al., 1996; Kanade, et al., 2006; Katoulis, et al., 1997; Paul, et al., 2009; Sawacha, et al., 2009), and their lack of improvement was possibly the result of the absence of gait-specific exercises in the intervention. The lack of significant changes in other gait parameters is most likely the result of an absence of pre-intervention gait pathology exhibited by the current participants, as well as a lack of gait-specific exercises in the intervention.

The intervention had no significant effect on dynamic foot morphology or plantar loading when all participants were analysed as one group. It was possible to stratify participants into high and low peak pressure groups based on a clinically-relevant pressure threshold, and this resulted in the observation of a peak pressure reduction beneath the lateral dominant forefoot in the high pressure group; however due to the small sample size, combined with an absence of change at any other foot region or parameter, this is likely to have been a random occurrence. While the intervention was not able to substantially reduce peak plantar loading, the absence of any increase following the intervention is clinically-significant when we consider the improvements observed in sensory threshold, which were therefore achieved without causing plantar tissue overloading.

The intervention had no significant effect on ankle plantar- or dorsiflexor isometric peak torque production. While the plantarflexor results from the current group of participants were similar to those exhibited by fallers in previous research (LaRoche, et al., 2010), this is not necessarily an indication of any dynamically-relevant ankle strength pathology prior to the intervention when it is considered that ankle moment and power generation during gait was found to be non-pathological (Chapter 6).

The intervention had a negligible effect on most quality of life measures. The score for bodily pain showed a trend toward improvement following the intervention, but this was non-significant.
Sensory function changed, motor function did not

It is clear from the findings of the current study that the intervention may have had a significant effect on sensory function in many participants, but a negligible effect on motor function. There are several potential explanations for this finding. Firstly, all participants had some degree of peripheral sensory dysfunction, since this was a requirement for inclusion in the study. However, it did not necessarily follow that all participants would have some degree of motor dysfunction, and the results of the current study illustrate an overall lack of severe motor pathology in the participants recruited for this study. This, as previously mentioned, is most probably the result of the strict inclusion criteria. The lack of severe motor dysfunction renders the goal of improving motor function largely irrelevant, particularly from a clinical standpoint.

However, some participants did exhibit motor irregularities in areas of common neuropathic dysfunction, including standing balance (Chapter 5) and plantar loading (Chapter 7). In the case of the former, some participants struggled to complete a full 20 second standing balance trial when both visual and somatosensory cues were diminished; and in the case of plantar loading, half of the participants exhibited high peak pressures that could be considered clinically-relevant due to their location at sites which frequently ulcerate. However, when further analysis of the individual results of each participant were made in both cases – and an extra group analysis was conducted in the case of the plantar loading results – it was discovered that despite the severity of dysfunction in these areas, the intervention still had no significant effect. Additionally, it was found that severity of sensory loss was not significantly correlated with any measure of motor function, a non-correlation which held for all four pre- and post-intervention assessments. Therefore, in the case of all measures of motor function, severity of sensory or motor dysfunction had no influence on how an individual responded to the intervention.

The second potential reason for the improvement in sensory function but lack of improvement in motor function – particularly in the participants who exhibited motor dysfunction – may have been inadequacies in terms of volume and intensity of the exercise intervention. A 12-week exercise intervention, comprised of twice-weekly supervised sessions, simply may not be sufficient to cause any adaptations in motor function. At a peripheral neural level, this may reflect a lack of adequate stimulation of motor nerve repair;
the study by Doyle and Roberts (2006) which showed axonal sprouting in eels following a two-week intervention required the eels to exercise for 480 hours, while the current participants only exercised for a total of 12 hours. Of course it should be noted that this study was conducted on eels, not humans; but the findings of this study may suggest that perhaps the volume and intensity of the intervention in the current study was not sufficient to cause repair of motor neurons in those participants that did exhibit motor dysfunction.

At a more central neural level, it is possible that the length and modality of the intervention was not sufficient to cause changes in cortical organisation of motor function, which may have been learned over an extended period of time in order to cope with reduced afferent input and peripheral motor dysfunction. From a different perspective, De Jong et al. (2003) investigated the effect of immobilisation of the hand following tendon surgery on cortical activation patterns when performing dynamic tasks immediately after the hand could move freely again. They found that after only six weeks of immobilisation, cerebral activation patterns were not efficient for their given hand movement tasks, and suggested that this was an indication of a reorganisation of motor functions in the motor cortex. While their study is vastly different to the current study in terms of pathology, modus of intervention and measured outcomes, it illustrates the point that the few participants with motor dysfunction which did not improve as a result of the intervention may have had deeply-seeded inefficient cortical organisation of motor function that could not be improved as a result of such a short, low-intensity intervention. However all of these points on peripheral neural repair and cortical function are purely theoretical and cannot be expanded on without quantitative proof.

The current group of participants did exhibit walking velocity and stride length values comparable to previous neuropathic populations (Courtemanche, et al., 1996; Kanade, et al., 2006; Katoulis, et al., 1997; Paul, et al., 2009; Sawacha, et al., 2009), and these measures of gross motor function remained unchanged following the intervention. Therefore the third potential explanation for the lack of improvement in areas of motor dysfunction was the type of exercises chosen in the current study. Allet et al. (2010a; 2010b) showed improvements in walking speed in neuropathic diabetics following a training programme which required participants to complete gait- and balance-relevant exercises, including walking across a beam and walking in a variety of different styles. Perhaps the fact that the exercises which comprised the current intervention were not gait-specific is the reason for the lack of improvement in walking speed. It can be suggested that it was naive to assume that a
programme which aimed to improve lower limb balance and strength would have a collateral effect on measures of gait and balance performance. Perhaps if more gait-specific exercises had been employed, an improvement in walking speed may have been observed; perhaps if the balance component of the intervention had included a loss of visual cues, those participants that continued to struggle with the eyes-closed balance conditions following the intervention would have shown improvement.

The research by Allet et al. (2010a; 2010b) suggests that it may be in the best interests of the researcher to design exercise interventions closely related to their outcome measures, in order to increase the likelihood of observing an intervention effect. However while such a study allows for the measurement of clinically-relevant outcomes – such as walking speed or time taken to cross a narrow surface – it does not answer the mechanisms behind these improvements, which the current study attempted to do. Unfortunately the improvement of measures of gross motor function did not materialise in the current study, and so the use of the relatively complex kinematic and kinetic techniques for investigating these measures was not as beneficial as desired.

Despite the absence of opportunity for the kinematic and kinetic measures to explain changes in motor function, these techniques did allow for a deeper understanding of these mechanisms. For example, the temporal spatial results calculated from gait assessments suggested that the participants exhibited reduced walking speeds, comparable to previous neuropathic populations. However, the full three-dimensional analysis of joint kinematics and kinetics revealed no significant pathology in these measures. So, despite exhibiting slower walking speeds than healthy populations, the current group of participants did not exhibit any dysfunction of dynamic joint movement. If the current study had only employed temporal spatial measures of gait, the concluding remarks would be that participants exhibited pathology in terms of walking speed that was not improved by the intervention. By understanding that the participants in fact had no gait dysfunction – other than walking conservatively – the focus is shifted from a supposition that the intervention was ineffective at improving gait to a realisation that perhaps their gait did not need to be improved in the first place.
**Statistical power**

Considering the small number of participants in the current study, the capacity to deliver statistically powerful results was severely compromised. The statistical software programme G*Power (v3.08; Faul et al., 2007) was used to calculate the potential power that could have been achieved in the current study given the low number of participants and a high effect size of 0.5 (J. Cohen, 1992). Based on this calculation, it was determined that the highest power that could have been achieved given this effect size was < 0.3.

Effect size was also calculated for a number of outcome measures between the 2nd pre-intervention and 1st post-intervention assessments using a modified version of Cohen’s method (J. Cohen, 1992; Thalheimer & Cook, 2002). Based on this effect size, post-hoc power was calculated using G*Power, and two representative examples of this post-hoc power analysis will now be discussed.

The improvements observed in sensory threshold at the hallux corresponded to a high effect size of -0.57. Using this value the number of participants that would have been required to obtain a high statistical power of >0.8 (J. Cohen, 1992) was estimated to be 27. Therefore, in order to firmly support the achievement of the experimental hypotheses it would have been necessary to acquire the same results as the current study from 27 participants. The acquisition of this statistical power would provide stronger impetus for the implementation of the current intervention as a means of improving peripheral sensory function in a wider neuropathic population. However as already discussed (Chapter 3) the attainment of this number of participants within the boundaries of the inclusion criteria was not possible, considering the 14-month period required to obtain the 12 participants that began the intervention study.

The results of the postural stability, gait, plantar loading and ankle strength experiments showed no significant improvement following the intervention. Among other reasons, it was suggested that this may be a reflection on the inability of the intervention to cause any motor function adaptation. Using isometric ankle plantarflexor strength as an example, we can estimate the number of participants that would be required to improve the power of these findings based on the observed effect size of 0.09. Using this value the number of participants that would have been required to obtain high statistical power of >0.8 (J. Cohen, 1992) was estimated to be >1000. Therefore, in order to firmly reject the null
hypothesis and avoid type-II error for this measure, it would have been necessary to acquire the same isometric plantarflexor results as the current study from approximately 1000 participants.

It can be suggested that the implementation of a pilot study, whereby a smaller group of participants could have been taken through the intervention prior to a larger group, would have shown that it was going to be unlikely to observe a significant intervention effect. Based on the findings of such a pilot study, the intensity of the intervention could have been adjusted and further power calculations could have been made to determine how many participants would be required to observe a significant effect. However due to the pragmatic difficulties in recruiting participants – which have already been discussed in this thesis – the conduct of such a pilot study was not feasible. It became quickly apparent in the participant recruitment phase that the population pool from which participants could be drawn was significantly smaller than expected, for reasons discussed elsewhere in this thesis. Therefore the small size of the group of participants prohibited any splitting into smaller groups in an attempt to guide the future direction of the study. Instead, it was decided to progress with the intervention in its current form based on the evidence in the literature regarding its potential effectiveness. However, it is accepted that a pilot study could have highlighted the inability of the intervention to cause adaptations in motor function at an early stage, and that subsequently changes could have been made to the intensity of the intervention prior to other participants starting the intervention. Therefore the absence of a pilot study is a limitation of the current study.

It is clear that the small sample size of the current study dictates that its findings – both those that support and refute the experimental hypotheses – are low in statistical power. This reduces the strength of any of the suppositions made regarding the effect of the intervention, and therefore is a limitation of the current study. However, it must be noted that although the statistical support for the implementation of the current intervention is weak, this does not take into consideration the clinically-relevant improvements exhibited by the current group of participants. This will now be discussed.
Clinical relevance of findings

The most clinically-relevant finding of the current study is the significant change in sensory function observed following the intervention. There were no significant changes in sensory threshold at any foot region between the two pre-intervention assessments, but following the intervention sensory threshold was seen to improve at most of the foot regions. Apart from the 3\textsuperscript{rd} metatarsal head region, average sensory threshold for the group fell below the 5.07 value used as the principle inclusion criteria for the current study, a value chosen due to the relevance of this threshold as a sign of loss of protective sensation (Batista, et al., 2005; Charanya, et al., 2004; Laing, 1994). The fact that a number of participants would not have met the inclusion criteria for the current study had they exhibited their post-intervention sensory threshold during the screening process is a clinically-significant finding.

Recommendations

Recommendations for clinicians

The findings of the current study suggest that, if attempting to improve peripheral sensory function, it may be appropriate to prescribe an exercise intervention comprised of lower limb balance and low-impact strength training to neuropathic diabetic patients that do not already have an absence of any peripheral touch sensation. However, as previously discussed the low statistical power of the current study prevents any definitive statement of treatment efficacy.

It is not necessarily the case that the intervention in its present form would only be effective in populations that meet the inclusion criteria for the current study; it is possible that patients with rheumatoid conditions such as gout, healed ulcers or cardiovascular conditions could equally benefit from the intervention without fear of stressing their respective conditions. In the case of patients with previous plantar ulcers, attention should be paid to these sites over the course of the intervention to ensure that this tissue remains free of callous. In the case of patients with cardiovascular disease, best clinical practice would dictate that clinicians should conduct the exercises in the presence of a cardiologist or a skilled cardiac rehabilitation specialist. While the cardiovascular requirements of a patient completing the
General Discussion, Recommendations and Conclusions

current intervention are most likely to be minimal, the presence of cardiovascular risk factors heightens the chance of a cardiac event, even during normal daily activities.

Supervision is addressed in the next set of recommendations, so it will not be elaborated on here. However an important consideration for clinicians is the fact that all exercise sessions were individually supervised, i.e. on a one-to-one basis, at a given participant’s home or place of business. Logistically, this may be too difficult for a clinician who has multiple patients and only limited fiscal and time resources. However it is not necessary to conduct an intervention in this manner; numerous studies have shown positive clinical improvements in patients suffering from a variety of pathologies when supervised group training has been implemented (Bravo et al., 1996; Cagliyan et al., 2007; Donat & Ozcan, 2007; P. Williams & Lord, 1997). As will now be discussed, the individual assessment of each exercise session in the current study was an unavoidable logistical necessity rather than a desired one.

Recommendations for researchers

A major strength of the current intervention study was the complete supervision of all exercise sessions by the current author, unequivocally ensuring that all exercises were completed at the correct intensity, duration and frequency in every session. Because of this supervision, we can be certain that all participants received the same intervention, at the same frequency and intensity, and that there was 100% adherence to the exercise programme. The degree of supervision of the exercise intervention was a priority when designing the intervention, since the evidence for home-based, unsupervised exercise interventions is very poor in diabetic populations (Dunstan et al., 2006; Praet, et al., 2008). As an example of this, the work by Dunstan et al. (2006) involved two months of supervised resistance training in Type-2 diabetics, after which improvements in glycaemic control were observed. Following the supervised intervention, the groups were divided into home-based and training centre-based exercise groups. Participants from both groups also attended monthly meetings, where they received information regarding physical activity and nutrition. The home-based group was provided with exercise equipment, while the training centre-based group was provided with 12-month gym memberships and offered supervision at their tri-weekly training sessions. The authors found that, after a year, the training centre-based group maintained their
improvements in glycaemic control achieved following the initial two month supervised sessions while the home-based group did not.

There are numerous reasons for why individuals respond better to supervised training programmes than unsupervised; it can be argued that simply the presence of another person is a critical factor, and if this other person is someone that the individual feels accountable to then they are more likely to comply. The only reason the current study can boast a 100% adherence rate is the fact that the current author would, twice-weekly, arrive at the home or place of business of each participant at a pre-arranged time and together the exercise intervention for that day would be completed. Conduct of every exercise at the correct intensity, duration and frequency was ensured, since the current author controlled these parameters at all times; this would not have been possible if the sessions had not been individually supervised. If an intervention is unsupervised, or only partly supervised, it cannot be totally ensured that the prescribed intervention was actually received by the participants.

Therefore there is no doubt that the supervision of exercise sessions is a far superior option when conducting an exercise intervention study. However, absolute personal supervision of all exercise sessions does have its limitations. Depending on the size of the intervention group, personal supervision can be enormously time-consuming and expensive. Without funding from the Health Research Council of New Zealand and the University of Auckland, the current exercise intervention could not have occurred in its current form due to the prohibitive cost associated with travelling between participants’ homes and businesses over a 12 month period. This method was employed when it was discovered that participants were entering the study in very small numbers due largely to the strict inclusion criteria, so the creation of groups with whom to conduct group exercise sessions became implausible. Since it was already proving difficult to recruit suitable participants into the study, and considering the progressive quality of their pathology, it was desirable to start participants in the intervention study as soon as possible. While increasing the amount of work required completing the intervention considerably, as mentioned the personal supervision of each exercise session enabled the current author to strictly control the quality and quantity of exercises performed by each participant. However, as soon as groups larger than 15 are employed in an exercise intervention study, either more exercise rehabilitation experts would be required or group sessions would have to be employed.
Another recommendation for researchers wishing to conduct a similar intervention study is that it may be beneficial to customise the intensity of the exercise sessions to each participant. This could be accomplished by taking a baseline measurement of balance and lower limb strength, and then tailoring the subsequent session to a certain percentage of baseline capabilities. In the current intervention, each participant received the same intensity, duration and frequency of exercise. While the accomplishment of this intensity was a struggle for some participants, two participants complained toward the end of the intervention that exercises had become too easy. Extra benefit could be obtained by also altering the intensity of exercises over the course of the intervention based on capability measured at different time points, rather than arbitrarily increasing the difficulty of the intervention at monthly intervals, as was conducted in the current study. By tailoring the intervention to each individual participant in this manner, perhaps further improvements in sensorimotor function could have been observed.

Due to the low sample size of the current study, the statistical power of the observed changes in sensory function following the intervention was low. As mentioned, the same results for the changes in sensory function at the hallux – the foot site which exhibited the largest effect size following the intervention – would need to be found in a sample of 27 participants in order to exhibit a statistical power of >0.8. Therefore the attainment of a larger sample size than the current study should be a priority in future research in order to increase potential power. It was the original intention of the current study to attain a sample size of 50, which did not eventuate due to aforementioned difficulties in recruiting participants that matched the inclusion criteria. It would be less difficult to recruit this number of participants if the inclusion criteria were ‘relaxed’; however, these criteria were specifically designed to ensure that the sensorimotor dysfunctions exhibited by the patients could only be explained by their diabetic neuropathy. By including patients with conditions such as gout, which can cause losses in sensory function irrespective of the presence of diabetic neuropathy (Rosenbaum, et al., 2006), the research question would have been confounded since we would not be certain whether changes in sensory function were the result of improvements in neuropathic or rheumatic symptoms.

Perhaps by including patients with underlying cardiovascular disease (CVD), more participants could be included into future studies and a sufficient number of participants required to obtain high statistical power could be recruited. As discussed in Chapter 3, it was
decided at the beginning of the current study that patients with CVD would not be included
due to their contraindications to exercise. However, now that the physical requirements of the
intervention are well understood – based on the anecdotal experience gained from conducting
the intervention in a population without CVD – the cautious inclusion of these participants
under the supervision of cardiac professionals may be warranted for future studies.

Recommendations for future research directions

There are four areas of future research that may have helped to explain the changes –
or lack thereof – observed in the current study. Firstly, further investigation into the effect of
the intervention on peripheral neural tissue is of high interest. As mentioned in Chapter 4, it
remains unknown whether the improvements in peripheral sensation were the result of an
improvement in the function of pre-existing nerves or a neurogenesis of new sensory nerves.
It was hypothesised in Chapter 4 that neurogenesis was improbable, and that neural repair was
the most likely causative factor. However without measuring this at a cellular level this is
only speculation. The measurement of the density of intraepidermal sensory nerve fibres at
various lower limb sites via biopsy (Loseth, et al., 2010; Quattrini, et al., 2007; Tavee &
Zhou, 2009) would be one way of ascertaining the presence of neurogenesis as a result of an
intervention. Assuming that the same improvements in sensory function as the current study
were observed, the absence of any evidence of neurogenesis would support the theory that
repair of pre-existing living nerves must have occurred. There are of course limitations to
these biopsies: they are generally obtained by punching a hole in the dermal tissue (Quattrini,
et al., 2007), which could clearly be an ethical issue in neuropathic patients with reduced
healing capacity (Greenman, Panasyuk, et al., 2005). A less invasive alternative would be
advanced imaging of dermal tissue (Malone et al., 2002), which incidentally could also offer
information on peripheral capillarisation.

Secondly, no improvements were observed in motor function in those participants who
exhibited dysfunction. As already discussed in this chapter, one possible explanation of this
lack of change is rigidity in terms of cortical organisation of motor function – metaphorically,
a ‘reluctance’ at the cortical level to learn new patterns of behaviour since the old patterns are
so deeply embedded. The additional measurement of cortical function could offer further
information on the organisation of the motor cortex in these populations. A method which
could be used is the measurement of regional cerebral blood flow using positron emission tomography (PET) techniques (de Jong, et al., 2003), with increased blood flow indirectly indicating increased activity in given regions of the motor and somatosensory cortex. The use of functional magnetic resonance imaging (fMRI) could also be used to investigate regional cortical activation (Hofbauer et al., 2006). If logistically possible, participants could be measured with such techniques while performing standing balance tests, under different visual and somatosensory conditions, before and after an intervention such as that conducted in the current study. An age-matched group without sensory dysfunction could act as controls. Based on the result of such an analysis, statements regarding the effect of neuropathy on cortical organisation of motor function could be made, as could the effect of an exercise intervention on this organisation.

Thirdly, it is also of interest to investigate the effect of an intervention on the underlying muscular and soft tissues which comprise the foot and ankle joint complex. The measurement of ankle strength in the current study represents a gross measure of motor function, and does not allow for a more precise understanding of the effect of the intervention on muscle tissue. Such an analysis could include the measurement of metabolites within muscle tissue via imaging techniques, with these measures acting as markers of the function of muscle metabolism (Greenman, et al., 2005). It is also possible to measure the cross-sectional area of muscles using ultrasound techniques (Andersen, et al., 2004; Severinsen et al., 2007), where the cross-sectional area represents muscle size and statements regarding muscle atrophy or hypertrophy can be made. Regarding soft tissue, increased plantar stiffness is related to increases in peak pressures and therefore an increase in the risk of plantar ulceration in neuropathic populations (Brash et al., 1999; Gefen, 2003; Klaesner et al., 2002; Mueller et al., 2003). The measurement of soft tissue properties is possible via imaging (Brash, et al., 1999; Charanya, et al., 2004) and indentation (Klaesner, et al., 2002) techniques, the latter of which measures the deformation of a given load of a given size on the plantar surface of the foot, and from this derives tissue stiffness. Clearly the goal of measuring this outcome pre-post an exercise intervention would be to document reduced tissue stiffness, which would indicate a reduced risk of plantar ulceration.

A future intervention study in neuropathic populations which implemented these three areas of research would be incomplete without the measurement of peripheral vascular flow. The current study is limited by the absence of this measure as a potential explanatory factor.
for the improvements observed in sensory function following the intervention. Magnetic resonance imaging (MRI) techniques can measure blood flow in a steady state (Hashimoto & Ohtsuka, 2005), but it is more common in diabetic populations to employ laser Doppler flowmetry techniques (Kilo et al., 2000; Krishnan et al., 2004) or spectral imaging techniques (Greenman, et al., 2005). The measurement of peripheral vascular flow, combined with more advanced peripheral neural tissue measures, could explain any improvements in sensory function which result from future exercise interventions in neuropathic populations.
**Final Conclusions**

Despite low group homogeneity in terms of sensory threshold, significant improvements in this measure were found following the exercise intervention; however it was observed that the participants with the most severe sensory loss exhibited no change. It was hypothesised that these findings were best explained by an improvement in the function of pre-existing sensory nerves, most probably due to improved vascular flow, rather than neurogenesis. Because of the low sample size of the current study, any statements regarding the efficacy of the intervention in improving sensory function in a wider neuropathic population are severely compromised. Future research should incorporate advanced peripheral and cortical neural imaging techniques, as well as measures of peripheral vascular flow, in order to further understand the observed changes in sensory function.

No significant group improvements in motor function were observed as a result of the intervention. It was hypothesised that this lack of change was best explained by the absence of severe motor pathology in most participants, most probably due to the strict inclusion criteria for this study, and/or the low intensity and volume of the training stimulus. Future low-impact exercise interventions in this population should increase the training stimulus in order to improve the likelihood of observing adaptations in those that exhibit motor dysfunction.

No significant group improvements in quality of life were observed as a result of the intervention. It was hypothesised that the lack of significant group changes in these measures was best explained by the absence of quality of life pathology in the current group of participants, most probably due to a combination of the strict inclusion criteria and the theory that participants may have adopted coping mechanisms for their chronic condition in the years preceding the intervention.
Originality of Research

This is the first study in which a group of neuropathic diabetic participants were taken through an exercise intervention which focussed on improving balance and strength of only the lower limb. Specifically, it is the first study in the neuropathic literature to use a balance board as the modus of instability in an exercise intervention.

This is the first study in which significant, quantifiable improvements in sensory function were observed following a low-impact exercise intervention in a neuropathic diabetic population.

This is the first study in which the effect of an exercise intervention on the three-dimensional kinematic and kinetic qualities of neuropathic gait was investigated. It is also the first study in which the CoP - CoM variable was employed as a measure of dynamic balance during gait in this population.

This is the first study in which the effect of an exercise intervention on foot morphology and plantar loading was investigated in a neuropathic diabetic population.
Appendix 1

Kinematic and Kinetic Model
Introduction

The following appendices outlines the kinematic and kinetic model employed in the current study in greater detail than that provided in the main body of the thesis. As outlined in Chapter 5, trajectory data were digitised, gaps filled and data filtered prior to model execution. Where examples are given from the model itself, the left anatomical ‘side’ is used. However if a discrepancy exists between left and right sides in the method of calculation of the given parameter, both calculations are shown.

The model was a modified version of the Cleveland Clinic model (Orthatrak 4.2 manual, Motion Analysis Corporation, U.S.A.), written in Vicon BodyLanguage using the software programme Vicon BodyBuilder (Vicon Motion Systems Inc., U.K.). The explanations given regarding order and syntax in which the BodyLanguage commands are written are generally taken from the Vicon BodyBuilder manual (Vicon, 2002). Following execution of the model, calculated variables were output in ASCII format from Vicon BodyBuilder for further analysis in Microsoft Excel.

Glossary of model terms and symbols

Definitions of Vicon BodyLanguage functions are taken from the Vicon BodyBuilder manual v1.2 (Vicon, 2002).

$ BodyLanguage symbol, instructing the model to search at the .mp file for the parameter directly following the ‘$’ symbol. For example, $BodyMass is the pre-defined weight of the participant that was entered into the .mp file prior to data analysis.

% BodyLanguage symbol, instructing the model that the subsequent marker directly following the ‘%’ symbol is in the local coordinate system.

ABS BodyLanguage function, which determines the absolute distance between the two markers which are contained in the brackets immediately following the
command. For example, ABS(LKNE, LKNM) determines the absolute distance between the lateral and medial left knee markers.

**DIST** BodyLanguage function, which determines the distance between the two markers subsequently listed in brackets immediately following the command. For example, DIST(LASI, RASI) determines the distance between the two ASIS markers.

**REACTION** BodyLanguage function, which incorporates all reaction forces applied to the segment in question by any child segments that are attached to it, as well as the effect of segment mass, gravity and the motion of the segment.

**POWER** BodyLanguage function, which determines resultant joint powers by incorporating powers flowing between parent and child segments.

### Macros

Macros were stated at the beginning of the model and referred to when necessary. The current model employed one macro, SEGVIS, which was used to determine the origin of a given segment and output the coordinates of a point 100mm along its \(xyz\) axes:

```plaintext
macro SEGVIS(Segment)
ORIGIN#Segment = 0(Segment)
XAXIS#Segment = 0(Segment) + (1(Segment) * 100)
endmacro
```

where \(ORIGIN#Segment = 0(Segment)\) sets the origin of the segment; and \(XAXIS#Segment\) is equal to a point 100mm along the \(x\) axis of the segment. Similar statements are completed for the \(y\) and \(z\) axes. The SEGVIS macro is used when calculating joint angles for the trunk and pelvis.
Parameter (.mp) file

The parameter or .mp file stores information relevant to each participant. Variables contained in the .mp file may be either manually entered or calculated and stored by the model. In the current model, participant body mass (kg), foot length (mm), gender (1 = male, 2 = female) and diameter of kinematic markers used (mm) were manually entered prior to the model being executed. Following the static trial, a number of calculated variables were stored in the parameter file, and these are indicated in their relevant section of this appendix. Once stored in the parameter file, these variables can be referred to by the model for subsequent calculations.

Anthropometric measures

Mass of lower limb segments

The mass (M) of the lower limb segments were slightly modified from the original Cleveland Clinic model, in order to reflect improvements upon the classical data (Clauser, et al., 1969; Dempster, 1955) previously used. Such improvements include the addition of separate mass parameters for males and females, which are both shown below (de Leva, 1996):

\[
\begin{align*}
\text{If} \,$Gender = 1 \,(\text{male}) \\
MLThigh &= 0.1416 \,* \,$BodyMass \\
MLShank &= 0.0433 \,* \,$BodyMass \\
MLFoot &= 0.0137 \,* \,$BodyMass \\
MLUArm &= 0.0271 \,* \,$BodyMass \\
MLFArm &= 0.0162 \,* \,$BodyMass \\
\text{If} \,$Gender = 2 \,(\text{female}) \\
MLThigh &= 0.1478 \,* \,$BodyMass \\
MLShank &= 0.0481 \,* \,$BodyMass \\
MLFoot &= 0.0129 \,* \,$BodyMass \\
MLUArm &= 0.0255 \,* \,$BodyMass \\
MLFArm &= 0.0162 \,* \,$BodyMass
\end{align*}
\]
Calculation of limb lengths and widths

A number of limb length and width variables were either manually entered by the tester or calculated and stored in the parameter file following the static trial. Foot length and width were measured with the patient in a standing position using an anthropometer (Lafayette Instrument Company, U.S.A.). Foot length was taken as the distance between the most posterior aspect of the heel to the most anterior aspect of the hallux. Foot width was taken as the distance between the most medial and most lateral aspects of the forefoot, which typically coincided with the medial and lateral heads of the 1st and 5th metatarsal heads, respectively.

Thigh and shank longitudinal lengths were determined using the DIST BodyLanguage function, which calculates the distance between two markers. In order to determine left thigh and shank length the following commands were used:

\[
L_{\text{ThighLength}} = \text{DIST}(\text{LASI, LKNE})
\]

\[
L_{\text{ShankLength}} = \text{DIST}(\text{LKNE, LANK})
\]

where LASI, LKNE and LANK refer to the left ASIS, left lateral knee and left lateral ankle markers, respectively. Based on these lengths, total leg length was calculated:

\[
L_{\text{LegLength}} = \text{DIST}(\text{LASI, LKNE}) + \text{DIST}(\text{LKNE, LANK})
\]

Upper arm and lower arm length were also calculated using the same method as for the thigh and shank, using their respective markers.

In order to determine the width of the knee and ankle, the distance between the lateral and medial markers placed about these joints were calculated, and the diameter of the markers subtracted:

\[
L_{\text{KneeWidth}} = \text{ABS}(\text{LKNE} \cdot \text{LKNM}) - 2 \times \text{MarkerDiameter}
\]

\[
L_{\text{AnkleWidth}} = \text{ABS}(\text{LANK} \cdot \text{LANM}) - 2 \times \text{MarkerDiameter}
\]
Local and global coordinate systems

Temporary local coordinate systems were created at the thigh, shank and foot. Data from these coordinate systems were then transferred into the global coordinate system prior to being output from the model. The foot is used as a representative example for brevity.

Foot

Local coordinate systems were created at the foot via a temporary foot segment TempLFoot:

\[ TempLFoot = [LHEE, LMET1 - LHEE, LMET1 - LMET5, xyz] \]

where the heel is the origin; the first segment axis \((x)\) runs parallel to or coincident with the line connecting the heel to the 1\(^{st}\) metatarsal; the second segment axis \((y)\) runs perpendicular to this line and a line connecting the 5\(^{th}\) and 1\(^{st}\) metatarsal heads; while the third segment axis \((z)\) runs perpendicular to the first two segment axes.

For the static trial, the ankle and knee joint centres were expressed in the local coordinate system of the temporary segment TempLFoot:

\[
\frac{\%LAnkleJCfoot}{LAnkleJCfoot} = \frac{LAJC}{TempLFoot} \\
\frac{\%LKneeJCfoot}{LKneeJCfoot} = \frac{LKJC}{TempLFoot}
\]

and then transformed into the global coordinate system of the temporary segment for dynamic trials:

\[
LAnkleJCfoot = \frac{\%LAnkleJCfoot}{TempLFoot} \\
LKneeJCfoot = \frac{\%LKneeJCfoot}{TempLFoot}
\]
Calculation of virtual markers and joint centres

Hip

The calculation of left and right joint centre position in the Cleveland Clinic model is based on regression formulae (Davis et al., 1991). To determine the parameters required for the calculation of the hip joint centres, a number of separate parameters needed to be calculated. The parameter $C$ refers to the distance between the ASIS marker and the hip joint centre in the frontal plane, while the parameter $LATD$ refers to the distance from the left ASIS marker to the trochanter:

\[ C = \text{LegLength} \times 0.115 - 15.3 \]
\[ LATD = 0.1288 \times \text{LegLength} - 48.56 \]

The distance between the ASIS markers was used to determine $MidASIS$, which was half of this distance:

\[ \text{InterASISDist} = \text{DIST}(\text{LASI}, \text{RASI}) \]
\[ MidASIS = \text{InterASISDist} / 2 \]

Marker diameter was divided by two in order to determine the distance to the centre of the marker, and subsequently labelled $MkrRadius$:

\[ MkrRadius = \frac{\text{MarkerDiameter}}{2} \]

where $\text{MarkerDiameter}$ is the diameter of the marker as manually entered into the .mp file.

The regression formulae used by the Cleveland Clinic model for the calculation of the hip joint centre requires the trigonometric calculation of distances based on angles derived from hip studies (Davis, et al., 1991). The angle $BETA (\beta; 18^\circ)$ refers to the angle created by a line connecting the midpoint between the two ASIS anatomical points with the midpoint between the two PSIS anatomical points, and a line extending horizontally from the midpoint between the two ASIS anatomical points. The angle $THETA (\theta; 28.4^\circ)$ refers to the angle
created by the line $C$ and a line extending vertically from a given ASIS anatomical point. Figure A1.1, taken from Davis et al. (1991), shows the line $C$ as well as the angles $\beta$ and $\theta$.

**Figure A1.1:** Figure showing the line $C$ and the angles $\beta$ and $\theta$; from Davis et al. (1991), Fig. 3, p583. The line $C$ and the angle $\theta$ are shown in the coronal plane view, while the angle $\beta$ is shown in the sagittal plane view. *LATD*, or ASIS to trochanter distance, is not shown in this figure.

Cosine and sine functions of these angles are then calculated prior to their inclusion in the final hip joint centre calculation:

\[
\begin{align*}
COSBETA &= 0.951 \\
SINBETA &= 0.309 \\
COSTHETA &= 0.880 \\
SINTHETA &= 0.476 \\
COSTHETASINBETA &= COSTHETA \times SINBETA \\
COSTHETACOSBETA &= COSTHETA \times COSBETA
\end{align*}
\]

where $COSBETA$ is equal to cosine($18^\circ$); $SINBETA$ is equal to sine($18^\circ$); $COSTHETA$ is equal to cosine($28.4^\circ$); $SINTHETA$ is equal to sine($28.4^\circ$); $COSTHETASINBETA$ is equal to cosine($28.4^\circ$) $\times$ sine($18^\circ$); and $COSTHETACOSBETA$ is equal to cosine($28.4^\circ$) $\times$ cosine($18^\circ$).

Once all required parameters were calculated, they could be entered into the hip joint centre calculation. Hip joint centre position is calculated in three planes (xyz), which are
separated by commas in the equation. Both right and left hip joint centre calculations are shown below, since the two differ slightly in the third part of the equation:

\[
RHJC = \{ C \cdot \text{COSTHETACOSBETA} - (LATD + MkrRadius) \cdot \text{SINBETA}, C \cdot \text{COSTHETASINBETA} - (LATD + MkrRadius) \cdot \text{COSBETA}, -C \cdot \text{SINTHETA} + \text{MidASIS}\} \cdot \text{Pelvis}
\]

\[
LHJC = \{ C \cdot \text{COSTHETACOSBETA} - (RATD + MkrRadius) \cdot \text{SINBETA}, C \cdot \text{COSTHETASINBETA} - (RATD + MkrRadius) \cdot \text{COSBETA}, \text{C} \cdot \text{SINTHETA} - \text{MidASIS}\} \cdot \text{Pelvis}
\]

where the output from these calculations is the \(xyz\) coordinates of the left and right hip joint centres in the global coordinate system.

**Knee**

The knee joint centre was calculated in the static trial based on the position of the lateral and medial knee markers:

\[
\%LKJC = \frac{\{(LKNE + LKNM) / 2\}}{LThighCluster}
\]

where \(\{(LKNE + LKNM) / 2\}\) is the midpoint between the lateral and medial knee markers, and \(/ LThighCluster\) converts the global position of the joint centre into the local coordinate system of \(LThighCluster\). Following the static trial the lateral and medial knee markers were removed, and for dynamic trials the positions of these markers and the knee joint centre was recreated by the thigh marker triad and converted from the local coordinate system back to a global position using the following commands:

\[
LKNE = \%LKNE \cdot LThighCluster
\]

\[
LKNM = \%LKNM \cdot LThighCluster
\]

\[
LKJC = \%LKJC \cdot LThighCluster
\]
Ankle

The calculation of the ankle joint centre was modified for the current study. Whereas the original Cleveland Clinic model calls for the removal of the lateral and medial ankle markers following the static trial, these were kept on in the current study for static and dynamic trials. This method enables the calculation of the ankle joint centre position based on dynamic markers $LANK$ and $LANM$:

$$LAJC = \frac{(LANK + LANM)}{2}$$

where $(LANK + LANM) / 2$ is the midpoint between the lateral and medial ankle markers.

Creation of segments

This section details the steps required for the creation of each segment, including the pelvis, trunk, thigh, shank, foot, upper arm and forearm. It includes the definition of segment components and orientation of axes. Each segment is detailed separately since required components generally differ between segments.

Pelvis

The origin of the pelvis is defined using the midpoint of the two ASIS markers, and labelled as $PELF$:

$$PELF = \frac{(LASI + RASI)}{2}$$

The pelvis segment orientation is then defined using both physical and virtual markers:

$$Pelvis = [PELF, RASI - LASI, PELF - SACR, zxy]$$
where $PELF$ is the origin; the first segment axis ($z$) is parallel or coincident to a line connecting the left and right ASIS markers; the second segment axis ($x$) is perpendicular to this line and a line connecting the sacrum and $PELF$; while the third segment axis ($y$) is set perpendicular to the first two segment axes.

**Trunk**

The origin of the trunk was defined as being half way between the sacrum marker and the virtual marker $PELF$:

$$TrunkOrigin = (PELF + SACR) / 2$$

The neck was defined as being located at the midpoint between the two shoulder markers:

$$Neck = (LSHO + RSHO) / 2$$

The trunk segment axes were then defined based on these two components:

$$Trunk = [TrunkOrigin, RSHO - LSHO, Neck - TrunkOrigin, zyx]$$

where $TrunkOrigin$ is the origin; the first segment axis ($z$) is parallel to or coincident with a line connecting the two shoulder markers; the second segment axis ($y$) is perpendicular to this line and a line connecting the origin of the trunk with the neck; while the third segment axis ($x$) is perpendicular to the first two segment axes.

**Thigh**

The thigh segment orientation was defined using virtual markers:

$$LThigh = [LKJC, LKJC - LHJC, LKNM - LKNE, xyz]$$
where the $LKJC$ is the segment origin; the first segment axis ($x$) runs parallel to or coincident with a line connecting the hip joint centre to the knee joint centre; the second segment axis ($y$) runs perpendicular to this line and a line connecting the lateral and medial knee markers; while the third segment axis ($z$) runs perpendicular to the first two segment axes.

**Shank**

The shank segment orientation was defined using virtual markers:

$$LTibia = [LAJC, LAJC - LKJC, LANM - LANK, xyz]$$

where the $LAJC$ is the segment origin; the first segment axis ($x$) runs parallel to or coincident with the line connecting the knee joint centre to the ankle joint centre, the second segment axis ($y$) runs perpendicular to this line and a line connecting lateral and medial ankle markers, while the third segment axis ($z$) runs perpendicular to the first two segment axes.

**Foot**

As mentioned, the section of the model pertaining to the ankle and foot was modified for use in the current model. This modification was necessary since the original Cleveland Clinic model is unable to adequately describe movements about the ankle joint in three directions, due to a lack of markers on the foot segment during dynamic trials. Where previously the model included two dynamic foot markers, namely the heel and 3rd metatarsal head, two markers were added to the 1st and 5th metatarsal heads respectively. In addition, as previously mentioned the ankle markers remained on during dynamic trials, which is also a modification to the Cleveland Clinic model. The availability of five physical foot markers during dynamic trials provided adequate kinematic information for a more efficacious expression of foot movement than was previously available in the original model.

During the static trial, the ankle and knee joint centres were expressed in the local coordinate system of this temporary segment:
\[
%LAnkleJCfoot = LAJC / LFoot
\]
\[
%LKneeJCfoot = LKJC / LFoot
\]

and then transformed into the global coordinate system of the temporary segment for dynamic trials:

\[
LAnkleJCfoot = %LAnkleJCfoot * LFoot
\]
\[
LKneeJCfoot = %LKneeJCfoot * LFoot
\]

As previously detailed, the location of the ankle and knee joint centres with respect to the temporary foot coordinate system TempLFoot was required for the definition of the segment axes. Based on these positions, the orientation of the foot segment proper could be described:

\[
LFoot = [LHEE, LKneeJCfoot - LAnkleJCfoot, LANK-LANM, yxz]
\]

where \( LHEE \) is the origin; the first segment axis (\( y \)) runs parallel to or coincident with the line connecting the ankle joint centre and knee joint centre in the foot coordinate system; the second segment axis (\( x \)) runs perpendicular to this line and a line connecting the medial and lateral ankle markers; and the third segment axis (\( z \)) runs perpendicular to the first two segment axes.

**Upper arm**

Firstly, the midpoint of the upper arm was defined as being the midpoint between the shoulder and elbow markers:

\[
LArm = (LELB - LSHO) / 2
\]

Following this, the upper arm segment axes were defined:

\[
LUArm = [LELB, LArm - LTRI, LELB - LSHO, yzx]
\]
where $LELB$ is the origin; the first segment axis ($y$) is parallel to or coincident with the line connecting the triceps marker with the midpoint of the upper arm; the second segment axis ($z$) is perpendicular to this line and a line connecting the shoulder and elbow markers; while the third segment axis ($x$) is perpendicular to the first two segment axes.

**Lower arm**

The lower arm segment was only required in order to calculate whole body centre of mass, and consisted of only two markers, being the lateral elbow and the wrist. Therefore the left lower arm was defined by:

$$L_{LowerArm} = LWRI \cdot LELB$$

where $LWRI$ was the segment origin, and the line connecting $LELB$ with $LWRI$ being the long axis of the lower arm segment.

**Segment hierarchy**

Before kinetic analysis, it was necessary to define a hierarchy of segments. Without the connection between parent and child joints, it would not be possible to calculate forces acting across these joints. For this model, the pelvis segment is defined as the root segment. Beginning with the trunk, the segment hierarchy was as follows:

$$Trunk = \{Trunk, Pelvis, TrunkOrigin\}$$

where the $Trunk$ segment is the child, the $Pelvis$ is the parent, and the two connect at the $TrunkOrigin$.

Continuing to the lower limb:

$$LThigh = \{LThigh, Pelvis, LHJC\}$$
where the \textit{LThigh} segment is the child, the \textit{Pelvis} segment is the parent, and the two connect at the \textit{LHJC}, or left hip joint centre. Continuing down the chain:

\[
\text{LShank} = [\text{LShank, LThigh, LKJC}]
\]

where the \textit{LShank} segment is the child, the \textit{LThigh} segment is the parent, and the two connect at the \textit{LKJC}, or left knee joint centre. Continuing down the chain:

\[
\text{LFoot} = [\text{LFoot, LShank, LAJC}]
\]

where the \textit{LFoot} segment is the child, the \textit{LShank} segment is the parent, and the two connect at the \textit{LAJC}, or left ankle joint centre.

\section*{Calculation of segment mass properties}

This section details the calculation of segment mass properties, including the position of the segment centre of mass and, where necessary, its moment of inertia. These calculations are based on cadaver studies (Chandler, et al., 1975; Clauser, et al., 1969; Dapena, 1978; Dempster, 1955). The thigh segment is shown as a representative example of these calculations for brevity. Following these descriptions, the calculation required for the estimation of whole-body centre of mass is detailed.

\textit{Thigh}

The location of the thigh centre of mass was defined by:

\[
\%LThighCoM = (\text{LHJC} / \text{LThigh} - \text{LKJC} / \text{LThigh}) \times 0.567 + \text{LKJC} / \text{LThigh}
\]

where \%\textit{LThighCoM} is the location of the centre of mass in the segment local coordinate system; \((\text{LHJC} / \text{LThigh} - \text{LKJC} / \text{LThigh})\) is a line representing the thigh, which is then multiplied by 0.567, the ratio which defines the location of the centre of mass (Dempster, 1955). The addition of \(+ \text{LKJC} / \text{LThigh}\) to the end of the command tells the model the
location of the origin; in this example, centre of mass location is defined by a ratio of 0.567 along the left thigh segment, starting from the left knee joint centre. As for all segments, the $xyz$ position of the centre of mass was then stored by the model in the parameter file.

Segmental centre of mass was also calculated by the model during dynamic trials:

\[
L_{\text{Thigh CoM}} = (L_{\text{HJC}} - L_{\text{KJC}}) \times 0.567 + L_{\text{KJC}}
\]

with the principal difference between the two previous equations being that the first equation is expressed in the segment local coordinate system, while the second equation is expressed in the segment global coordinate system.

In order to determine the moment of inertia of the thigh segment, the individual moments of inertia occurring about each axis of segment rotation were first calculated:

\[
I_{\text{FlxExtLThigh}} = M_{\text{LThigh}} \times L_{\text{ThighLength}} \times 0.323 \times L_{\text{ThighLength}} \times 0.323
\]
\[
I_{\text{AbdAddLThigh}} = M_{\text{LThigh}} \times L_{\text{ThighLength}} \times 0.323 \times L_{\text{ThighLength}} \times 0.323
\]
\[
I_{\text{IntExtLThigh}} = M_{\text{LThigh}} \times L_{\text{ThighLength}} \times 0 \times L_{\text{ThighLength}} \times 0
\]

where $I_{\text{FlxExtLThigh}}$, $I_{\text{AbdAddLThigh}}$ and $I_{\text{IntExtLThigh}}$ are flexion/extension, abduction/adduction and internal/external rotation moments of inertia, respectively; $M_{\text{LThigh}}$ refers to the mass of the left thigh; while $L_{\text{ThighLength}}$ is thigh length and 0.323 (or 0 in the last equation) is the radius of gyration. $L_{\text{ThighLength}} \times 0.323$ (or 0) gives the perpendicular distance to the axis of rotation, which is completed twice in each equation since:

\[
I = \text{mass} \times \text{perpendicular distance to axis of rotation}^2
\]

where $I$ is the moment of inertia. Once the individual components were calculated, whole segment moment of inertia could be stored as one parameter:

\[
L_{\text{Thigh MoI}} = \{I_{\text{IntExtLThigh}}, I_{\text{AbdAddLThigh}}, I_{\text{FlxExtLThigh}}\}
\]

where $L_{\text{Thigh MoI}}$ is the moment of inertia for the left thigh.
Once mass, the location of the centre of mass and the moment of inertia of the segment was calculated, these properties were incorporated into the definition of segment properties by the following command:

\[ L\text{Thigh} = [L\text{Thigh}, M\text{LThigh}, %L\text{ThighCoM}, L\text{ThighMoI}] \]

where \( L\text{Thigh} \) is the segment; \( M\text{LThigh} \) is the segment mass; \( %L\text{ThighCoM} \) is the location of the centre of mass; and \( L\text{ThighMoI} \) is the moment of inertia.

**Calculation of whole body centre of mass**

Whole body centre of mass position was found by multiplying the positions of segmental centres of mass by their respective ratio of segment mass to total body mass, and then summing all these individual segment calculations:

\[
\text{CoM} = (0.581 \times T\text{CoM}) + (0.027 \times LU\text{ArmCoM}) + (0.027 \times RU\text{ArmCoM}) + (0.023 \times LF\text{ArmCoM}) + (0.023 \times RF\text{ArmCoM}) + (0.099 \times L\text{ThighCoM}) + (0.099 \times R\text{ThighCoM}) + (0.046 \times L\text{ShankCoM}) + (0.046 \times R\text{ShankCoM}) + (0.014 \times L\text{FootCoM}) + (0.014 \times R\text{FootCoM})
\]

The output from this calculation is a \( xyz \) set of coordinates describing centre of mass position as a weighted sum trajectory in the global coordinate system.

**Calculation of segment and joint angles**

**Segment angles**

Euler angles were calculated for the trunk and pelvis segments relative to the global coordinate system using the faux-segment Anatomy, described as such since it is a non-anatomical segment. The global coordinate system was defined by:

\[
\text{Global} = \{[0,0,0], [1,0,0], [0,0,3], xyz\}
\]
which is then used as an insertion into the faux-segment \textit{Anatomy}:

\[
\text{Anatomy} = [0(\text{Global}), -3(\text{Global}), -2(\text{Global}), xzy]
\]

where 0(\text{Global}), -3(\text{Global}), -2(\text{Global}) refers to the direction of each of the axes within the global coordinate system. Depending on the position of the participant is facing within the global coordinate system in a given trial, the direction of some axes may be altered:

\[
\text{Test} = \text{PELF} - \text{SACR}
\]

\[
\text{If Test}(2) > 0 \text{ Then} \\
\text{Anatomy} = [0(\text{Global}), -3(\text{Global}), -2(\text{Global}), xzy]
\]

\[
\text{Else} \\
\text{Anatomy} = [0(\text{Global}), -3(\text{Global}), 2(\text{Global}), xzy]
\]

where Test is a line connecting the sacrum marker and PELF, the virtual marker located at the midpoint between the two ASIS markers. In the above BodyLanguage code, the model tests whether the y axis of Test, written as Test (2), is a positive number. If it is a positive number, the direction of the y axis is altered from positive to negative. The SEGVIS macro is then applied, in order to establish xyz coordinates for the faux-segment Anatomy:

\[
\text{SEGVIS}(\text{Anatomy})
\]

Using the global coordinate system, the trunk segment angles are calculated:

\[
\text{Trunk} \_ A = \langle \text{Anatomy, Trunk, xyz} \rangle \\
LT\text{runk} \_ A = \langle -1(\text{Trunk} \_ A), -2(\text{Trunk} \_ A), 3(\text{Trunk} \_ A) \rangle
\]

where -1(Trunk \_ A) is the x axis, -2(Trunk \_ A) is the y axis, and 3(Trunk \_ A) is the z axis. The brackets < > are used to define a rotation. Pelvis segment angles were also calculated relative to the global coordinate system:

\[
\text{Pelvis} \_ A = \langle \text{Anatomy, Pelvis, xyz} \rangle \\
LP\text{elvis} \_ A = \langle -1(\text{Pelvis} \_ A), -2(\text{Pelvis} \_ A), 3(\text{Pelvis} \_ A) \rangle
\]
where \(-1(Pelvis_A)\) is the \(x\) axis, \(-2(Pelvis_A)\) is the \(y\) axis, and \(3(Pelvis_A)\) is the \(z\) axis.

**Joint angles**

Euler angles were calculated for the hip, knee and ankle joints. These angles represent rotations of the child segment relative to the parent segment, about the origin of the parent segment:

\[
Joint\ Angle = \langle Child\ Segment,\ Parent\ Segment,\ xyz\rangle
\]

where \(xyz\) refers to the axes of the parent segment defined previously. Based on this convention, hip angles were defined by:

\[
LHip_A = \langle LThigh, Pelvis, xyz\rangle
\]

\[
RHip_A = \langle RThigh, Pelvis, xyz\rangle
\]

where \(LThigh\) and \(RThigh\) are the child segments, \(Pelvis\) is the parent segment and \(xyz\) is the order of axes. Following definition of parent and child segments, individual axes of rotations and their direction were defined:

\[
LHip_A = \langle 1(LHip_A), -2(LHip_A), 3(LHip_A)\rangle
\]

\[
RHip_A = \langle -1(RHip_A), 2(RHip_A), 3(RHip_A)\rangle
\]

where the numbers 1, 2 and 3 refer to \(x\) (internal / external rotation), \(y\) (ab / adduction) and \(z\) (flexion / extension) axes respectively. Note the \(x\) axis is positive for the left and negative for the right. This is due to the fact that when both limbs complete the same movement they move in opposing directions; for example, when both limbs internally rotate they turn to face each other. In this example, internal rotation of the left hip would be positive, while internal rotation of the right hip would be negative. These direction conventions are stated at this point in the model to ensure that angular output is comparable between limbs.

The \(y\) axis is negative for the left hip and positive for the right hip for the same reasons outlined in the above paragraph. In this case, abduction of the left hip would be
negative, while abduction of the right hip would be positive. Flexion/extension directions are the same for both left and right hips, where flexion is positive and extension is negative for the \( z \) axis.

Knee angles were defined by:

\[
L_{Knee\_A} = <L_{Shank}, L_{Thigh}, xyz>
\]
\[
R_{Knee\_A} = <R_{Shank}, R_{Thigh}, xyz>
\]

where \( L_{Shank} \) and \( R_{Shank} \) are the child segments, \( L_{Thigh} \) and \( R_{Thigh} \) are the parent segments and \( xyz \) is the order of axes. Individual axes of rotations and their direction were then defined:

\[
L_{Knee\_A} = <1(L_{Knee\_A}), -2(L_{Knee\_A}), -3(L_{Knee\_A})>
\]
\[
R_{Knee\_A} = <-1(R_{Knee\_A}), 2(R_{Knee\_A}), -3(R_{Knee\_A})>
\]

where the numbers 1, 2 and 3 refer to \( x \) (internal / external rotation), \( y \) (ab / adduction) and \( z \) (flexion / extension) axes respectively. The \( x \) axis is positive for the left knee and negative for the right knee, for the reason outlined above. In this case, internal rotation of the left knee would be positive, while internal rotation of the right knee would be negative. The \( y \) axis is negative for the left knee and positive for the right knee. In this case, abduction of the left knee would be negative, while abduction of the right knee would be positive. Flexion/extension directions are the same for both left and right knees, where flexion is negative and extension is positive for the \( z \) axis.

Ankle angles were defined by:

\[
L_{Ankle\_A} = <L_{Foot}, L_{Shank}, xyz>
\]
\[
R_{Ankle\_A} = <R_{Foot}, R_{Shank}, xyz>
\]

where \( L_{Foot} \) and \( R_{Foot} \) are the child segments, \( L_{Shank} \) and \( R_{Shank} \) are the parent segments and \( xyz \) is the order of axes. Individual axes of rotations and their direction were then defined:
\[ L\text{Ankle}_A = \langle 1(L\text{Ankle}_A), 2(L\text{Ankle}_A), 3(L\text{Ankle}_A) \rangle \]
\[ R\text{Ankle}_A = \langle -1(R\text{Ankle}_A), -2(R\text{Ankle}_A), 3(R\text{Ankle}_A) \rangle \]

where the numbers 1, 2 and 3 refer to \( x \) (inversion / eversion), \( y \) (ab / adduction) and \( z \) (dorsiflexion / plantarflexion) axes respectively. The \( x \) axis is positive for the left ankle and negative for the right ankle; the \( y \) axis is positive for the left ankle and negative for the right ankle; while the \( z \) axis is positive for both limbs.

**Kinetics**

**Reactions**

In Vicon BodyLanguage, the \textit{REACTION} function is used to combine force, moment and point of application into one expression. In the current model the \textit{REACTION} \textit{ForcePlate} was comprised of:

\[ \text{ForcePlate} = \text{ForcePlate}(1), \text{ForcePlate}(2), \text{ForcePlate}(3) \]

where \textit{ForcePlate}(1) refers to the three components of ground reaction force, \textit{ForcePlate}(2) refers to the \( x \), \( y \), and \( z \) moments, and \textit{ForcePlate}(3) refers to the \( x \), \( y \), and \( z \) point of ground reaction force application.

**Conversion of moments from Nmm to Nm**

The use of Newton-millimetres (Nmm) as the unit for the description of moments is standard in Vicon software. However since moments are most commonly reported in Newton-metres (Nm), moment data derived from the current model were converted from Nmm to Nm by dividing moment data by 1000:

\[ \text{Moment} = \text{ForcePlate}(2) / 1000 \]
Calculation of point of force application

Moments derived from ground reaction force data are measured about the centre of the force plate, which is defined in the global coordinate system relative to the origin of the system. For the current model, the origin of the global coordinate system was the corner of force plate one, and the centre of each plate expressed as a distance in millimetres (mm) relative to this point:

\[
\text{PoA} = \text{Centre} + \left\{ -\frac{\text{Moment (2)}}{\text{Force (3)}}, \frac{\text{Moment (1)}}{\text{Force (3)}}, -\text{Centre (3)} \right\}
\]

where \(x\) and \(y\) are the two coronal axes, and \(z\) is the vertical axis.

These distances are used by the model to calculate the point of force application. When nothing is on the force plate, the point of force application is equal to the force plate centre \(xyz\) positions. As soon as a set threshold of 10N is exceeded in any of the three force axes (Vicon, 2002), the point of force application is defined by:

<table>
<thead>
<tr>
<th></th>
<th>(x) distance to origin (mm)</th>
<th>(y) distance to origin (mm)</th>
<th>(z) distance to origin (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Force Plate 1</td>
<td>307.5</td>
<td>454.5</td>
<td>0</td>
</tr>
<tr>
<td>Force Plate 2</td>
<td>415</td>
<td>1214</td>
<td>0</td>
</tr>
<tr>
<td>Force Plate 3</td>
<td>415</td>
<td>1829</td>
<td>0</td>
</tr>
</tbody>
</table>

where \(x\) and \(y\) are the two coronal axes, and \(z\) is the vertical axis.
Calculation of joint reaction forces and joint moments

The calculation of joint forces requires the use of the REACTION function. The resultant joint reaction force is then normalised by dividing by the body mass of the participant, and therefore the unit of this force is N/kg:

\[ \text{LHF} = \frac{l(\text{REACTION (LThigh)})}{\text{BodyMass}} \]

where \(\text{LHF}\) refers to left hip joint reaction force; \(l\) refers to the force component of the previously-defined ForcePlate reaction; and \(\text{LThigh}\) is the segment.

The reaction function is also used to calculate joint moments, in much the same manner as for the calculation of joint reaction forces:

\[ \text{LHM} = 2(\text{REACTION (LThigh)}) \]

where \(\text{LHM}\) refers to left hip joint moment; \(2\) refers to the moment component of the previously-defined ForcePlate reaction; and \(\text{LThigh}\) is the segment. As previously described, the unit of joint moments as defined by the model is Newton metres (Nm).

Calculation of joint powers

In order to calculate joint power, Vicon BodyLanguage uses the POWER function. This function calculates the joint power based on the joint moment and its angular velocity. Angular velocity is calculated 0.04s about each frame of data for use in this calculation (Vicon, 2002). The positive or negative power flow from parent onto child is expressed in the POWER calculation:

\[ \text{LHipPower} = \frac{\text{POWER(\text{Pelvis, LThigh})}}{\text{BodyMass}} \]

where \(\text{Pelvis}\) is the parent and \(\text{LThigh}\) is the child. The resultant joint power is then divided by \(\text{BodyMass}\) in order to normalise the data to watts per kilogram, or W/kg.
Appendix 2

Centre of Pressure Calculations
Introduction

This appendix details the calculations required to determine several postural stability outcome measures, including calculation of the CoP, distance, area and non-linear measures. This appendix is an elaboration on Chapter 5 of the main thesis body.

Calculation of the CoP

CoP trajectories were calculated from filtered force data. In order to calculate CoP, the following formulae were used (Bertec force plate manual, Bertec Corporation, U.S.A.):

\[
\text{CoP}_{AP} = \frac{(-\text{height offset} \times F_x - M_y)}{F_z} + \text{global offset}
\]

\[
\text{CoP}_{ML} = \frac{(-\text{height offset} \times F_y + M_x)}{F_z} + \text{global offset}
\]

where \(F\) = force; \(M\) = moment; \(x\) = AP direction; \(y\) = ML direction; \(z\) = vertical direction; and height offset refers to the thickness of the cover of each force platform, which was 7mm for the standard surface conditions and a variable height based on the individual participant for the foam conditions. The global offset refers to an addition which was made to each CoP trajectory in each direction in order to move it from its normal origin – the centre of the force plate – to the global origin, used for all kinematic analysis. This enabled comparisons between the CoP and centre of mass (CoM), the latter also being expressed relative to the global origin.

In order to calculate net CoP (CoPNet) trajectories from the two force platforms, the following formulae were used (Termoz et al., 2007):

\[
\text{CoPNet}_{AP} = \frac{(FPa \text{CoP}_{AP} + FPb \text{CoP}_{AP})}{2}
\]

\[
\text{CoPNet}_{ML} = \frac{(FPa \text{CoP}_{ML} + FPb \text{CoP}_{ML})}{2}
\]
where CoPNet for a given direction is the mean of the two CoP trajectories from each force plate. Subsequent calculations performed on CoP data were completed for both individual force platforms as well as CoPNet. For the sake of brevity, only the CoPNet trajectory in the AP direction (or the resultant direction where appropriate) will be used in formulae examples, since formulae for the ML direction are the same.

Once CoP trajectory data was calculated, the mean of each CoP trajectory was defined by (Prieto, et al., 1996):

\[
CoPNet_{AP_{mean}} = mean(CoPNet_{AP})
\]

Once the mean CoP was calculated for each direction, the CoP trajectory data was expressed relative to the mean and temporarily labelled CoPNetAPn (Prieto, et al., 1996):

\[
CoPNet_{AP_n} = CoPNet_{AP} - CoPNet_{AP_{mean}}
\]

Finally, prior to outcome measures being calculated, CoP trajectories were normalised to foot length and expressed as a percentage:

\[
CoPNet_{AP_{relative}} = \left( \frac{CoPNet_{AP_n}}{foot\ length} \right) \times 100
\]

Once CoP trajectory data was expressed relative to the mean and normalised, CoP outcome measures were calculated using the subsequent methods.

**CoP distance measures**

Mean distance and standard deviation measures give information on the degree of postural steadiness, and are calculated with respect to the mean of the CoP trajectory (Prieto, et al., 1996):
The standard deviation of the CoP trajectory provides a measure of variability, and is determined by calculating the root mean square of the relative CoP trajectory (Prieto, et al., 1996):

\[ \text{CoPNet}_{\text{AP\_dist}} = \text{mean}(\text{CoPNet}_{\text{AP\_relative}}) \]

\[ \text{CoPNet}_{\text{AP\_SD}} = \sqrt{\text{CoPNet}_{\text{AP\_relative}}^2} \]

In addition to means and standard deviations, the total displacement of the CoP during a trial was also calculated as the sum of the differences between consecutive CoP data points (Prieto, et al., 1996):

\[ \text{CoPNet}_{\text{AP\_disp}} = \sum \text{CoPNet}_{\text{AP\_relative}}[n + 1] - \text{CoPNet}_{\text{AP\_relative}}[n] \]

where \( n \) = CoP trajectory data point.

Following the calculation of the displacement, it was possible to calculate the average velocity of the CoP during a given trial. This was achieved by dividing the displacement by the length of the trial in seconds (Prieto, et al., 1996):

\[ \text{CoPNet}_{\text{AP\_vel}} = \frac{\text{CoPNet}_{\text{AP\_disp}}}{\text{trial length}} \]

---

**Ellipse area calculations**

In addition to distance measures, CoP time-series data was also analysed using area measurement techniques, specifically the area of an ellipse encompassing a 95% confidence interval from the CoP trajectory. In order to calculate this variable the following formulae were used (L. M. Doyle & Roberts, 2006; Prieto, et al., 1996):
\[ \text{Area} = \pi ab \]

where \( a \) is the major radius and \( b \) is the minor radius, as defined by:

\[
a = \sqrt{\left[ F_{0.05[2,n-2]} \left( \text{CoPNet}_{APSD}^2 + \text{CoPNet}_{MLSD}^2 + D \right) \right]} \\
b = \sqrt{\left[ F_{0.05[2,n-2]} \left( \text{CoPNet}_{APSD}^2 + \text{CoPNet}_{MLSD}^2 - D \right) \right]}
\]

where \( F_{0.05[2,n-2]} = 3 \), the \( F \)-statistic at the 95% confidence interval, and \( D \) is defined by:

\[
D = \sqrt{(\text{CoPNet}_{APSD}^2 + \text{CoPNet}_{MLSD}^2)} \\
- \sqrt{4((\text{CoPNet}_{APSD} \times \text{CoPNet}_{MLSD})^2 - \text{CoPNet}_{APMLSD}^2)}
\]

where \( \text{CoPNet}_{APMLSD}^2 \) is the covariance, defined by:

\[
\text{CoPNet}_{APMLSD}^2 = \text{mean}(\text{CoPNet}_{AP \text{relative}} \times \text{CoPNet}_{ML \text{relative}})
\]

The above equations are simplified down to (Prieto, et al., 1996; Salavati, et al., 2009):

\[
\text{Ellipse Area} = 2\pi F_{0.05[2,n-2]} \sqrt{\text{CoPNet}_{APSD}^2 \text{CoPNet}_{MLSD}^2 - \text{CoPNet}_{APMLSD}^2}
\]

**Relationship between CoM and CoP**

In conjunction with the analysis of centre of pressure parameters, the relationship between the position of the whole body centre of mass and the centre of pressure was also...
examined. In order to compare these variables, it was first necessary to resample the centre of pressure data to match the kinematic data (100Hz). This was accomplished using the Matlab function *resample*, which effectively saves every $n$th frame of data as dictated by the user, in this case every 10th frame. Following resampling, the whole body centre of mass trajectory in the $x$ (AP) and $y$ (ML) directions were subtracted from their centre of pressure counterparts in order to calculate the CoP - CoM variable:

$$\text{CoP}_{AP}\text{CoM}_{AP}\text{Dist} = \text{CoPNet}_{AP100Hz} - \text{CoM}_{AP}$$

where $\text{CoPNet}_{AP100Hz}$ is the resampled centre of pressure data, and $\text{CoM}_{AP}$ is the position of the whole body centre of mass in the AP direction. The CoP - CoM measure is the root mean square of the $\text{CoP}_{AP}\text{CoM}_{AP}\text{Dist}$ trajectory (Hsue, et al., 2009):

$$\text{CoP}_{AP}\text{CoM}_{AP}\text{Dist}_{RMS} = \sqrt{\text{CoP}_{AP}\text{CoM}_{AP}\text{Dist}^2}$$

In order to reduce any ramping effect, the first and last 50 frames of $\text{CoP}_{AP}\text{CoM}_{AP}\text{Dist}$ were disregarded when calculating the mean in the above formula.

**Cross-correlation analyses**

Cross-correlation analyses were conducted between several related variables, including net CoP and whole body CoM as well as individual CoP trajectories and their relevant joint moments. This analysis was performed using the Matlab function *xcov*, which determines the cross-correlation coefficient between two chosen time series of the same length relative to their respective means across a user-defined number of lags. For the current study, cross-correlation coefficients were determined between the CoP and other calculated outcome measures over the course of a trial, with a separate coefficient calculated for each lag from -100 to +100 frames (-1 second to +1 second) including zero (Li & Caldwell, 1999; Termoz, et al., 2008; Winter, et al., 1996):
\[ C = \frac{(x_t - \bar{x})(y_{t+\text{lag}} - \bar{y})}{\sqrt{(x_t - \bar{x})^2 (y_t - \bar{y})^2}} \]

where \( C \) is the cross-correlation at a given lag, and \( x_t \) and \( y_t \) are the two time series being correlated.

The maximum and minimum cross-correlation coefficients were determined, as were the lags at which these maxima and minima occurred. The cross-correlation coefficients, or \( r \) values, ranged between -1 (perfect negative correlation) to 1 (perfect positive correlation). Lags were output in terms of number of frames and then subsequently converted to time in seconds.

**Methodological observation**

In a paper by Termoz et al. (2008), the authors examined postural sway during quiet standing in healthy participants and those affected by Parkinson’s disease. Two force plates were employed, from which a net CoP trajectory was calculated. The formula used for this calculation was:

\[
\text{CoPNet} = \left( \text{CoP}_{\text{left}} \times \frac{F_z_{\text{left}}}{F_{\text{left}} + F_{\text{right}}} \right) + \left( \text{CoP}_{\text{right}} \times \frac{F_z_{\text{right}}}{F_{\text{left}} + F_{\text{right}}} \right)
\]

where \( \frac{F_z_{\text{left}}}{F_{\text{left}} + F_{\text{right}}} \) and its right counterpart calculate the fraction of body weight on each side, thereby assigning weighting to each CoP trajectory depending on the ratio of loading of a given limb.

Initially, this method was employed in net CoP calculations for the current thesis; however this was discarded in favour of the average method, whereby the position of the left and right CoP trajectories were averaged to give the net CoP position. The reasoning behind
this switch in methodology was two-fold. Firstly, it was found that results for given a outcome measure became more erroneous as the separation between left and right CoP trajectories for a given direction increased. This error was profoundly evident in the ML direction, where the CoP position of the two respective trajectories was separated by at least 0.15m, but not as evident in the AP direction since the separation was never as large. Secondly, the theory behind the weighting of net CoP position based on relative limb loading needs further examination. If, for example, the position of the CoP in the ML direction were to move laterally beneath a given limb by 0.01m over a period of time, it stands to reason that since the CoP is a resultant measure of the movement of all body segments one would expect the CoM would also be moving in the direction of the lateral shift. This CoM movement would therefore alter limb loading, which would shift by a given amount onto the laterally-moving limb. The expression of the net CoP position as being the average of the left and right CoP positions is therefore reflective of the fact that the relative loading between the limbs must have shifted. By including a weighting component in the net CoP calculation based on this relative loading, one is doubly-compensating for the shift in limb loading which has additive effects to the final net CoP position. In essence, this will mean that the movement of the net CoP in a given direction will be exaggerated. The authors do not explain their reasoning for this method of net CoP calculation (Termoz, et al., 2008). Further examination of this theory could include an investigation of the relationship between shifting relative limb loading and CoP movement, but this is beyond the scope of the current thesis.
Appendix 3

Balance Results Omitted from Chapter Five
Romberg and foam ratio results

Romberg ratio results are shown in Tab. A3.1. Foam ratio results are shown in Tab. A3.2. Velocity values are omitted from tables since they were equal to those observed for CoP displacement.
Table A3.1: Romberg ratio results for standard and foam surface conditions

<table>
<thead>
<tr>
<th>Day</th>
<th>AP Direction</th>
<th>ML Direction</th>
<th>Foam Surface</th>
<th>AP Direction</th>
<th>ML Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Standard Surface</td>
<td>Foam Surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Distance</td>
<td></td>
<td></td>
<td>Displacement</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ellipse area</td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>1.4 ± 0.6</td>
<td>1.3 ± 0.6</td>
<td>1.6 ± 0.4</td>
<td>1.6 ± 0.5</td>
<td>1.7 ± 0.7</td>
</tr>
<tr>
<td>Pre-2</td>
<td>1.9 ± 1.4</td>
<td>1.7 ± 0.9</td>
<td>1.6 ± 0.4</td>
<td>1.5 ± 0.5</td>
<td>1.7 ± 0.6</td>
</tr>
<tr>
<td>Post-1</td>
<td>1.3 ± 0.3</td>
<td>1.2 ± 0.5</td>
<td>1.8 ± 0.4</td>
<td>1.5 ± 0.4</td>
<td>2.0 ± 0.6</td>
</tr>
<tr>
<td>Post-2</td>
<td>1.3 ± 0.4</td>
<td>1.2 ± 0.3</td>
<td>1.8 ± 0.4</td>
<td>1.7 ± 0.6</td>
<td>2.2 ± 0.7</td>
</tr>
<tr>
<td>Pre-1</td>
<td>1.6 ± 0.4</td>
<td>1.1 ± 0.1</td>
<td>1.7 ± 0.7</td>
<td>1.4 ± 0.5</td>
<td>1.9 ± 0.9</td>
</tr>
<tr>
<td>Pre-2</td>
<td>1.8 ± 0.6</td>
<td>1.2 ± 0.3</td>
<td>1.7 ± 0.6</td>
<td>1.4 ± 0.3</td>
<td>2.3 ± 1.0</td>
</tr>
<tr>
<td>Post-1</td>
<td>1.6 ± 0.3</td>
<td>1.1 ± 0.3</td>
<td>2.6 ± 1.0</td>
<td>0.3 ± 1.1</td>
<td>2.7 ± 0.9</td>
</tr>
<tr>
<td>Post-2</td>
<td>1.8 ± 0.3</td>
<td>0.1 ± 0.6</td>
<td>2.3 ± 1.0</td>
<td>0.5 ± 1.9</td>
<td>0.40</td>
</tr>
</tbody>
</table>

Notes: All values are presented as mean ± standard deviation. All p-values are presented as mean ± standard deviation.
Table A3.2: Foam ratio results for eyes open and eyes closed

<table>
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<tr>
<th>Day</th>
<th>AP Direction</th>
<th>Eyes Open</th>
<th>ML Direction</th>
<th>Eyes Closed</th>
<th>ML Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day</td>
<td>Avg</td>
<td>Avg Δ</td>
<td>p</td>
<td>Avg</td>
</tr>
<tr>
<td>Distance</td>
<td>Pre-1</td>
<td>2.1 ± 0.5</td>
<td>-</td>
<td>-</td>
<td>2.3 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>2.4 ± 0.9</td>
<td>0.4 ± 0.6</td>
<td>0.12</td>
<td>2.5 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>1.9 ± 0.5</td>
<td>-0.5 ± 0.7</td>
<td>0.07</td>
<td>2.7 ± 1.1</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>1.7 ± 0.6</td>
<td>-0.3 ± 0.3</td>
<td>0.07</td>
<td>1.8 ± 0.6</td>
</tr>
<tr>
<td>Displacement</td>
<td>Pre-1</td>
<td>2.5 ± 0.3</td>
<td>-</td>
<td>-</td>
<td>1.7 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>2.4 ± 0.6</td>
<td>-0.1 ± 0.4</td>
<td>0.78</td>
<td>1.7 ± 0.5</td>
</tr>
<tr>
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<td>Post-1</td>
<td>2.1 ± 0.5</td>
<td>-0.3 ± 0.6</td>
<td>0.16</td>
<td>1.8 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>2.0 ± 0.4</td>
<td>-0.2 ± 0.6</td>
<td>0.46</td>
<td>1.4 ± 0.4</td>
</tr>
<tr>
<td>Ellipse area</td>
<td>Pre-1</td>
<td>5.2 ± 2.1</td>
<td>-</td>
<td>-</td>
<td>5.2 ± 1.8</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>6.2 ± 3.1</td>
<td>0.9 ± 1.8</td>
<td>0.21</td>
<td>9.2 ± 7.0</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>5.2 ± 2.9</td>
<td>-1.0 ± 3.0</td>
<td>0.48</td>
<td>7.8 ± 3.5</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>3.6 ± 2.2</td>
<td>-2.2 ± 1.6</td>
<td>0.03</td>
<td>5.8 ± 3.3</td>
</tr>
</tbody>
</table>
Cross-correlation results

Cross-correlation and latency results between hip I/E moment vs. ML CoP movement, hip Abd/Add moment vs. ML CoP movement, hip F/E moment vs. AP CoP movement, knee F/E moment vs. AP CoP movement, ankle I/E moment vs. ML CoP movement and ankle F/E moment vs. AP CoP movement are shown in Tabs. A3.3 – A3.8.
Table A3.3: Cross-correlation and latency between hip I/E rotation moment and ML CoP movement

<table>
<thead>
<tr>
<th></th>
<th>Dominant Limb</th>
<th>Non-Dominant Limb</th>
<th></th>
<th>Dominant Limb</th>
<th>Non-Dominant Limb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avg (r)</td>
<td>Avg Δ</td>
<td>p</td>
<td>Avg (r)</td>
<td>Avg Δ</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SS</td>
<td>Pre-1</td>
<td>0.48 ± 0.40</td>
<td>-</td>
<td>-0.49 ± 0.24</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>0.54 ± 0.27</td>
<td>0.78</td>
<td>-0.42 ± 0.31</td>
<td>0.07 ± 0.24</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.61 ± 0.33</td>
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<td>-0.42 ± 0.34</td>
<td>0.00 ± 0.30</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.44 ± 0.39</td>
<td>-0.14 ± 0.31</td>
<td>0.46</td>
<td>-0.34 ± 0.21</td>
</tr>
<tr>
<td>SSEC</td>
<td>Pre-1</td>
<td>0.50 ± 0.39</td>
<td>-</td>
<td>-0.43 ± 0.25</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>0.58 ± 0.30</td>
<td>0.08 ± 0.38</td>
<td>0.67</td>
<td>-0.46 ± 0.29</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
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<td>0.06 ± 0.24</td>
<td>0.33</td>
<td>-0.48 ± 0.29</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.53 ± 0.40</td>
<td>-0.01 ± 0.24</td>
<td>0.75</td>
<td>-0.34 ± 0.24</td>
</tr>
<tr>
<td>FS</td>
<td>Pre-1</td>
<td>0.39 ± 0.21</td>
<td>-</td>
<td>-0.29 ± 0.24</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>0.48 ± 0.24</td>
<td>0.09 ± 0.08</td>
<td>0.04</td>
<td>-0.35 ± 0.23</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.43 ± 0.33</td>
<td>-0.05 ± 0.18</td>
<td>0.48</td>
<td>-0.35 ± 0.29</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.36 ± 0.28</td>
<td>0.10 ± 0.20</td>
<td>0.46</td>
<td>-0.23 ± 0.22</td>
</tr>
<tr>
<td>FSEC</td>
<td>Pre-1</td>
<td>0.42 ± 0.26</td>
<td>-</td>
<td>-0.35 ± 0.17</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>0.43 ± 0.26</td>
<td>0.01 ± 0.12</td>
<td>1.00</td>
<td>-0.37 ± 0.25</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.44 ± 0.33</td>
<td>0.02 ± 0.16</td>
<td>0.78</td>
<td>-0.32 ± 0.26</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.32 ± 0.32</td>
<td>0.00 ± 0.11</td>
<td>0.92</td>
<td>-0.31 ± 0.22</td>
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</table>
Table A3.4: Cross-correlation and latency between hip Abd/Add moment and ML CoP movement

<table>
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<th>Day</th>
<th>Dominant Limb</th>
<th>Non-Dominant Limb</th>
<th>Dominant Limb</th>
<th>Non-Dominant Limb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avg (r)</td>
<td>Avg Δ</td>
<td>p</td>
<td>Avg (r)</td>
</tr>
<tr>
<td>SS</td>
<td>Pre-1</td>
<td>0.30 ± 0.29</td>
<td>-</td>
<td>-0.23 ± 0.35</td>
</tr>
<tr>
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<td>Pre-2</td>
<td>0.28 ± 0.23</td>
<td>-0.02 ± 0.27</td>
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</tr>
<tr>
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<td>Post-1</td>
<td>0.26 ± 0.32</td>
<td>-0.02 ± 0.25</td>
<td>0.89</td>
</tr>
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<td>Post-2</td>
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<td>0.11 ± 0.20</td>
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</tr>
<tr>
<td>SSEC</td>
<td>Pre-1</td>
<td>0.25 ± 0.19</td>
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<td>-0.34 ± 0.27</td>
</tr>
<tr>
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<td>Pre-2</td>
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<td>0.09 ± 0.29</td>
<td>0.26</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.39 ± 0.27</td>
<td>0.04 ± 0.20</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.24 ± 0.23</td>
<td>-0.06 ± 0.27</td>
<td>0.92</td>
</tr>
<tr>
<td>FS</td>
<td>Pre-1</td>
<td>0.31 ± 0.24</td>
<td>-</td>
<td>-0.30 ± 0.27</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>0.26 ± 0.29</td>
<td>-0.04 ± 0.26</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.33 ± 0.17</td>
<td>0.07 ± 0.19</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.18 ± 0.21</td>
<td>-0.08 ± 0.24</td>
<td>0.46</td>
</tr>
<tr>
<td>FSEC</td>
<td>Pre-1</td>
<td>0.32 ± 0.25</td>
<td>-</td>
<td>-0.39 ± 0.21</td>
</tr>
<tr>
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<td>Pre-2</td>
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<td>0.06 ± 0.25</td>
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</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.39 ± 0.23</td>
<td>0.01 ± 0.23</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.31 ± 0.31</td>
<td>-0.02 ± 0.18</td>
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</table>
Table A3.5: Cross-correlation and latency between hip F/E moment and AP CoP movement

<table>
<thead>
<tr>
<th>Day</th>
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<th>Latency</th>
<th>Non-Dominant Limb</th>
<th>Dominant Limb</th>
<th>Non-Dominant Limb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dominant Limb</td>
<td></td>
<td>Non-Dominant Limb</td>
<td>Dominant Limb</td>
<td>Non-Dominant Limb</td>
</tr>
<tr>
<td></td>
<td>Avg (r) Avg Δ p</td>
<td>Avg (r) Avg Δ p</td>
<td>Avg (s) Avg Δ p</td>
<td>Avg (s) Avg Δ p</td>
<td>Avg (s) Avg Δ p</td>
</tr>
<tr>
<td>SS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>-0.71 ± 0.11</td>
<td>-</td>
<td>-0.54 ± 0.30</td>
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<td>-</td>
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<tr>
<td>Pre-2</td>
<td>-0.56 ± 0.18</td>
<td>0.15 ± 0.21</td>
<td>-0.47 ± 0.33</td>
<td>0.06 ± 0.18</td>
<td>1.00</td>
</tr>
<tr>
<td>Post-1</td>
<td>-0.59 ± 0.24</td>
<td>-0.03 ± 0.21</td>
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<td>-0.56 ± 0.28</td>
<td>-0.08 ± 0.35</td>
</tr>
<tr>
<td>Post-2</td>
<td>-0.61 ± 0.18</td>
<td>0.05 ± 0.27</td>
<td>0.75</td>
<td>-0.59 ± 0.25</td>
<td>-0.13 ± 0.32</td>
</tr>
<tr>
<td>SSEC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>-0.73 ± 0.15</td>
<td>-</td>
<td>-0.57 ± 0.26</td>
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<td>-</td>
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<tr>
<td>Pre-2</td>
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<td>0.23 ± 0.21</td>
<td>0.03</td>
<td>-0.55 ± 0.27</td>
<td>0.02 ± 0.17</td>
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<tr>
<td>Post-1</td>
<td>-0.68 ± 0.18</td>
<td>-0.18 ± 0.20</td>
<td>0.05</td>
<td>-0.56 ± 0.25</td>
<td>-0.01 ± 0.13</td>
</tr>
<tr>
<td>Post-2</td>
<td>-0.66 ± 0.13</td>
<td>0.09 ± 0.21</td>
<td>0.46</td>
<td>-0.42 ± 0.24</td>
<td>0.06 ± 0.35</td>
</tr>
<tr>
<td>FS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-1</td>
<td>-0.68 ± 0.11</td>
<td>-</td>
<td>-0.59 ± 0.19</td>
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</tr>
<tr>
<td>Pre-2</td>
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<td>0.07 ± 0.13</td>
<td>0.21</td>
<td>-0.54 ± 0.23</td>
<td>0.05 ± 0.28</td>
</tr>
<tr>
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<td>-0.12 ± 0.15</td>
<td>0.07</td>
<td>-0.64 ± 0.21</td>
<td>-0.10 ± 0.26</td>
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<td>0.25</td>
<td>-0.60 ± 0.16</td>
<td>0.04 ± 0.27</td>
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<tr>
<td>FSEC</td>
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<td></td>
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<tr>
<td>Pre-1</td>
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<td>-0.60 ± 0.21</td>
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<td>0.05 ± 0.14</td>
<td>0.40</td>
<td>-0.56 ± 0.17</td>
<td>0.04 ± 0.22</td>
</tr>
<tr>
<td>Post-1</td>
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<td>-0.01 ± 0.18</td>
<td>0.58</td>
<td>-0.65 ± 0.17</td>
<td>-0.09 ± 0.20</td>
</tr>
<tr>
<td>Post-2</td>
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<td>-0.06 ± 0.15</td>
<td>0.46</td>
<td>-0.67 ± 0.17</td>
<td>-0.04 ± 0.12</td>
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</tbody>
</table>

260
Table A3.6: Cross-correlation and latency between knee F/E moment and AP CoP movement

<table>
<thead>
<tr>
<th>Day</th>
<th>Dominant Limb</th>
<th>Non-Dominant Limb</th>
<th>Dominant Limb</th>
<th>Latency</th>
<th>Non-Dominant Limb</th>
</tr>
</thead>
<tbody>
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<td></td>
<td>Cross-Correlation</td>
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<td></td>
<td></td>
<td>Latency</td>
</tr>
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<td>Avg (r)</td>
<td>Avg Δ</td>
<td>p</td>
<td>Avg (r)</td>
<td>Avg Δ</td>
</tr>
<tr>
<td>SS</td>
<td>Pre-1</td>
<td>0.96 ± 0.02</td>
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<td>-</td>
<td>0.90 ± 0.09</td>
</tr>
<tr>
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<td>Pre-2</td>
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<td>0.12</td>
<td>0.82 ± 0.28</td>
</tr>
<tr>
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<td>Post-1</td>
<td>0.96 ± 0.02</td>
<td>0.04 ± 0.09</td>
<td>0.16</td>
<td>0.90 ± 0.14</td>
</tr>
<tr>
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<td>Post-2</td>
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<td>-0.07 ± 0.10</td>
<td>0.03</td>
<td>0.92 ± 0.04</td>
</tr>
<tr>
<td>SSEC</td>
<td>Pre-1</td>
<td>0.94 ± 0.05</td>
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<td>-</td>
<td>0.94 ± 0.04</td>
</tr>
<tr>
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<td>Pre-2</td>
<td>0.92 ± 0.04</td>
<td>-0.02 ± 0.08</td>
<td>0.40</td>
<td>0.89 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.97 ± 0.01</td>
<td>0.05 ± 0.04</td>
<td>0.03</td>
<td>0.91 ± 0.15</td>
</tr>
<tr>
<td></td>
<td>Post-2</td>
<td>0.95 ± 0.04</td>
<td>-0.02 ± 0.05</td>
<td>0.46</td>
<td>0.92 ± 0.07</td>
</tr>
<tr>
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<tr>
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<td>0.07 ± 0.08</td>
<td>0.02</td>
<td>0.91 ± 0.04</td>
</tr>
<tr>
<td></td>
<td>Post-1</td>
<td>0.90 ± 0.05</td>
<td>-0.02 ± 0.07</td>
<td>0.40</td>
<td>0.91 ± 0.07</td>
</tr>
<tr>
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<td>Post-2</td>
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<td>0.01 ± 0.07</td>
<td>0.92</td>
<td>0.91 ± 0.06</td>
</tr>
<tr>
<td>FSEC</td>
<td>Pre-1</td>
<td>0.92 ± 0.04</td>
<td>-</td>
<td>-</td>
<td>0.89 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>Pre-2</td>
<td>0.91 ± 0.04</td>
<td>0.00 ± 0.06</td>
<td>0.89</td>
<td>0.90 ± 0.05</td>
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<tr>
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Table A3.7: Cross-correlation and latency between ankle I/E moment and ML CoP movement

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<td>p</td>
<td>Avg (r)</td>
<td>Avg Δ</td>
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Table A3.8: Cross-correlation and latency between ankle F/E moment and AP CoP movement

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<td>Avg Δ</td>
<td>p</td>
<td>Avg (r)</td>
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<td>-0.96 ± 0.04</td>
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<td>-0.97 ± 0.03</td>
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<td>-0.98 ± 0.01</td>
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<td>-</td>
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<td>-0.96 ± 0.03</td>
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</tr>
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<td>-0.90 ± 0.03</td>
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Appendix 4

Gait Results Omitted from Chapter Six
Range of movement results

Range of movement results for the trunk, pelvis, hip, knee and ankle are exhibited in Tabs. A4.1 – A4.4.
Table A4.1: Trunk and pelvis range of movement during gait

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<td>Pre-2</td>
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<tr>
<td>Post-1</td>
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<td>0 ± 2</td>
</tr>
<tr>
<td>Post-2</td>
<td>8 ± 2</td>
<td>0 ± 1</td>
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<td>-1 ± 1</td>
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<tr>
<td>Post-1</td>
<td>5 ± 2</td>
<td>0 ± 1</td>
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<tr>
<td>Post-2</td>
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<tr>
<td>Pre-2</td>
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<td>0 ± 1</td>
</tr>
<tr>
<td>Post-1</td>
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<td>0 ± 0</td>
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Table A4.2: Hip range of movement during gait

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<th>p</th>
<th>Avg (°)</th>
<th>Avg Δ</th>
<th>p</th>
<th>CoV (%)</th>
<th>p</th>
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<td><strong>Non-Dominant Limb</strong></td>
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<tr>
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<td>-</td>
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<td>13 ± 8</td>
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<td>13 ± 4</td>
<td>-</td>
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<td>17 ± 7</td>
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</tr>
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<td>14 ± 3</td>
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<td>12 ± 8</td>
<td>0.40</td>
<td>13 ± 4</td>
<td>0 ± 3</td>
<td>0.67</td>
<td>13 ± 7</td>
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<td>17 ± 12</td>
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<tr>
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Table A4.3: Knee range of movement during gait

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<th>CoV (%)</th>
<th>p</th>
<th>Avg (°)</th>
<th>Avg Δ</th>
<th>CoV (%)</th>
<th>p</th>
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<tr>
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<td>11 ± 11</td>
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<td>17 ± 4</td>
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<td>14 ± 7</td>
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<tr>
<td>Pre-2</td>
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<td>-1 ± 3</td>
<td>14 ± 7</td>
<td>0.40</td>
<td>17 ± 6</td>
<td>0 ± 3</td>
<td>16 ± 12</td>
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<tr>
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<td>16 ± 12</td>
<td>0.67</td>
<td>16 ± 5</td>
<td>-1 ± 4</td>
<td>9 ± 4</td>
<td>0.16</td>
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<td>9 ± 10</td>
<td>0.75</td>
<td>18 ± 5</td>
<td>1 ± 3</td>
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<td>3 ± 7</td>
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<td>1 ± 3</td>
<td>9 ± 3</td>
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<td>-2 ± 5</td>
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<tr>
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<td>18 ± 12</td>
<td>0.17</td>
<td>12 ± 5</td>
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<tr>
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<td>67 ± 6</td>
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<td>0.35</td>
<td>69 ± 7</td>
<td>0 ± 4</td>
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### Table A4.4: Ankle range of movement during gait

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<th>Dominant Limb</th>
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<td>Avg Δ</td>
<td>CoV (%)</td>
</tr>
<tr>
<td>Pre-1</td>
<td>18 ± 6</td>
<td>-</td>
<td>12 ± 7</td>
</tr>
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<td>Post-2</td>
<td>26 ± 7</td>
<td>0 ± 4</td>
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Joint moment results

Peak joint moment values and the timing of their occurrence for the hip, knee and ankle joints are shown in Tabs. A4.5 – A4.10. Peak joint powers and the timing of their occurrence for the hip, knee and ankle joints are show in Tabs. A4.11 – A4.12.
Table A4.5: Peak hip moment during stance phase of gait

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<td>Day</td>
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<tr>
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<td>Avg (Nm/kg)</td>
<td>Avg Δ</td>
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<tr>
<td>Internal Rotation</td>
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<td>External Rotation</td>
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</tr>
<tr>
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<td>Pre-2</td>
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<td>0.01 ± 0.04</td>
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<tr>
<td>Post-2</td>
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<td>0.02 ± 0.09</td>
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<td>Post-2</td>
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<td>Flexion</td>
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<td>Pre-2</td>
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Table A4.6: Timing of peak hip moment during stance phase of gait

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<th>CoV (%)</th>
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<td>p</td>
<td>Avg (% Stance)</td>
<td>Avg Δ</td>
<td>p</td>
<td>Avg (% Stance)</td>
<td>Avg Δ</td>
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<td>79 ± 17</td>
<td>10 ± 23</td>
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<td>66 ± 25</td>
<td>-13 ± 18</td>
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<td>67 ± 19</td>
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<td>41 ± 20</td>
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<td>1 ± 4</td>
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<td>1 ± 2</td>
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<td>1 ± 3</td>
<td>0.35</td>
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<td>0.08</td>
<td>4 ± 1</td>
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<td>-</td>
<td>-</td>
<td>2 ± 1</td>
<td>-</td>
<td>83 ± 2</td>
<td>-</td>
<td>-</td>
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<tr>
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<td>-1 ± 1</td>
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<td>1 ± 1</td>
<td>0.48</td>
<td>83 ± 2</td>
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<td>84 ± 1</td>
<td>0 ± 2</td>
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Table A4.7: Peak knee moment during stance phase of gait

|       | Day | Dominant Limb | | | | | | Non-Dominant Limb | | | |
|-------|-----|---------------|---|---|---|---|---|---|---|---|---|---|
|       |     | Avg (Nm/kg)   | Avg Δ | p | CoV (%) | p | Avg (Nm/kg) | Avg Δ | p | CoV (%) | p |
| Abduction |     |               |       |   |        |   |             |       |   |        |   |
| Pre-1 | 0.09 ± 0.08 | - | - | -149 ± 534 | - | 0.08 ± 0.07 | - | - | 56 ± 46 | - |
| Pre-2 | 0.09 ± 0.08 | 0.00 ± 0.05 | 1.00 | 54 ± 32 | 0.07 | 0.05 ± 0.03 | -0.03 ± 0.07 | 0.48 | 40 ± 28 | 0.67 |
| Post-1 | 0.15 ± 0.12 | 0.06 ± 0.05 | 0.03 | 56 ± 56 | 0.58 | 0.12 ± 0.10 | 0.06 ± 0.09 | 0.05 | 47 ± 47 | 0.78 |
| Post-2 | 0.11 ± 0.11 | -0.07 ± 0.04 | 0.03 | 74 ± 106 | 0.75 | 0.08 ± 0.04 | -0.05 ± 0.07 | 0.03 | 42 ± 41 | 0.75 |
| Adduction |     |               |       |   |        |   |             |       |   |        |   |
| Pre-1 | -0.26 ± 0.11 | - | - | -21 ± 14 | - | -0.35 ± 0.18 | - | - | -23 ± 13 | - |
| Pre-2 | -0.34 ± 0.15 | -0.09 ± 0.13 | 0.07 | -20 ± 9 | 0.89 | -0.37 ± 0.16 | -0.02 ± 0.06 | 0.67 | -9 ± 6 | 0.07 |
| Post-1 | -0.24 ± 0.18 | 0.11 ± 0.07 | 0.01 | -61 ± 112 | 0.40 | -0.28 ± 0.16 | 0.08 ± 0.05 | 0.01 | -17 ± 12 | 0.12 |
| Post-2 | -0.32 ± 0.16 | -0.09 ± 0.09 | 0.05 | -18 ± 19 | 0.35 | -0.40 ± 0.18 | -0.08 ± 0.04 | 0.03 | -20 ± 14 | 0.60 |
| Flexion |     |               |       |   |        |   |             |       |   |        |   |
| Pre-1 | 0.19 ± 0.08 | - | - | 23 ± 17 | - | 0.20 ± 0.09 | - | - | 27 ± 17 | - |
| Pre-2 | 0.20 ± 0.10 | 0.02 ± 0.09 | 0.21 | 18 ± 13 | 0.58 | 0.23 ± 0.12 | 0.02 ± 0.08 | 0.58 | 18 ± 6 | 0.21 |
| Post-1 | 0.18 ± 0.07 | -0.02 ± 0.07 | 0.21 | 18 ± 13 | 0.89 | 0.28 ± 0.12 | 0.05 ± 0.09 | 0.09 | 12 ± 6 | 0.12 |
| Post-2 | 0.22 ± 0.08 | 0.01 ± 0.04 | 0.60 | 20 ± 7 | 0.92 | 0.23 ± 0.14 | -0.08 ± 0.11 | 0.17 | 31 ± 19 | 0.12 |
| Extension |     |               |       |   |        |   |             |       |   |        |   |
| Pre-1 | -0.49 ± 0.18 | - | - | -16 ± 15 | - | -0.50 ± 0.16 | - | - | -16 ± 13 | - |
| Pre-2 | -0.53 ± 0.26 | -0.04 ± 0.18 | 1.00 | -20 ± 16 | 0.40 | -0.50 ± 0.14 | 0.00 ± 0.13 | 1.00 | -12 ± 6 | 0.48 |
| Post-1 | -0.59 ± 0.27 | -0.07 ± 0.09 | 0.12 | -13 ± 8 | 0.21 | -0.47 ± 0.21 | 0.04 ± 0.18 | 0.58 | -27 ± 36 | 0.07 |
| Post-2 | -0.56 ± 0.19 | 0.07 ± 0.22 | 0.46 | -14 ± 9 | 0.92 | -0.54 ± 0.22 | -0.10 ± 0.22 | 0.25 | -21 ± 7 | 0.92 |
### Table A4.8: Timing of peak knee moment during stance phase of gait

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<td>Avg Δ</td>
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<td>7 ± 21</td>
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<td>Post-2</td>
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<td>2 ± 22</td>
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<td>Flexion</td>
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<tr>
<td>Pre-2</td>
<td>16 ± 19</td>
<td>-15 ± 29</td>
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<td>27 ± 25</td>
<td>11 ± 27</td>
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<td>3 ± 11</td>
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<td>Pre-2</td>
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<td>3 ± 18</td>
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<td>Post-1</td>
<td>27 ± 8</td>
<td>-12 ± 17</td>
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Table A4.9: Peak ankle moment during stance phase of gait

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</tr>
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<td>Inversion</td>
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<td>-</td>
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<tr>
<td>Pre-2</td>
<td>-0.09 ± 0.05</td>
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</tr>
<tr>
<td>Post-1</td>
<td>-0.10 ± 0.04</td>
<td>-0.01 ± 0.04</td>
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<tr>
<td>Post-2</td>
<td>-0.06 ± 0.06</td>
<td>0.04 ± 0.05</td>
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<tr>
<td>Post-1</td>
<td>0.20 ± 0.11</td>
<td>-0.08 ± 0.13</td>
</tr>
<tr>
<td>Post-2</td>
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Table A4.10: Timing of peak ankle moment during stance phase of gait

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276
Table A4.11: Peak joint powers during stance phase of gait

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Table A4.12: Timing of peak joint powers during stance phase of gait

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<td>1 ± 1</td>
<td>0.12</td>
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Appendix 5

Monofilament Protocol Sheet
### Foot Sensitivity Assessment for Exercise Intervention Study

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**The modified 4,2,1, Algorithm according to Dyck for sensory threshold testing**

- Semmes-Weinstein Monofilaments are available in 20 different grades (1.65-6.65). According to Dyck one begins with an intermediate filament strength (4.56).
- If the filament is sensed a filament 4 levels below the first one is used. (Otherwise, the fourth higher filament is used) When a turning point is reached two steps are taken back until the next turning point is reached. Then only one step is used to find the third turning point that will define the sensory threshold.
- Each monofilament will be applied 10 times with 7 real and 3 zero- or placebo-stimuli in random order (grey boxes). As soon as more than 20% of the stimuli are falsely recognized (3 mistakes) the next filament has to be used.
Appendix 6

Participant Information Sheet and Consent Form
Ethical approval

Ethical approval was sought and obtained from the Ministry of Health Northern-X ethics committee (study # NTX/07/11/116). In addition, since clinicians from Counties-Manukau District Health Board (CMDHB) were assisting with participant recruitment, ethical approval was also sought and obtained from the CMDHB research office. The participant information sheet and consent forms for this study are presented below.
Participant Information Sheet

**Project title:** The effect of an exercise and footwear intervention on the symptoms of diabetic neuropathy

**Principal Investigator:** Jason Gurney  
Department of Sport and Exercise Science  
Tamaki Campus  
University of Auckland  
Telephone 373 7599 ext. 82560

You are invited to participate in the above named research project, which is being conducted by Jason Gurney, a PhD candidate at the University of Auckland. He has been involved in researching diabetic foot complications and educating community groups on this topic since 2003.

A major complication of diabetes is the loss of sensation under the foot, known as **neuropathy**, which causes a diabetic to lose the ability to sense potentially tissue-damaging loads under the foot during walking.

The purpose this research project is to investigate whether an exercise and footwear intervention might be able to improve the symptoms related to diabetic neuropathy, and as a result of this reduce ulceration risk. This will be accomplished by the following:

- Taking a sample of diabetics who suffer from neuropathy and dividing them into two groups, both of whom will receive a 12-week **exercise intervention**.
- During this intervention, one group will receive a standard **footwear intervention** and the other a more specific footwear intervention which has been shown to improve the function of lower-leg muscles.

The study will follow the following timeline:

Baseline Measures #1  
Baseline Measures #2  
Finish Exercise Programme  
Final Testing

Start Exercise Programme  
Post-Programme Testing

In total, your participation will include:

- 4 biomechanical testing sessions;
- 24 supervised exercise sessions;

In total we wish to include over 50 diabetic participants. For the intervention, each participant will act as their own ‘control’ group. In order to assess equipment reliability, non-diabetic participants with normal lower limb function are also required.
Participant Eligibility and Recruitment

In order to assess equipment reliability, non-diabetic participants with normal lower limb function are required. For the intervention, all persons who have type I or II diabetes with diabetes duration of over five years and who haven’t developed any ulceration or have had ulcerations under either the forefoot or the heel, which have fully healed. Each participant must be diagnosed as having sensory neuropathy, as shown by an inability to sense the 5.07 Semmes-Weinstein monofilament anywhere on the sole of the foot.

Persons should not have or be

- any kind of acute or not fully healed foot ulceration
- pain during or following walking
- rheumatoid arthritis
- a partial or full amputation of the lower extremity
- a fracture of the lower extremity within the last 2 years
- a severe ankle or knee injury within the last 3 years
- severe abnormalities of leg anatomy
- your eyesight having significantly decreased recently
- pregnant for a period of more than 4 months, since pregnancy at a later stage could affect gait.

Some of these points can be answered easily. If you’re interested but don’t feel sure if you fulfil the criteria please check with us.

Participants will be recruited by the Principal Investigator, with assistance from Counties Manukau DHB diabetes nurses and doctors.

If you require an interpreter please let the researcher know as soon as possible. We will provide an interpreter if you require one.

Procedures – Exercise Programme

*Participants will have two weekly sessions of low-impact supervised exercise at a convenient time and place of their choosing.*

Some key points about the exercise programme:

- The exercise programme will last for 12 weeks.
- The programme will be suited to each participant
  - Therefore the exercise you complete will be within your physical capabilities to ensure safety and effectiveness of the programme
  - Your physical capabilities will be assessed by experienced exercise rehabilitation staff
- Exercise sessions will consist of low-impact strength and balance exercises – again at intensities within your physical capabilities
- You are free to leave the study at any time if you feel you are unable to participate for any reason
Procedures – Biomechanical Testing

Your agreement to have all the procedures used in this project performed on you will be obtained in writing on a Consent Form. The project will be conducted in the Gait Laboratory (Room 178) located on the ground floor of Building 750 at the Tamaki Campus, Opposite the Unisports Centre, University of Auckland, St. Johns.

Prior to data collection, your body condition will be checked for any particular features which might exclude you from participation.

To investigate the effect of the exercise and footwear intervention, several tests will be performed:

- We will take a number of foot prints and barefoot walking impressions using a pressure-sensitive platform;
- We will conduct a 3-D analysis during barefoot walking, while you perform a number of walking trials at a self-selected or predetermined pace;
- We will conduct an ankle perturbation test, where your foot and ankle will be moved very slightly (20°) at a high speed using a specific ankle perturbation device;
- We will measure muscle and nerve activity using electromyography techniques, both during walking and during the ankle perturbation test;
- We will assess the soft tissue under your foot using ultrasound and similar techniques;
- We will also assess blood records in order to monitor changes in blood proteins as a result of the exercise programme;
- We will assess ankle muscle strength, where you will move your ankle up and down at a controlled speed and we will measure the strength which you produce;
- We will assess sensation threshold on the bottom surface of your foot, using filaments made from nylon. These will be pressed to the bottom surface of your foot and you will be asked if you can sense them;
- We will assess quality of life, using a questionnaire, which you will fill out during each biomechanical testing session.

No invasive techniques will be applied. The time needed for the total examination will be not longer than 1.5 hours.

You will be allowed to stop for a break at any stage during the testing if you need to. Food and drinks, including diabetic-appropriate foods as recommended by Diabetes New Zealand, will be made available for you. Further details will be provided by the Principal Investigator.
Reimbursement of Costs

- As a participant you have a right to claim any **transport costs** incurred by your participation in biomechanical testing sessions.
  - The Principal Investigator should be contacted if transport is required to any biomechanical testing sessions.
- **Parking** at the Unisports Centre, University of Auckland Tamaki Campus is free of charge.
- The Principal Investigator does not offer any other financial assistance to participants of this study.

Use of Data

- Your participation in this study is very helpful for the progression of scientific research in the area of diabetes. All data collected during this research will be analysed and published as part of a PhD thesis written by the Principal Investigator, as well as research articles published in international peer-reviewed scientific journals.
- All research conducted using data obtained by participants in this study will involve the Principal Investigator, and no transfer of data to any other research group will occur.
- The data will be stored on personal computers in a locked office, as well as in a locked filing cabinet, for a period of 10 years.
- At any point during or following the study, data collected from you during the study can be destroyed at your request.

Benefits, risks and safety

- With partaking in this study you will receive a comprehensive diagnosis of your foot and lower-limb function with regard to the effects of your diabetic neuropathy on them.
- We will provide you with detailed information about possible changes in foot shape and risk factors you might be exposed to. This information can be extremely valuable for your future foot care. If you have a podiatrist, in the event that we identify areas with high loading we will inform them in writing about this so the fit of your shoes can be further improved.

Below are some possible adverse effects you may experience as a result of participation in this study:

- Ulceration or re-ulceration as a result of increased physical activity
- Participation may increase risk of cardiovascular injury as a result of increased physical activity
- Other physical injuries, such as muscle strains or joint sprains, may occur during physical activity
- Increases in physical activity may cause other negative side-effects, such as dizziness and tiredness
In order to minimize your risk of experiencing the above adverse effects, the following steps will be taken by the research team:

- Weekly foot assessments by the Principal Investigator
- Weekly supervised exercise sessions with the Principal Investigator to ensure correct and safe technique and exercise intensity levels
- During supervised exercise sessions and biomechanical measurement sessions there will always be a staff member present who is trained and certified in first-aid
- If dizziness or other negative side-effect are experienced at any point during the exercise programme the participant will be free to stop training and, if desired, discontinue their participation in the study

**Right to Withdraw**

If at any point you wish to withdraw from the study for any reason, you are free to do so. This withdrawal will at no point affect your continuing or future health care. Collected data (if any) will be destroyed at your request.

**Accident Compensation**

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act.

If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

Should you have any questions about ACC, contact your nearest ACC office: freephone 0800 735 566, the ACC website www.acc.co.nz/claimscare/making-a-claim/medicalmisadventure/index.html or the investigator.

**Your Rights**

- Your participation is entirely voluntary. You do not have to take part in this study, and if you choose not to take part this will not affect any future care or treatment.
- If you do agree to take part you are free to withdraw from the study at any time, without having to give a reason and this will not affect your continuing or future health care.
- You may have your data withdrawn from the study within three months of data collection. The removal of data can be achieved by
contacting Jason Gurney at the University of Auckland, Department of Sport and Exercise Science.

- You may obtain results regarding the outcome of the project from the experimenters upon completion of the study.
- You will be required to provide your informed consent by signing a Consent Form.
- Your identity will be kept strictly confidential. Since the data obtained in the current study might assist in the future treatment of your diabetes we will store it including your name. Your identity will be strictly omitted in subsequent publication of the research findings.
- Discomfort and incapacity has not been reported from any of the procedures that will be used in this project, however, if the procedures cause you concern, you may withdraw from the project at any stage.

If you have any queries or concerns regarding your rights as a participant in this research study, you can contact an independent Health and Disability Advocate. This is a free service provided under the Health and Disability Commissioner Act:

- Telephone (NZ wide): 0800 555 050
- Free Fax (NZ wide): 0800 2787 7678 (0800 2 SUPPORT)
- Email: advocacy@hdc.org.nz

If you would like to participate in this research project or if you have any questions about the project, please contact Mr. Jason Gurney at the address/phone number provided below:

Mr Jason Gurney  
Department of Sport and Exercise Science  
Room 178A, Building 750A, University of Auckland Tamaki Campus  
Telephone 373 7599 extn 82560

The Head of Department is:

Dr Heather Smith  
Department of Sport and Exercise Science  
University of Auckland Tamaki Campus  
Telephone 373 7599 extn: 84681  
h.smith@auckland.ac.nz

This study has received ethical approval from the Northern X Regional Ethics Committee.
CONSENT FORM

Project title: The Effect of an Exercise and Footwear Intervention on Diabetic Neuropathy

Principal Researcher/Supervisor: Jason Gurney

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I have been given and have understood the explanation of this research project and my role as a subject. In particular I have been informed that:

1. I have read and I understand the information sheet dated 12/02/2009 for volunteers taking part in the study designed to investigate differences in foot function in diabetic populations. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.

2. I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study.

3. I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my continuing or future health care.

4. I understand that I may withdraw my data from the study at any point during or following the study. I understand that to do this I will need to contact the Principal Investigator using the contact details provided in the Participant Information Sheet.
5. I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

6. I understand that the treatment, or investigation, will be stopped if it should appear harmful to me.

7. I have had time to consider whether to take part.

8. I know who to contact if I have any side effects to the study.

9. I know who to contact if I have any questions about the study.

10. I may obtain results regarding the outcome of the project upon completion of the study.

11. I consent to the researchers accessing my medical notes only for the purpose of accessing information relevant to this study.

12. I consent to the researchers accessing Medlab records for blood protein records.

13. I consent to my data being stored for 10 years and used on studies of a similar type for which ethical approval will be sought from an accredited N.Z. ethics Committee.

14. I wish to receive a copy of the results YES/NO

I agree to take part in this research.

Signed: ____________________________

Name (please print): ____________________________

Date: ____________________

Project explained by: Name (please print): ____________________________

Project role: ____________________________

Signature: ____________________________

Date: ____________________

290
Appendix 7

Pressure distribution system reliability study
Reliability study

This study was conducted in 2007 and subsequently published in Gait and Posture in 2008. For copyright reasons the plain-text version of the article is presented. The reference for this article is: Gurney, J. K., Kersting, U. G., & Rosenbaum, D. (2008). Between-day reliability of repeated plantar pressure distribution measurements in a normal population. Gait and Posture, 27, 706-709.
BETWEEN-DAY RELIABILITY OF REPEATED PLANTAR PRESSURE DISTRIBUTION MEASUREMENTS IN A NORMAL POPULATION

Abstract
The objective of this study was to determine the reliability of repeated plantar pressure distribution measurements during normal gait across multiple testing sessions. Testing sessions were conducted on five separate days at approximately the same time of day. Nine subjects (5 male, 4 female, age 26 ± 8.4 years) who were free of any musculoskeletal injury were recruited. A capacitive pressure distribution platform (EMED AT, Novel GmbH, Munich, Germany), sampling at 50 Hz was used to collect plantar pressure patterns during barefoot walking at a self-selected speed. Four parameters were investigated: peak pressure, maximum force, impulse, and contact time, and these were investigated in 10 areas of the foot after using the PRC mask method of subdividing the foot into ten anatomical areas of interest. Individual means of all the five repeated trials for each foot were calculated, and these values were used to calculate intraclass correlation coefficients (ICC) and coefficients of variation (CoV) for all parameters. The results of this investigation show a generally good level of reliability, the quality of which is dependent on the region of the foot and the parameter investigated. Areas with typically high loading characteristics, such as the central forefoot showed a higher level of reliability in the ICC’s (>0.9) than less loaded areas such as the medial midfoot (<0.8). The conclusion of this study is that plantar pressure distribution measurements can be used in comparative evaluations since the measures of repeatability are satisfactory for the parameters and foot regions usually used in the investigation of clinical populations such as neuropathic diabetics.

Introduction
Plantar pressure measurements are an established tool for the evaluation of foot function. These measurements assess the effect of structural changes, which may occur as a complication of pathologies such as diabetes, and have therefore been suggested as one of the key tools in ulcer risk estimation (P.R. Cavanagh, et al., 1993). The vast majority of diabetic foot complications that result in amputation do begin with formation of foot ulcers, which might be prevented by appropriate treatment and early detection with methods such as plantar pressure distribution measurements (P.R. Cavanagh, et al., 2000).
Reliability of pressure distribution systems

In 1991, Hughes and colleagues investigated the reliability of the EMED pressure measurement system by collecting plantar pressure data during gait within one testing session. After analysing a coefficient of variation between repeated trials, Hughes et al. found that the reliability of the pressure data collected increased as the number of trials collected increased. Their advice to users of such systems was a collection of a minimum of three trials per experimental session in order to ensure a good level of reliability (Hughes, et al., 1991).

Hostens et al. investigated the repeatability of an XSensor pressure measurement system in measuring back and seating pressures on agricultural machines across four days and found good repeatability (Hostens et al., 2001). Between-day repeatability of in-shoe pressure measurement during gait in normal subjects was recently evaluated by Putti et al. Measures were taken twice, with an average gap of 12 days between test days. This analysis found a high repeatability between days across a number of parameters (Putti et al., 2007). To our knowledge, however, the reliability of the parameters used to describe foot loading characteristics during barefoot walking has not been evaluated across several repeated testing sessions.

The ability of the equipment to consistently and reliably measure the same loading characteristic is crucial for clinical diagnoses (Finch, 1999), as it is for the comparison of repeated measurements, for example in pre- vs. post-operative comparisons (Mittal, et al., 2006; Nyska et al., 1998; Patel & Wieman, 1994).

Therefore, the present project investigated the reliability of plantar pressure measurements performed on different days in a group of normal, symptom-free subjects.

Methods

Nine subjects (5 male, 4 female, age 26 ± 8.4 years) were recruited from staff and students of the University of Auckland Biomechanics Laboratory. All subjects gave consent to be tested and were free of neuromusculoskeletal disorders at the time of testing.
Testing sessions were conducted on five separate days at approximately the same time of day. If, for example, a subject was tested mid-morning on the first session, efforts were made to ensure each subsequent testing session was conducted mid-morning. All testing was conducted within a nine-day period, and the time taken to collect data from each subject had a range of 7-9 days with an average of 7.6.

A capacitive pressure distribution platform (EMED AT, Novel GmbH, Munich, Germany), embedded in the ground flush with the floor surface and collecting at 50 Hz was used to collect plantar pressure patterns during barefoot walking at a self-selected speed (Bryant, et al., 1999; Hayafune, et al., 1999; Murphy, et al., 2005). The resolution of this system is two sensors per square cm, and the sensor area of the platform measures 360 x 190 mm, with a total of 1377 sensors, and a pressure range of 10 to 1270 kPa. Five trials were collected for both the left and right foot, a sufficient number of trials for the attainment of reliable withinsession data (Hughes, et al., 1991). Approximately five steps were taken prior to and following platform contact.

All subjects were given time to familiarise themselves with the process of walking over the platform (Rosenbaum & Becker, 1997). Subjects were asked to not look at the platform as they walked but instead to walk ‘normally’ and not to be concerned with the platform (Bryant, et al., 1999; Bus, et al., 2005). If a subject obviously aimed at the platform and altered the gait pattern to ensure full contact, the trial was not included for further analysis.

Data analysis was conducted with the Novel Database Pro software package (version 11.38, Novel GmbH, Munich, Germany). In order to achieve a detailed description of foot loading during walking, four parameters were investigated: peak pressure, maximum force, impulse, and contact time. These parameters were considered to be the most commonly used in the functional foot assessment of those with pathological conditions such as neuropathic diabetes. These parameters were investigated in 10 areas of the foot after using the PRC mask method of subdividing the foot into anatomical areas of interest. This mask involves the regional division of the foot for data analysis purposes in to lateral and medial heel, lateral and medial midfoot, lateral, central and medial forefoot, hallux, 2nd toe and 3rd-5th toes (see Figure 1). As described by Novel, the boundary between the heel and midfoot is located 73% of foot length, measured from the toes to the heel. The boundary between the midfoot and forefoot
is located 45% along this length. Lateral and medial borders of the heel and midfoot are defined by a vertical axis running from the centre of the heel to the centre of the second toe. The first, second and lateral metatarsals (medial, central and lateral forefoot) are separated by lines which are parallel to this axis, and these regions are defined as being 30% (medial), 25% (central) and 45% (lateral) of the medio-lateral axis (Novel GmBh, Munich, Germany). The use of this automated masking algorithm has been supported by previous research by Cavanagh and Ulbrecht (1994).

Figure 1: PRC mask applied to divide the foot into anatomical areas of interest.

Statistical data analysis was conducted in the statistical software package SPSS (version 10.0). Individual means of all the five repeated trials for each foot were calculated, and these values were used to calculate between-days intraclass correlation coefficients (ICC) and coefficients of variation (CoV) for all parameters, since these were shown by Atkinson and Neville to be accepted methods of measuring reliability between testing sessions. The type of
ICC used for this analysis was a one-way random ICC, since the difference in results between test days was random (Atkinson & Nevill, 1998).

Results

The results of the ICC and CoV analysis show a generally good level of reliability, the quality of which is dependent on the region of the foot and the parameter investigated. In terms of peak pressure, the ICC range across all regions of the foot was 0.687 (lateral toes) to 0.909 (central forefoot). The average ICC value for all regions of the foot was 0.847. Maximum force ICC values ranged between 0.708 (lateral forefoot) to 0.955 (lateral midfoot). Impulse ICC values ranged between 0.738 (medial midfoot) and 0.964 (lateral midfoot). Contact time ICC values ranged between 0.766 (lateral midfoot) and 0.924 (lateral toes). The parameter which showed the highest average ICC value was impulse (0.880), and the lowest average value was observed in the peak pressure parameter (0.801) (Table 1).

Table 1: Intraclass Correlation Coefficients

<table>
<thead>
<tr>
<th>Region</th>
<th>Peak Pressure</th>
<th>Max. Force</th>
<th>Impulse</th>
<th>Contact Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>• med. hindfoot</td>
<td>0.803</td>
<td>0.889</td>
<td>0.873</td>
<td>0.814</td>
</tr>
<tr>
<td>• lat. hindfoot</td>
<td>0.817</td>
<td>0.911</td>
<td>0.894</td>
<td>0.833</td>
</tr>
<tr>
<td>• med. midfoot</td>
<td>0.788</td>
<td>0.776</td>
<td>0.738</td>
<td>0.788</td>
</tr>
<tr>
<td>• lat. midfoot</td>
<td>0.862</td>
<td>0.955</td>
<td>0.964</td>
<td>0.766</td>
</tr>
<tr>
<td>• med. forefoot</td>
<td>0.850</td>
<td>0.945</td>
<td>0.938</td>
<td>0.882</td>
</tr>
<tr>
<td>• central forefoot</td>
<td>0.909</td>
<td>0.905</td>
<td>0.929</td>
<td>0.846</td>
</tr>
<tr>
<td>• lat. forefoot</td>
<td>0.689</td>
<td>0.708</td>
<td>0.767</td>
<td>0.802</td>
</tr>
<tr>
<td>• hallux</td>
<td>0.781</td>
<td>0.898</td>
<td>0.905</td>
<td>0.905</td>
</tr>
<tr>
<td>• 2nd toe</td>
<td>0.822</td>
<td>0.807</td>
<td>0.860</td>
<td>0.909</td>
</tr>
<tr>
<td>• lateral toes</td>
<td>0.687</td>
<td>0.805</td>
<td>0.930</td>
<td>0.924</td>
</tr>
<tr>
<td>• mean</td>
<td><strong>0.801</strong></td>
<td><strong>0.860</strong></td>
<td><strong>0.880</strong></td>
<td><strong>0.847</strong></td>
</tr>
</tbody>
</table>

CoV values for the regional peak pressures ranged between 7% (lateral hindfoot) and 20.5% (lateral toes). The average CoV value for all regions of the foot was 11.3%. Maximum force CoV values ranged between 5.5% (medial hindfoot) and 25.7% (medial midfoot). Impulse CoV values ranged between 7.0% (central forefoot) and 30.9% (medial midfoot). Contact time CoV values ranged between 2.2% (central forefoot) and 10.6% (medial midfoot). Impulse showed the highest average CoV value (14.1%), while contact time showed the lowest average CoV value (5.8%) (Table 2).
Tab 2: Coefficients of Variation (CoV=SD/mean in %)

<table>
<thead>
<tr>
<th>Parameter →</th>
<th>Peak Pressure</th>
<th>Max. Force</th>
<th>Impulse</th>
<th>Contact Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• med. hindfoot</td>
<td>7.8</td>
<td>5.5</td>
<td>8.2</td>
<td>6.5</td>
</tr>
<tr>
<td>• lat. hindfoot</td>
<td>7.0</td>
<td>5.8</td>
<td>7.5</td>
<td>6.3</td>
</tr>
<tr>
<td>• med. midfoot</td>
<td>16.9</td>
<td>25.7</td>
<td>30.9</td>
<td>10.6</td>
</tr>
<tr>
<td>• lat. midfoot</td>
<td>11.5</td>
<td>15.7</td>
<td>17.5</td>
<td>5.5</td>
</tr>
<tr>
<td>• med. forefoot</td>
<td>10.0</td>
<td>9.0</td>
<td>9.6</td>
<td>2.5</td>
</tr>
<tr>
<td>• central forefoot</td>
<td>8.1</td>
<td>7.8</td>
<td>7.0</td>
<td>2.2</td>
</tr>
<tr>
<td>• lat. forefoot</td>
<td>10.3</td>
<td>10.1</td>
<td>8.8</td>
<td>2.5</td>
</tr>
<tr>
<td>• hallux</td>
<td>14.8</td>
<td>11.1</td>
<td>13.3</td>
<td>6.5</td>
</tr>
<tr>
<td>• 2nd toe</td>
<td>15.4</td>
<td>17.7</td>
<td>16.2</td>
<td>6.5</td>
</tr>
<tr>
<td>• lateral toes</td>
<td>20.5</td>
<td>21.7</td>
<td>21.6</td>
<td>8.5</td>
</tr>
<tr>
<td>• mean</td>
<td><strong>12.2</strong></td>
<td><strong>13.0</strong></td>
<td><strong>14.1</strong></td>
<td><strong>5.8</strong></td>
</tr>
</tbody>
</table>

Areas with typically high loading characteristics, such as the central forefoot (>0.9) and medial and lateral hindfoot (>0.8), showed a higher level of reliability in the ICC’s than the less loaded areas, such as the medial midfoot (<0.8). As mentioned, contact times showed the lowest variation, with CoV’s between 2 and 11%. Regional peak pressure values appeared to be sufficiently robust for repeated measurements with CoV’s below 15% in the predominant loading areas.

Discussion

This investigation showed that high between-day reliability could be achieved between testing days in normal, symptom-free subjects. This trend was particularly true in regions of the foot where relatively high loading typically occurs during gait, such as the hindfoot and forefoot. Generally speaking, a lower reliability was found in the typically less-loaded areas, such as the medial midfoot. The medial midfoot also showed the highest coefficient of variation across parameters, ranging from 10.6% (contact time) to 30.9% (impulse). However, the coefficient of variation for the central forefoot ranged only between 2.2% (contact time) and 8.1% (peak pressure).

The findings of this study are clinically significant since areas of very high pressure under the foot are good indicators of potential damage being caused to the underlying tissue, particularly in symptomatic diabetic feet (P.R. Cavanagh, et al., 1998). Therefore a high reliability between testing days in these foot regions as it has been shown by the present
results is highly desirable for clinical screening purposes. Cornwall and McPoil investigated
the effect of different foot orthotics on initial loading times during gait. They found that the
between-trial reliability (ICC) was high for the forefoot regions, but less so for other regions,
which is in accordance to the present results although for a different parameter (Cornwall &
McPoil, 1997).

It has to be realized, however, that the presented results apply only for the specific
instrumentation that was used here and cannot generally be transferred to other available
pressure distribution measurement systems. These may be based on different sensor
technologies and may not achieve a comparable reliability. Also, the PRC masking method
may limit our ability to generalize the conclusions from this study to a wider population. The
PRC mask method, chosen for its strong reputation as a valid method of dividing the foot in
to anatomical areas of interest, still makes assumptions regarding the boundaries of particular
regions. Also, areas such as the medial midfoot may become under-represented by such
masking algorithms, and therefore when investigating afflictions such as pes planovalgus an
investigator may need choose a mask which is more suitable for this investigation. However,
since the investigation being attempted in this study was of a non-specific nature, the more
generic PRC mask was chosen.

A possible confounding factor with these results is that the present subjects did not
experience neuromusculoskeletal symptoms, particularly of the lower extremity. Subjects
with such complaints may be incorporated into a future study on the reliability of plantar
pressure measurements; however due to time and ethical considerations this was not
performed. It was also most desirable to, in the first instance, ensure that between-day
reliability could be found in subjects who have no pathological basis for exhibiting variable
gait and/or alterations to plantar pressure patterns.

**Conclusion**

The results of this study confirm that plantar pressure distribution measurements with the
instrumentation applied here can be used in comparative evaluations since the measures of
repeatability are satisfactory for the chosen parameters and foot regions that are normally
used in clinical investigations. The determined measures for variability (CoV) may serve for
power estimation in clinical intervention experiments.
References


