Unilateral Strength Training and Mirror Therapy for Enhancing Lower Limb Motor Function After Stroke

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Declaration

I declare that this thesis is the result of my own independent research and work, except where otherwise stated and referenced accordingly. This thesis has not been previously accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

This thesis is submitted to the Institute of Technology, Sligo in partial fulfilment of the requirements for the Degree of Doctor of Philosophy.

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Abstract

Stroke is the leading cause of adult disability. Hemiparesis and spasticity are common impairments, resulting in ankle dorsiflexion dysfunction and gait asymmetry. Often the most-affected side is too weak to engage in rehabilitation programmes. Cross-education and mirror therapy (MT) are novel treatments that unilaterally train the less-affected limb, showing promising therapeutic effects in the more-affected limb. The inclusion of mirror visual feedback during cross-education training can further augment the cross-education effect in healthy populations. However, little is known about the application of a combination of these therapies in a clinical setting. Therefore, a gap remains in the literature regarding whether mirror visual feedback of the training limb can further augment cross-education and motor function recovery post-stroke.

The first objective of this thesis was to assess existing evidence for the application of cross-education post-stroke. The systematic review (Chapter 2.0) suggests that there is moderate to strong evidence for applying cross-education after stroke. The second objective was to establish a reliable protocol for assessing strength. The reliability study (Chapter 3.0) established a reliable protocol for assessing three important strength parameters; Peak Torque, Rate of Torque Development and the novel parameter Average Torque of a single isometric contraction. The third objective was to investigate the therapeutic effects of applying a combination of cross-education and MT post-stroke. A combination of ankle dorsiflexion cross-education and MT was applied to one stroke patient (Chapter 4.0), with meaningful outcomes in strength, spasticity, motor function and self-perceived participation. Subsequently, cross-education and cross-education with MT were applied to stroke patients (Chapter 5.0). Both therapies resulted in a significant improvement in spasticity, with the combination therapy showing a trend for improving motor function. These findings present the first evidence that cross-education with MT can be applied post-stroke and may achieve lower limb rehabilitative outcomes.

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Dedication

I dedicate this thesis to my parents. Thank you for always encouraging me to do my best regardless of the outcome. I also dedicate this thesis to my grandfather Donald, who lived with severe hemiparesis for 30 years after suffering a stroke at the young age of 40. A man who managed to laugh out loud regardless and would race me home, in his wheelchair, from the school bus as a child. Who could have known back then that I would have the privilege of working to help people rehabilitate after stroke?

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List of Abbreviations

10MWT	10 Metre Walk Test
AROM	Active Range of Motion
AT	Average Torque
CV	Coefficient of Variation
EMG	Electromyography
ES	Effect Size
fMRI	Functional Magnetic Resonance Imaging
ICC	Intraclass Correlation Coefficient
ICF	International Classification of Functioning, Disability and Health framework
LA	Less-affected
LHS	London Handicap Scale
MA	More-affected
MAS	Modified Ashworth Scale
MCID	Minimal Clinically Important Difference
MDC	Minimal Detectable Change
MMSE	Mini Mental State Exam
MT	Mirror Therapy
MVC	Maximal Voluntary Contraction
MVIC	Maximal Voluntary Isometric Contraction
Nm	Newton metres
Nm/s	Newton metres per second
PT	Peak Torque
RTD	Rate of Torque Development
SD	Standard Deviation
SRD	Smallest Real Difference
TE	Typical Error
TMS	Transcranial Magnetic Stimulation
TUG	Timed Up & Go
W	Work

1.0 Introduction and Theoretical Background

1.1 Introduction

Stroke, defined as neural damage as a result of interrupted blood flow to the brain [1], is the leading global cause of adult disability [2]. Neural damage following a stroke causes a loss of input to motoneurons which often manifests as various deficits seen on the opposite side of the body to the hemispheric location of the ischemic attack [3]. Of the fifteen million people who suffer a stroke each year, five million (33%) are permanently disabled [2]. Six to twelve months after stroke, 35% of patients who presented with lower limb hemiparesis will still show reduced functional ability which has an extensive impact on independent management of activities of daily living [4-6] and is further associated with high levels of anxiety and poorer perception of health related quality of life [7]. Hemiparesis, a one sided muscle weakness [8, 9], and spasticity, increased involuntary muscle tone [10], are the most commonly reported physical impairments [11-14]. Hemiparesis following stroke is commonly more noticeable in distal muscle groups [3]. Spasticity develops in 25%-30% of stroke patients and in the lower limbs occurs predominantly in the ankle (66%) [11, 15], contributing to common gait impairments [16]. Ankle dorsiflexion dysfunction is a particularly common issue due to such weakness and spasticity after stroke. It has been reported that maximal dorsiflexor torque of the most-affected (MA) limb can be reduced to as little as 38% of the less-affected (LA) limb [17] and dorsiflexor weakness post-stroke is a primary contributor to decreased gait velocity and temporal symmetry [18].

Presently performed lower extremity rehabilitation techniques are based on repetitive methods, e.g. active assisted and passive manual movements, primarily addressing the MA limb directly [19]. Therapy sessions mainly take place in acute or outpatient settings

and prove to be expensive, labour intensive, and require travel for patients in rural regions [20, 21]. Consequently, there is a need for community or home-based post-stroke rehabilitation techniques that are evidence based, cost effective, patient centred and allow for early supported discharge services to be employed [12]. Resistance training of the MA side has been shown to improve muscle force and motor function without increasing spasticity and pain [3, 22-24]. However, in many cases the impairment of the MA limb is too great to be engaged in active exercise, which denies the possibility of independent home training as therapist assistance is needed at all times [21, 25]. Home-based rehabilitation is associated with improved functional outcomes and reduced reliance on health services [26]. Furthermore, both supervised and unsupervised home-based exercise can result in significant physical improvement [27]. Innovative rehabilitation techniques that primarily engage the LA limb may have potential to reduce the expense and labour required during traditional physical interventions post-stroke.

Cross-education, the performance improvement in the untrained homologous muscle after unilateral exercise training [28, 29], was first described by Scripture et al. in 1894 [30]. Since then, the phenomenon has captured the interest of many researchers. A recent meta-analysis [31] of 31 cross-education studies in healthy subjects found definite evidence supporting the existence of the phenomenon, with the magnitude of strength increase being on average 11.9% of initial untrained limb strength. To the healthy person there is no obvious relevance of the phenomenon as they usually strive to improve function and strength in both limbs simultaneously. From the perspective of

rehabilitation, however, the relevance of cross-education emerges as a way to benefit the recovery of function after unilateral orthopaedic injury or neurological damage [32]. The use of cross-education as a treatment option for the lower extremity in stroke rehabilitation is a relatively new concept. Dragert & Zehr [33] were the first to investigate the application of cross-education in a stroke population, reporting strength increases of 34% in the trained LA limb and 31% in the untrained MA limb after 6 weeks of maximal isometric dorsiflexion strength training. The strength improvements also had a positive effect on functional tasks. A recent systematic literature review [34] (detailed in Chapter 2.0) supports the findings and confirms that neuromuscular cross–educational effects can be effective in the lower extremity post-stroke. In summary, cross-education has been proven to produce significant strength and functional benefits after stroke.

It has been hypothesised that the cross-education effect in the lower extremity may be further augmented by combining the strengthening therapy with mirror therapy (MT) [35, 36]. Mirror therapy has been shown to improve motor function and activities of daily living post-stroke [37, 38]. During MT, a mirror is placed in the patient's mid-sagittal plane, thus reflecting the LA side as if it were the MA side [39]. The therapeutic approach is based on visual stimulation. When observing the mirror, movements of the LA limb create the illusion of normal movements of the affected limb. It has been suggested that cross-education may be further augmented with the addition of MT in a clinical population [40]. A recent study [40] has shown that the cross-education effect in a non-clinical population is indeed further augmented by combining cross-education with MT. The study concluded that untrained limb strength increased significantly more in the

mirror training group (61%) when compared to strength training only without the mirror (34%). To date, this combination of therapies has not been investigated in a chronic stroke population. Therefore, the effects on spasticity and motor function remain unexplored. This is the first study to investigate the potential for cross-education of strength plus MT for improving post-stroke motor function in the lower limb.

1.2 Theoretical Framework

1.2.1 Cross-Education

Cross-education, the performance improvement in the untrained homologous muscle after unilateral exercise training [28, 29, 41], was first described by Scripture at al. (1894) [30]. After implementing a unilateral strength training intervention that lasted only 13 days, Scripture at al. [30] reported a strength increase of 43% in the untrained limb. The magnitude of contralateral strength transfer has previously been reported to be on average 52% of the strength increase observed in the trained limb [42]. The contraction type, speed, the novelty of the strength task, the chosen intensity, as well as training of the non-dominant or dominant limb play a decisive role in the extent of the strength transfer [28, 31, 43-47]. A meta-analysis [31] of 31 cross-education studies found evidence suggesting that the increase in untrained limb strength is on average 11.9% of initial untrained limb strength (9.4% in the upper limb and 16.4% in the lower limb). It is accepted that cross-education is not limited to specific muscles groups. The effect can be noted for both the upper and lower body, for large muscle groups to small muscle groups [44, 48] and for both males and females of varying ages [29, 49].

1.2.2 Mechanisms of Cross-Education

Although the existence of contralateral strength transfer has been proven, a conclusion regarding the precise mechanisms could not yet be presented. Current literature suggests that adaptations contributing to the cross-education effect are most likely to occur on a cortical or supraspinal level [42, 43], although peripheral muscular adaptations may not be ruled out [50]. The consensus is that there are numerous sites of adaptation following unilateral strength training. The following section addresses the potential mechanisms of cross-education.

Muscle Mechanisms

It is firmly accepted that strength training results in peripheral muscular adaptations such as hypertrophy and increased enzyme and contractile protein activity in the trained limb [51]. Not only does unilateral strength training have such effects in the trained limb, it also results in maintenance and performance improvement in the contralateral untrained limb. There is evidence that unilateral strength training has the potential to minimise muscle atrophy in an immobilised contralateral untrained limb [41, 52, 53]. However, unlike that of the trained limb, peripheral adaptations in the untrained homologous muscle (e.g. hypertrophy, modification in contractile protein composition or adaptations in muscle enzyme concentrations) could not be shown in any trial so far [42, 54-58]. Studies using electromyography (EMG) have reported a minimal degree of muscle activity in the untrained limb during unilateral training [40, 45, 57, 59] and the contralateral motor unit activation is probably too minimal to induce muscular adaptation [42]. Furthermore, the cross-education effect occurs even without such contralateral activity [47, 60, 61]. Direct adaptations to skeletal muscle following

unilateral strength training are seen as highly unlikely; however, the authors of a review on cross-education warn that muscular processes should be also incorporated [42].

Spinal Mechanisms

Force generation or motor output is influenced by spinal networks affecting reflex actions, descending commands and motor drive to agonist, synergists and antagonists [62]. The Hoffmann reflex (H-reflex) has been used to assess excitability of the Ia afferent motor neuron pathway in the untrained limb [63-65]. However, the limited number of studies that have explored the function of spinal reflexes in the contralateral untrained limb after unilateral strength training have reported conflicting results. While Lagerquist et al. [63] reported no change in H-reflex amplitude of the untrained limb following 5 weeks of unilateral plantarflexion strength training, Dragert & Zehr [65] report a decrease in maximal H-reflex amplitude in the antagonist muscle (soleus) of the untrained limb following 5 weeks of high-intensity unilateral dorsiflexion strength training. Thus, indicating an association between cross-education and spinal reflex adaptation.

Cortical Mechanisms

The planning and execution of movement takes place primarily in the frontal lobes of the cerebral cortex with direct control of motorneural output being in the primary motor cortex (M1) [42]. Interhemispheric connection between the left and right hemispheres of the brain is facilitated via the corpus callosum [66]. Such interhemispheric connection may provide a justifiable explanation for the cross-education effect [42, 67].

Several studies agree that unilateral strength training results in bilateral activation of the left and right primary motor cortex (M1) [42, 68-70]. Farthing et al. [54] explored the effects of unilateral strength training on changes in brain activity using functional magnetic resonance imaging (fMRI). The results of the study provided further evidence that both cortical hemispheres are increasingly activated by unilateral strength training and that communication of neural activity may be passed between the left and right hemispheres [54].

Ruddy & Carson [71] put forward two theories involving neural plasticity that may help to define the cortical mechanisms of cross-education (Figure 1.1). Firstly, the "bilateral-access" theory describes the ability for both the trained and the untrained limb to access new motor engrams which are developed following unilateral training. This theory is based on the cross-education of skill-based tasks which involve motor learning, known as "bilateral-transfer" [50]. The "bilateral-access" theory may be applicable in the cross-education of strength as strength training and the ability to produce purposeful force may also be considered a motor learning task as effective force production involves recruitment of motor units, inhibition of antagonists and co-ordination of synergists [67]. The second theory, which may not be mutually exclusive to the first, is described as "cross-activation". This theory involves the idea that forceful unilateral contractions are driven by bilateral cortical activity. Such activity in both the contralateral and ipsilateral M1 result in lasting neural adaptations in both hemispheres. Key to both theories is the particular involvement of the ipsilateral M1 in facilitating the cross-education of strength [67, 71, 72].

To date the focus has been primarily on the involvement of the M1 in facilitating cross-education [73]. Cortical adaptations which mediate cross-education may not be restricted to the M1 [42]. Indeed, increased neural activity has been reported in ipsilateral supplementary motor areas, cingulate motor areas and prefrontal areas during unilateral movement [54, 74], illustrating their potential to contribute to inter-limb transfer of performance [73].

With the use of transcranial magnetic stimulation (TMS), Hortobagyi et al. [61] investigated whether interhemispheric inhibition (IHI) played a role in cross-education. The study reported a reduction in interhemispheric inhibition (IHI) from the trained to the untrained M1, coupled with a significant strength increase (28%) in the contralateral untrained index finger, following 8 weeks of unilateral finger strengthening. Hortobagyi et al. [61] concluded that repeated effortful unilateral contractions resulted in decreased IHI from the trained to the untrained hemisphere, suggesting that interhemispheric plasticity contributes to cross-education. Latella et al. [48] further explored the cortical mechanisms mediating cross-education using TMS, demonstrating that corticospinal inhibition reduced in both the trained and the contralateral untrained leg following 8 weeks of unilateral leg strengthening, again supporting the importance of cortical adaptations in the mediation of cross-education.

The inhibitory neurotransmitter gamma-amino-butyric-acid (GABA) contributes to the modulation of pyramidal neuron activity and GABAergic interneurons make up 10-25% of all cortical neurons [75]. Recent studies have indicated the involvement of GABAergic inhibitory neurons and their role in cross-education [76-78]. Activity of $GABA_A$–mediated

inhibitory interneurons and $GABA_B$ receptor activity in the untrained M1 are both reduced by bouts of unilateral resistance training [76-78], giving rise to increased corticospinal output from the ipsilateral untrained M1 [61, 77, 79, 80]. Short interval intracortical inhibition (SICI) is an inhibitory phenomenon that can be measured with TMS [81]. Following 3 weeks of unilateral leg strengthening, Goodwill et al [77] reported a significant increase in strength for the untrained leg along with a 21% decrease in SICI of the ipsilateral M1. Similarly, Latella et al. [48] reported a significant (16.4%) reduction in contralateral silent period (cSP) in the contralateral untrained leg along with a significant (20.4%) increase in strength in the untrained leg after 8 weeks of unilateral leg strengthening.

In summary, it would seem that adaptations at a cortical level drive the cross-education effect; however, specific adaptation sites and processes have not yet been incontestably defined. It may even be possible that contributing factors vary among individuals, muscle groups, and training protocols [42].

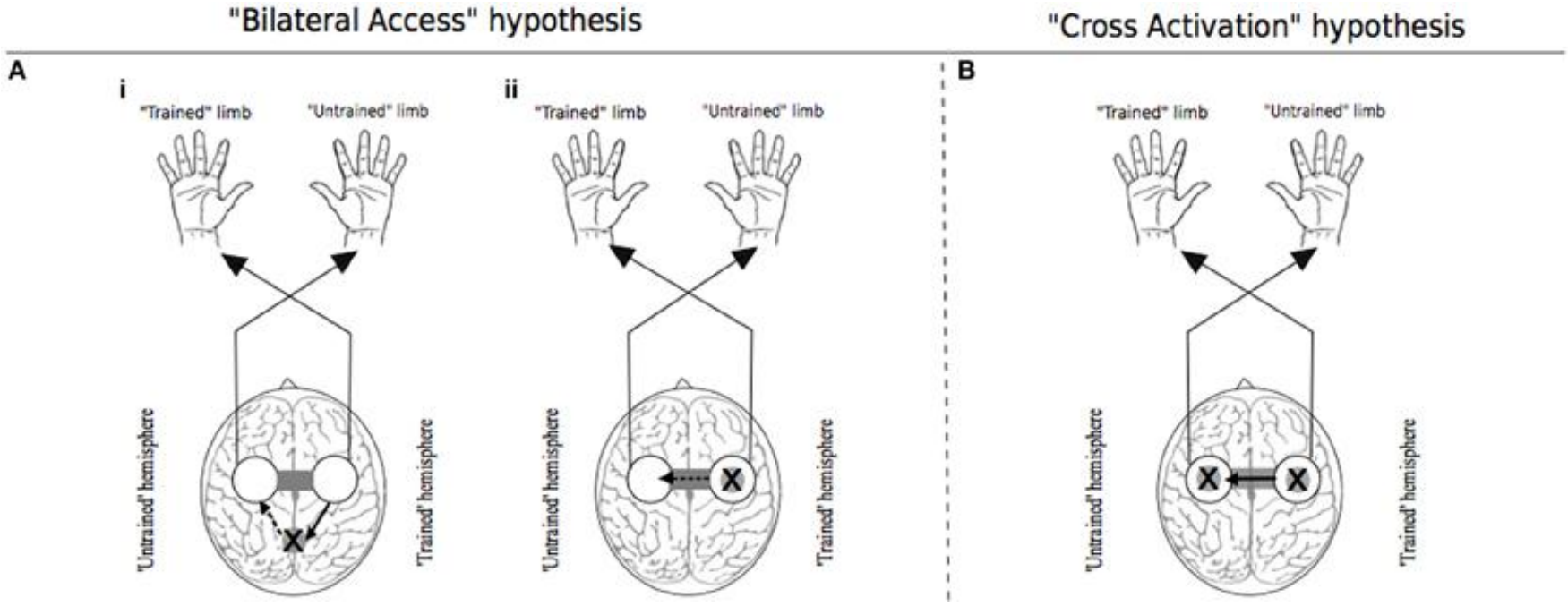

Figure 1.1: Bilateral Access Theory and Cross Activation Theory of Cross-education
In both illustrations "X" indicates the location of training induced adaptations, white circles indicate lateralised motor networks, solid arrows represent process occurring during unilateral training, dashed arrows indicate processes specific to the subsequent transfer phase during which movements are generated by the untrained limb. **Ai** illustrates the theory that engrams are established in brain centres that are accessible to motor networks of both the trained and untrained limbs. **Aii** demonstrates the theory whereby training related adaptations are lateralised to motor networks projecting to the trained limb but are accessible to motor networks projecting to the untrained limb via callosal transfer. **B** illustrates that "cross activation" of the homologous motor network gives rise to bilateral adaptations that facilitate performance improvements of the untrained limb.
[71, 72]

1.2.3 Clinical Application of Cross-Education

To the healthy person there is no obvious relevance of cross-education as they usually strive to improve function and strength in both limbs simultaneously. From the perspective of rehabilitation, however, the relevance of cross-education emerges as a way to benefit the recovery of function after unilateral orthopaedic injury or neurological damage [32]. Magnus et al. [82] demonstrated how cross-education can positively impact recovery after distal radius fracture. Following a unilateral strength training intervention combined with standard clinical rehabilitation, hand grip strength as well as range of motion significantly improved in the training group versus the control group (standard clinical rehabilitation only). The training group maintained 62% of the non-fractured limb strength at week 12 post-injury versus 45% in the control group [82]. Contrastingly, Zult et al. [80] applied cross-education strength training to subjects recovering from anterior cruciate ligament reconstruction and found that strength training of the uninjured lower limb as an adjuvant to standard care did not result in increased rate of recovery in the untrained injured limb compared to standard care alone.

Cross-Education and Stroke Rehabilitation

The use of cross-education as a treatment option in rehabilitation after neurological damage is a relatively new concept. Dragert & Zehr [33] investigated cross-education as a viable treatment option in rehabilitation following neurological damage as a result of a stroke. The study consisted of 19 participants who followed a high-intensity unilateral isometric dorsiflexor strength training programme. Following 6 weeks of maximal isometric voluntary dorsiflexion contractions of the less-affected (LA) limb, strength

increased significantly by 34% in the trained (LA) limb, and by 31% in the untrained most-affected (MA) limb. The strength improvements also had a positive effect on lower limb motor function [33]. Similarly, a study that employed a supplementary tilt table to allow unilateral task-orientated training of the LA limb, resulted in significant (23-45%) strength increases in the untrained MA dorsiflexors [83]. A recent systematic literature review [34] (Chapter 2.0), of which the author of this thesis was a principal researcher and co-author, supports these findings and confirms that neuromuscular cross–education effects can be achieved post-stroke. The review concluded that there is moderate to strong evidence that cross-education from the trained (LA) limb to the untrained (MA) limb can be applied in stroke patients and has an impact on the recovery of muscle strength.

There are indications that the improvement of strength following unilateral training of the LA limb also translates into motor function recovery. Urbin et al. [84] investigated the effects of cross-education training in stroke patients with upper limb hemiparesis. Following 4 weeks (16 sessions) of progressive unilateral wrist extensor strength training of the LA limb, results showed a significant increase (100%) in active range of motion (AROM) for the untrained (MA) limb. Although the study reported no specific post-intervention measurement of strength for the untrained limb, the findings suggest that cross-education may have further rehabilitative effects post-stroke.

Based on the findings of the above studies, it is reasonable to suggest that cross-education of strength has potential in post-stroke rehabilitation. More high quality

randomised controlled trials are recommended to further investigate the prospect of cross-education as a post-stroke rehabilitation treatment.

1.2.4 Mirror Therapy

During mirror therapy (MT) a mirror is placed in the patient's mid-sagittal plane, thus reflecting the LA side as if it were the MA side [39]. The therapeutic approach is based on visual stimulation whereby the subject observes the movements of the training unaffected limb in the mirror as if it were the opposite affected limb, creating the illusion that normally coordinated movements are happening in the affected limb.

Ramachandran & Rogers-Ramachandran [85] first applied MT in a successful attempt to alleviate phantom limb pain. Ramachandran's theory of phantom limb pain, often felt in amputees, is that it is a direct result of what he refers to as 'learned paralysis' [86]. In a normally functioning limb, a motor command to perform movement is quickly followed by proprioceptive sensory feedback. When a limb is missing, due to amputation, proprioceptive sensory feedback does not occur [87]. The absence of the correct sensory feedback elicits feedback modification which, along with visual feedback informing the brain that the limb is not moving, causes a confusion between motor and sensory interaction resulting in 'learned paralysis' [86].

The purpose of MT is to restore normal sensorimotor function by tricking the brain into believing the affected limb is moving according to motor command [87]. With the use of a simple mirror device to provide mirror visual feedback, Ramachandran & Rogers-Ramachandran [85] demonstrated how MT has the ability to reorganise cortical

representation of a painful phantom limb. After applying various forms of MT to subjects with upper limb amputation, the study describes subjects feeling sensations of the phantom limb moving, experiences of relief from painful spasms in the phantom limb and even complete disappearance of the phantom limb. With these findings providing proof of principle, Ramachandaran and Rogers-Ramachandaran [85] suggested similar therapeutic effects may be possible in other neurological conditions such as stroke.

1.2.5 Mechanisms of Mirror Therapy

The mechanisms underlying the positive effects of MT are proven to be neurophysiological. The following outlines three plausible and not mutually exclusive theories addressing the mechanisms of MT.

i) Visual feedback overrides proprioception [88]. Observation and illusion of the affected limb moving perfectly, by way of mirror visual feedback, brings about increased attention to the affected limb. In a similar way as constraint induced therapy, whereby the unaffected limb is restricted from use forcing the patient to focus more on using the affected limb, increased attention towards the affected limb may firstly improve motor networks and secondly encourage the patient to use the affected limb more during activities of daily living, both enhancing overall motor function [87].

ii) It has been established that cortical motor areas that are active during observation of a motor task are also involved in its active reproduction [89]. The neurological structure allowing this process is believed to be the mirror neuron system (MNS) [90]. Mirror neurons reside in the premotor cortex and are activated when either performing an action or simply observing an action

being performed. Action observation, the visual observation of a moving limb, is already used in neurorehabilitation as it is thought to facilitate the corticospinal pathway and improve motor function [91]. The visual observation of an actively performing limb in a mirror is therefore thought to stimulate the MNS and increase excitability in the corticospinal pathway, inducing motor learning and neurorehabilitation [87, 92]. Similarly, motor imagery (the mental simulation of an action or movement) activates neural pathways involved in motor control and has also been associated with therapeutic effects [89].

iii) Finally, it has been suggested that motor pathways project from the unaffected hemisphere of the brain ipsilaterally to the affected side of the body. Mirror visual feedback promotes the unmasking and recruitment of such ipsilateral motor pathways which may have been previously dormant, thus enhancing restoration of motor function after hemiparesis [93].

It would seem that the precise neurophysiological mechanisms of mirror therapy are still to be defined; however, the literature suggests that the therapeutic effects are a result of the interaction between perceptual and motor activity at a cortical level [40].

Mirror Therapy and Stroke Rehabilitation

The observation of mirror illusions may increase activation of the contralateral hemisphere and corticomuscular excitability [94-98]. By influencing corticomuscular

excitability, MT might directly stimulate motor recovery. Furthermore, the mirror illusion might prevent or reverse a learned non-use of the MA limb [99, 100].

Similar to the paralysis described in amputees, Ramachandran and Altschuler [86] proposed that as well as permanent neurological damage, a form of 'learned paralysis' may be present in patients who have experienced a stroke due to initial swelling and edema causing a loss of corticofugal communication to the MA limb, impairing sensorimotor function. Such 'learned paralysis' is present long after swelling has subsided and corticofugal communication is restored [86]. With this in mind, MT may be relevant in an attempt to restore motor function post-stroke.

Thieme et al. [37] conducted a Cochrane review with the purpose of assessing and comparing the effectiveness of MT on improvement of motor function after stroke and its impact on activities of daily living, pain and visuospatial neglect. The review of the literature found 14 relevant studies (a total of 567 participants), with an overwhelming majority of the studies focussing on upper limb interventions (13 out of the 14 studies). After analyses of the studies the authors concluded that MT was effective in terms of improving motor function, activities of daily living and pain for patients that had suffered a stroke [37]. However, there remains a need for well-designed randomised controlled studies with large sample sizes to further evaluate the effects of MT after stroke [37].

A more recent systematic review [38], with emphasis on lower limb MT studies involving the stroke population, revealed a total of only 4 high quality randomised controlled trials

[101-104] and one case study [105] that met the inclusion criteria for review. The results of the review indicated that MT can improve motor recovery, gait and range of motion after stroke [101-104]. However, the effectiveness of MT as a post-stroke rehabilitation treatment remains inconclusive until more robust evidence is available. Furthermore, the number of studies reporting on the long-term effects of MT remains inadequate [38].

Based on recommendations in the literature, the Institute of Technology (IT) Sligo Neuroplasticity Research Group have investigated the effects of MT combined with treadmill walking with positive findings in post-stroke patients [106]. The case study reports a reduction in lower limb spasticity with improved motor function following the 4-week intervention. More studies with larger sample sizes that include long-term follow-up are required to substantiate existing knowledge on the benefits of MT as a post-stroke treatment.

1.2.6 Cross-Education and Mirror Therapy Combined

Both cross-education of strength [33, 34] and MT [37, 38] have proven to promote strength and motor functional recovery post-stroke. A recent review [36] found substantial evidence that the use of a mirror during unilateral strength training may further enhance the cross-education effect.

Studies suggest that the MNS may not only be involved when implementing MT but also during cross-education interventions. When using a combination of both therapies the level of activity in involved brain areas can be increased, which may further augment the

contralateral performance improvements [35, 36]. Zult et al. [107] tested the hypothesis with a high standard trial including 27 healthy volunteers. The study showed that performing effortful wrist flexions while viewing the mirror image of the moving right hand reduces short-interval intracortical inhibition (SICI) in the ipsilateral M1 compared with no-mirror contractions and resting conditions with and without a mirror [107]. Although no effect of the mirror on corticospinal excitability of the right M1 could be demonstrated during the trial, increased corticospinal excitability has previously been demonstrated with less intense muscle contractions [98]. Zult et al. [107] hypothesised that the strong muscle contraction in their study (60% MVC) created a saturation effect and the unilateral contraction causes a level of excitation in the ipsilateral corticospinal path which cannot be further increased by mirror viewing. Zult et al. [107] concluded that the mirror induced changes of SICI in the ipsilateral M1 supports the idea that unilateral strength training combined with mirror visual feedback might be more effective than unilateral strength training on its own.

The proof of principle for combining the two therapies was provided by Zult et al. [40] during a trial including 23 healthy adults randomised into a mirror-training group and non-mirror training group. Strength in the trained wrist flexor increased by 72% in both groups, while strength increase in the untrained wrist flexor was significantly higher in the mirror training group (61%) than the non-mirror training group (34%). The study also reported a 15% decrease in cSP in the mirror training group, with no decrease in the non-mirror training group, which coincided with a higher magnitude of strength transfer in the mirror group. Considering cSP has been shown to lengthen in the contralateral hemisphere to the paretic side following stroke [108], these findings may again highlight

the importance of the modulation of inhibitory pathways in evoking cross-education, especially after stroke.

While Zult et al. [40] provide initial evidence that mirror visual feedback of a training limb can augment the cross-education effect in healthy subjects, further research is needed to explore the possible use of the combination therapy in the rehabilitation process of patients with unilateral impairments. Furthermore, Thieme et al. [37] identified a need for further research focusing on outcome measures of activities of daily living. Based on recent evidence, this thesis addresses the gap in the research and provides new information regarding the application of the combination of cross-education and MT in chronic stroke patients with hemiparesis.

1.3 Thesis Objectives

Based on recent recommendations that the inclusion of MT may have the potential to enhance the cross-education effect, the primary aim of this thesis was to explore if mirror visual feedback influences the cross-education effect when unilaterally strength training the LA lower limb post-stroke. Specifically, of interest were the therapeutic effects of the combined therapies and its potential as a treatment in post-stroke rehabilitation. The secondary aim of this thesis was to build on previous cross-education of strength studies to provide greater evidence of the benefits of cross-education training for post-stroke rehabilitation. Currently, there is limited knowledge on the therapeutic effects of both cross-education and MT for the lower limb in a stroke population. Therefore, this thesis focussed on applying the combined therapies and measuring the effects on lower limb motor function in stroke patients. Additionally,

given that the majority of studies investigating strength outcomes use Peak Torque (PT) as the primary strength measure, and that Rate of Torque Development (RTD) and Average Torque (AT) may be more meaningful measures in a rehabilitative clinical setting [109, 110], this thesis set about to design a reliable isometric strength testing protocol that can be implemented in a stroke population. Furthermore, in line with recommendations that innovative patient centred therapies that allow for early supported discharge and ultimately reduce national health care costs [12] are needed, as an adjunct this thesis aimed to design and prototype a mirror strength training device and training protocol that can be implemented in the patient's own home with minimal therapist supervision.

The objectives of this thesis are addressed as follows:

1. Chapter 1.0 includes an in depth review of the literature regarding the theoretical background of cross-education, MT, the application of cross-education as a post-stroke treatment and identifies a gap in the literature regarding the novel combination of cross-education and MT for enhancing post-stroke motor function recovery.
2. Chapter 2.0 presents a published systematic review of the literature, identifying moderate to strong evidence for the application of cross-education as a potential treatment post-stroke.
3. Chapter 3.0 addresses the need to develop a strength testing protocol that can be applied to a chronic stroke population and tests the reliability of PT, RTD and AT as objective parameters for assessing strength.

4. Chapter 4.0 reports a case study evaluating the effects of applying the combination of cross-education strength training with MT on an individual with chronic stroke.
5. Chapter 5.0 outlines a Randomised Controlled Feasibility Pilot Study that compares the combination therapy to cross-education alone and explores the hypothesis that MT influences the cross-education effect to improve lower limb motor function in chronic stroke patients.
6. Chapter 6.0 details the design of a mirror strengthening device that is based on the principles explored in this thesis. The development of the device is currently funded by a feasibility grant with the intention to bring a lower and upper limb mirror strengthening device to commercialisation stage.

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2.0 Cross-Education of Strength has a Positive Impact on Post-Stroke Rehabilitation: A Systematic Literature Review

Ehrensberger, M., Simpson, D., Broderick, P., Monaghan, K. Cross-education of strength has a positive impact on post-stroke rehabilitation: a systematic literature review. Topics in Stroke Rehabilitation, 2016. 23(2): 126-35

2.1 Abstract

Background: Since its discovery in 1894 cross-education of strength, a bilateral adaptation after unilateral training, has been shown to be effective in the rehabilitation after one-sided orthopedic injuries. Limited knowledge exists on its application within the rehabilitation after stroke. This review examined the evidence regarding the implication of cross-education in the rehabilitation of the post-stroke hemiplegic patient and its role in motor function recovery.

Methods: Electronic databases were searched by two independent assessors. Studies were included if they described interventions which examined the phenomenon of cross-education of strength from the less-affected to the more-affected side in stroke survivors. Study quality was assessed using the PEDro scale and the Cochrane risk of bias assessment tool.

Results: Only two controlled trials met the eligibility criteria. The results of both studies show a clear trend towards cross-educational strength transfer in post-stroke hemiplegic patients with 31.4% and 45.5% strength increase in the untrained, more-affected dorsiflexor muscle. Results also suggest a possible translation of strength gains towards functional task improvements and motor recovery.

Conclusion: Based on best evidence synthesis guidelines the combination of the results included in this review suggest at least a moderate level of evidence for the application of cross-education of strength in stroke rehabilitation. Following this review, it is recommended that additional high quality randomised controlled trials are conducted to further support the findings.

2.2 Introduction

Cross–education, the performance improvement in the untrained homologous muscle after unilateral exercise training [1, 2] was first described by Scripture et al. in 1894 [3]. Since then, the phenomenon captured the interest of many researchers with a literature review conducted by Carroll et al. [4] and a more recent meta-analysis conducted by Manca et al. [5].

The magnitude of contralateral strength transfer reported in previous research is ranking between 35 to 104% of initial strength [4]. The contraction type, speed, the novelty of the strength task, the chosen intensity as well as training of the non-dominant or dominant limb play a decisive role in the extent of strength transfer [1, 6-10]. A meta-analysis of studies by Manca et al. [5] found definite evidence for the phenomenon of cross-education. The degree of strength transfer is on average 11.9% of the initial strength in the untrained limb [5] and has also been reported to be 52% of the strength increase observed in the trained limb [4]. Although the existence of contralateral strength transfer has been proven; a conclusion regarding the underlying mechanisms could not yet be presented. Current literature suggests that adaptations, contributing to the cross-education effect, are most likely to occur on a supraspinal or cortical level [4, 6]. Several studies, concentrating on the motor cortex, could show that unilateral strength training results in bilateral activation of the left and right primary motor cortex (M1) [4, 11-13] . Hortobágyi [12] concludes that the described bilateral activation can cause plastic changes and mediates the cross-education effect. Adaptations on spinal level, facilitating contralateral strength transfer, remain unresolved [1, 4, 12]. Peripheral adaptations in the untrained homologous muscle (e.g. hypertrophy, modification in

contractile protein composition or adaptations in muscle enzyme concentrations) could not be shown in any trial so far [4, 14-18]. Accordingly, adaptations on this level are seen as highly unlikely; however, the authors of a review on cross-education warn that muscular processes should not be discarded completely, as measuring methods might lack sensitivity [4]. In summary cortical mechanisms are considered to be superior in the cross-education effect; however, specific adaptation sites and processes have not yet been determined. It may even be possible that contributing factors vary among individuals, muscle groups and training protocols [4].

To the healthy person, there is no obvious relevance of the phenomenon as they usually strive to improve function and strength in both limbs simultaneously. From the perspective of rehabilitation, however, the relevance of cross-education emerges as a way to benefit the recovery of function after unilateral orthopedic injury or neurological damage [19]. In a study by Magnus et al. [20], cross-education was proven to have positive impact on recovery after distal radius fracture. After a unilateral strength training intervention combined with standard clinical rehabilitation, hand grip strength as well as range of motion were significantly improved in the training group (TG) versus the control group (standard clinical rehabilitation). The TG showed 62% and the control group showed 45% of the non-fractured limb strength at week 12 post-injury [20].

Hemiparesis, a one sided muscle weakness, affects 80 – 85% of acute stroke patients [21, 22]. Six to twelve months after stroke 35% of patients who presented lower limb hemiparesis and 56% of those who presented upper limb hemiparesis will still suffer from the reduced functional ability [23]. Typically, hemiparesis causes asymmetry

between the more-affected (MA) and less-affected (LA) side [19] and often the impairment of motor function on the MA side is too great to be engaged in a strength training programme. One of the leading considerations for the clinical application of cross-education may therefore be to enhance post-stroke rehabilitation to reinstate bilateral limb symmetry [19].

The use of cross-education as a treatment option in stroke rehabilitation is a relatively new concept; therefore, limited research exists in the area. Restricted knowledge regarding the topic currently prevents its application within the clinical setting. The purpose of this literature review was to investigate the effects of cross-education of strength on the post-stroke hemiplegic patient and its role in rehabilitation and motor function recovery.

2.3 Methodology

2.3.1 Search Strategy

During December 2014 the following databases were searched: CINAHL, CENTRAL, Google scholar, HSE Library, MEDLINE, Open Grey, PEDro, and Web of Science. Two assessors (DS, ME) independently searched all databases from their date of inception to December 2014 using the key words presented in the search strategy (Table 2.1). The titles and abstracts were screened for suitability, if a decision could not be made on this information the full text was retrieved. Authors of included articles were contacted for further material and reference lists were searched for other relevant studies.

Table 2.1: Search Strategy Medline

#1:	stroke OR “stroke rehabilitation” OR “cerebrovascular accident”
#2:	“Ischaemic stroke” OR “cerebral infarction” OR “brain attack” OR “thrombotic stroke” OR “embolic stroke”
#3:	“brain aneurysm” OR “hemorrhagic stroke” OR “haemorrhagic stroke” OR haemorrhage OR haemorrhage
#4:	Hemiparesis OR hemiparetic OR hemiplegia OR “unilateral paresis”
#5:	1 OR 2 OR 3 OR 4
#6:	“cross education” OR cross-education OR “cross transfer” OR cross-transfer
#7:	“interlimb transfer” OR inter-limb transfer
#8:	“strength transfer” OR strength-transfer
#9:	“skill transfer “OR “intermanual transfer”
#10:	“unilateral training”
#11:	6 OR 7 OR 8 OR 9 OR 10
#12:	5 and 11

2.3.2 Inclusion & Exclusion Criteria

For studies/reviews to be included 1) the article had to be a controlled trial or a systematic review, 2) the article had to be in the English language, 3) participants had to be human and diagnosed stroke patients, 4) the described intervention had to be applied to the LA limb only, and 5) strength assessment of the MA side had to be included as an outcome measure. In other words, studies describing interventions which examined the phenomenon of cross-education of strength from the LA to the MA side in stroke survivors. Studies were excluded if 1) they followed other designs as mentioned above, 2) the full text article could not be retrieved in the English language, 3) participants were healthy or presented with conditions other than stroke (e.g. Cerebral Palsy), 4) interventions were applied bilaterally or to the MA limb only, and 5) outcome measures did not include strength assessment of the MA limb.

2.3.3 Risk of Bias Assessment

Both trials included in this review were assessed by two reviewers (DS, ME). The risk of bias was assessed using 2 different bias assessment tools, the first one being the risk of bias assessment tool from the Cochrane handbook for systematic reviews of interventions [24]. The risk of bias is described as “low risk”, “high risk” or “unclear risk” and was judged according to the “Criteria for judging risk of bias in the ‘Risk of bias’ assessment tool” [24]. The second tool used was the PEDro scale, the physiotherapy evidence database assessment tool which is based on the list developed by Verhagen et al. [25] using the Delphi consensus technique.

2.3.4 Data Extraction and Synthesis

Data were extracted and cross-checked by two assessors (DS, ME). Extracted data included 1) study design, 2) sample size, 3) inclusion/exclusion criteria, 4) participant age, 5) participant gender, 6) outcome measures, 7) summary of main results. Regarding outcome measures, strength gains in the untrained limb compared to baseline measurements and/or compared to strength gain in the trained extremity were of most interest. Secondly, motor recovery and functional impairment measures were considered. Pooled analysis of the data was not possible due to heterogeneity between studies.

2.4 Results

2.4.1 Identification of Studies

The electronic database search yielded 4203 results. Using the described inclusion and exclusion criteria, 53 full articles remained eligible for further screening. After screening,

2 studies were found to be relevant for this review. The hand search, including looking through the reference lists of chosen articles, didn't provide any additional results. The selection process is displayed in Figure 2.1

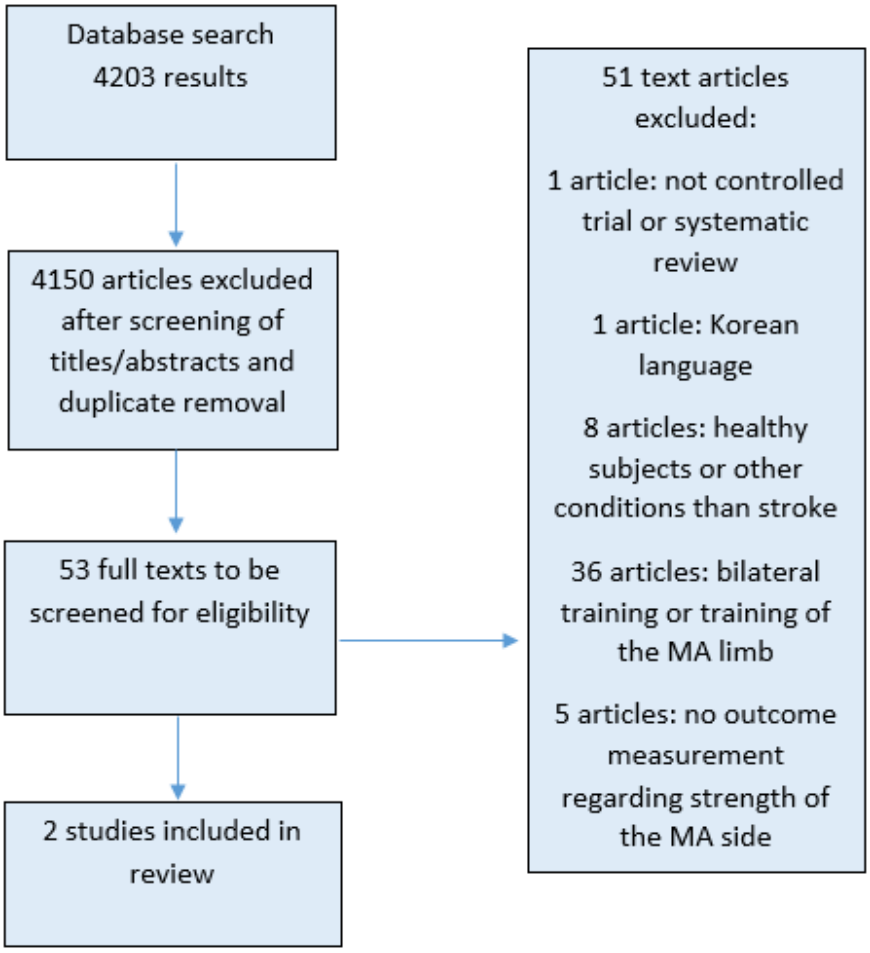

Figure 2.1: Flowchart of Study Selection Process

2.4.2 Description of Studies

Both studies consisted of a physical intervention to the less-affected (LA) side in stroke patients; strength measures of the more-affected (MA) sides were reported. Study characteristics are detailed in Table 2.2.

Table 2.2: Description of Each Study

Study	Study design	Sample Size	Gender	Mean age ± SD	Paretic side left/right	Stroke type ischemic/he-morrhagic	Inclusion/ Exclusion criteria	Intervention	Outcome measure
Kim et al. 2014	Single blinded randomized controlled trial	30	15F:15M	CG: 61.2±8.7 EG1: 59.2±7.7 EG2: 58.5 ±11.8	CG: 7/3 EG1: 4/6 EG2: 5/5	CG: 5/5 EG1:4/6 EG2: 7/3	Inclusion: First stroke, stable hemodynamic, Ashworth index <2 in all LE muscles, MMSE score > 24. Exclusion: Orthopedic impairment, cardiovascular impairment, thrombophlebitis significant perceptual, cognitive or communication impairment, diabetes, contraindication for tilt table.	• Tilt table intervention •CG: SFT + tilt table but no active intervention •EG1: SFT + standing training for less-affected leg • EG2: SFT + task-oriented training for less-affected leg • 5 sessions per week for 3 weeks	• LE muscle strength hand held dynamometer • Gait parameters: velocity, cadence, stride length, gait symmetry, double support percentage
Dragert & Zehr 2013	One-group, non-randomized control intervention	19	4F:15M	58.3 ± 12.2 (range 26 – 81 years)	12/7	NR	Inclusion: >6months after stroke, one-sided dorsiflexor weakness, stand free with or without assistive device, maintain activity level during the study. Exclusion: Medication affecting muscle tone <3months prior, chronic disease comorbidity.	• Dorsiflexion isometric strength training on LA side 5sets of 5 maximal isometric contractions held for 5seconds • 3 sessions per week for 6 weeks	• MVIC measured with load cell • EMG • M-wave • RI • Gait kinematics • Clinical measures: Modified Ashworth Scale, Time up and go, 10m walk test, Functional ambulation category, Berg balance scale, modified Fugl-Meyer

F = female, M = male, CG = control group, EG = experimental group, NR = not reported, MMSE = mini mental state examination, SFT = standard function training, LA = less-affected, LE = lower extremity, MVIC = maximal voluntary isometric contraction, EMG = electromyography, RI = reciprocal inhibition.

The first study (Kim et al. [26]) included is a single blinded randomised controlled trial with two experimental (EG1 & EG2) and one control group (CG). Thirty participants took part, 15 male and 15 female, with the average age (mean (SD)) of CG mean = 61.2(8.7), EG1 mean = 59.2(7.7), and EG2 mean = 58.5(11.8). Inclusion criteria consisted of: First episode of stroke, stable hemodynamics, Ashworth index <2 in all lower extremity (LE) muscles and a mini mental state examination (MMSE) score >24. Exclusion criteria consisted of: Orthopedic impairment, cardiovascular impairment, thrombophlebitis, significant perceptual, cognitive or communication impairment, diabetes and contraindications for tilt table. Pre- and post-intervention strength measures, taken with a hand-held dynamometer, include hip flexors, hip extensors, knee flexors, knee extensors, ankle dorsiflexors and ankle plantarflexors. Other measurements were spatiotemporal parameters of gait (gait velocity, cadence, stride length, gait symmetry ratio and double support period).

Kim et al. [26] compares 3 different types of tilt table interventions combined with standard functional training over a 3-week period. The standard functional training consisted of strengthening and stretching exercises of the limbs, postural control, and therapist guided techniques for normal movement and simple forward stepping for 30 minutes, 5 times per week. Additionally, all groups received tilt table intervention for 20 minutes a day: Control Group (CG) strapped bilaterally with safety belts, no exercise intervention; Experimental Group 1 (EG1) strapped with safety belts paretic side only, one-leg standing training with LA leg; Experimental Group 2 (EG2) strapped with safety belts paretic side only, progressive task-oriented training with the LA lower extremity. The additional tilt table intervention accumulated to 300 minutes over 3 weeks. Even

though Kim et al. [26] include strength outcome measurements, the intervention did not contain strength specific training.

The second study (Dragert & Zehr [27]) was a one group non-randomised controlled intervention, in which 19 participants (15 male and 4 female, age ranging from 26 to 81 years (mean age = 58.3 ± 12.2)) took part. Inclusion criteria consisted of: >6 months after stroke, one-sided dorsiflexor weakness, ability to stand free with or without assistive device and maintain the activity level during the study. Exclusion criteria included: Medication affecting muscle tone <3 months prior and chronic disease comorbidity. Pre- and post-intervention measures included maximal voluntary isometric contraction (MVIC) of the dorsiflexors and plantarflexors bilaterally, EMG of the soleus (SOL), tibialis anterior (TA) and vastus lateralis (VL), walking trial measurements (step cycle timing, EMG, joint kinematics in the MA knee and both ankles), and clinical measures (Timed Up and Go, Timed 10m walk, Modified Ashworth Scale, Functional ambulatory category, Berg balance scale, and Fugl-Meyer).

Dragert & Zehr [27] applied a mixed laboratory and home-based training protocol for the LA dorsiflexors. The strength training consisted of warm-up, followed by 5 sets of 5 maximal effort isometric repetitions held for 5 seconds with 2 seconds rest between contractions and 2 minutes rest between sets. Each participant had to complete 3 sessions (25 minutes) per week for 6 consecutive weeks, accumulating to 450 minutes of intervention.

In both studies included in this review, post-test measurements were compared to pre-test results to identify changes.

2.4.3 Description of Results

Kim et al. [26] found no significant differences between pre-test and post-test strength measures in the LA limb of all 3 groups. However, the MA side showed a significant strength improvement for all measured muscle groups in EG1 (one leg standing training) and EG2 (task oriented training). For the EG1 group (one leg standing training), strength gain ranged from 13.7% to 53.2% (mean = 22.6%) and dorsiflexor strength increased by 23% (p = <0.01). For the task–oriented training group improvements from 28.5% to 48% were noted (mean = 39.5%), with a dorsiflexor strength gain of 45.5% (p = <0.01). The CG had no significant strength increase. Furthermore, the strength gains in knee flexors, knee extensors, ankle dorsiflexors and ankle plantar flexors were significantly greater in EG2 than EG1. In all gait characteristics significant improvements could be shown for EG2 against CG. Also stride length, gait symmetry ratio and double support period significantly improved in EG2 compared to EG1. All characteristics except stride length showed a significant improvement in EG1 against CG. There were no significant changes noted in the CG. All results are shown in detail in Table 2.3.

In the trial by Dragert & Zehr [27], Dorsiflexor Maximal Voluntary Isometric Contraction (MVIC) significantly increased by 33.5% (p = 0.02) in the trained limb and by 31.4% (p = 0.009) in the untrained MA limb. After intervention, Timed Up and Go was significantly reduced from 18.61s to 17.41s (p = 0.05). There were no other significant changes observed in functional impairment or clinical measures. EMGmax increased significantly

in the tibialis anterior muscle in both limbs, an increase in muscle activation in the tibialis anterior of the MA side (p = 0.03) and in the soleus muscle of the LA and MA side (p = 0.005, p = 0.04) was recorded. Furthermore, the range of motion of the LA ankle increased significantly (p = 0.04), this improvement did not translate into the MA side.

Table 2.3: Results of Each Study

		Kim et al. 2014			Dragert & Zehr 2013
		CG	**EG1**	**EG2**	**EG**
Strength increase pre to post intervention MA side% (*p*- value)	Hip flexors	-14.2 (0.02)	53.2† (<0.01)	48† (<0.01)	
	Hip extension	-0.6 (0.0664)	16.6† (0.03)	28.5† (0.02)	
	Knee flexors	-0.2 (0.09)	14.7† (0.04)	43.9†‡ (<0.01)	
	Knee extension	-0.3 (0.29)	13.7† (0.03)	35.6†‡ (<0.01)	
	Ankle dorsiflexors	-1.4 (0.37)	23.0† (<0.01)	45.5†‡ (<0.01)	31.4 (0.009)
	Ankle plantarflexors	0.0 (0.6)	14.8† (0.03)	35.4†‡ (<0.01)	-4.5 (0.77)
Change in spatiotemporal parameters of gait pre to post intervention % (*p*- value)	Gait velocity	-0.2 (0.88)	9.8† (<0.01)	10.2† (<0.01)	
	Cadence	1.2 (0.39)	7.5† (<0.01)	8.6† (<0.01)	
	Stride length (MA side)	0.8 (0.45)	0.7 (0.661)	8.3†‡ (<0.01)	
	Gait symmetry ratio	-5.0 (0.07)	-50.6† (0.04)	-64.1†‡ (0.01)	
	Double support period (% cycle)	-1.4 (0.11)	-14.7† (0.04)	-28.0†‡(<0.01)	
Change in clinical measures % (*p*- value)	Timed Up & Go				-6.4 (0.05)

MA = more-affected, † = significantly different compared to CG, ‡ = significantly different compared to EG1.

2.4.4 Bias

The study by Kim et al. [26] is a single blinded randomised controlled trial (RCT), allowing for comparisons between intervention and control groups. Eight out of the 11 items in the PEDro scale [25] were satisfactory and the study was considered to have a low risk of bias according to the Cochrane risk of bias assessment tool [24]. However, allocation concealment and blinding of participants and therapists was not described. The fact that patients were allowed to choose the angle of the tilt table individually, might cause a variation in the exercise protocol between the three groups. The small sample size within this study was identified as a limiting factor.

The study by Dragert & Zehr [27] is a one group non randomised controlled intervention. The assessment of bias using the Cochrane risk of bias assessment tool and the PEDro scale proved difficult as a number of criteria within both tools could not be applied due to study design. Only 7 out of the 11 items of the PEDro scale were appropriate, 4 out of those 7 were reported to the assessor's satisfaction. Blinding of therapists, participants and outcome assessor is not reported. No control group outcome measures are obtained for comparison, which may compromise the interpretation of results as strength gain in the contralateral limb might be due to familiarization of test protocol or environment. Furthermore, the partly home-based intervention protocol could cause adherence issues. This potential problem was addressed via telephone communication between participants and therapist directly after home training sessions were completed; however, the risk of possible overtraining, under-training or incorrect technique remains. Participant profile showed a wide range of heterogeneity regarding age, time after stoke, lower extremity functional capacity etc. Participant drop-out

resulted in a small sample size (n=19); however, Dragert & Zehr [27] state that the Cohen's d effect size calculations suggests robust results. Overall the study scored 4 out of 11 in the PEDro scale, the risk of bias using the Cochrane risk of bias assessment tool was considered unclear. Detailed description of the bias assessment is shown in Tables 2.4 and 2.5.

Table 2.4: Cochrane Risk of Bias Assessment

Study	Random sequence generation	Allocation concealment	Blinding of key personnel & participants	Blinding of outcome assessment	Complete outcome data	Selective reporting	Other bias
Kim et al. 2014	Low risk: "group allocation determined by using a randomized procedure", method explained	Unclear risk, not reported	Unclear risk, not reported	Low risk "blinded evaluators"	Low risk	Low risk	Small sample number, Low risk: power analysis determined sample size. Subjects choose angle of tilt table individually, might cause a variation in exercise protocols
Dragert & Zehr 2013	N/A	N/A	Unclear risk, not reported	Unclear risk, not reported	Low risk	Low risk	Small sample number, Low risk: "Cohen's d effect size calculations suggests robust results"

Table 2.5: PEDro Risk of Bias Assessment

Item		Kim et al. 2014	Dragert & Zehr 2013
1	Eligibility criteria were specified	Yes	Yes
2	Subjects were randomly allocated to groups	Yes	N/A
3	Allocation was concealed	Not reported	N/A
4	The groups were similar at baseline regarding most important prognostic indicators	Yes	N/A
5	There was blinding of all subjects	Not reported	Not reported
6	There was blinding of all therapists who administered therapy	Not reported	Not reported
7	There was blinding of all assessors who measured at least one outcome	Yes	Not reported
8	Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	Yes	Yes
9	All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat"	Yes	Yes
10	The results of between-group statistical comparison are reported for at least one key outcome	Yes	N/A
11	The study provides both point measures and measures of variability for at least one key outcome	Yes	Yes
Total		8/11	4/11

2.4.5 Confounders

Dragert & Zehr [27] recruited participants via community stroke support groups, posters in medical offices/hospitals, and newspaper articles. This suggests participants were recruited on a voluntary basis which may result in participants with a high level of motivation and efficacy. Kim et al. [26] recruited all participants from a single inpatient setting which represents a limited sample population. The level of motivation and efficacy in participants was not measured or reported pre-test or post-test in both trials, therefore presenting a possible confounder of the results.

2.4.6 Strength of Results

In general, the standard of evidence in a RCT is regarded higher than in a one group non-randomised controlled study. Randomised controlled trials are quantitative, comparative, controlled experiments in which conclusions regarding the treatment effects may be drawn with less bias than in all other study designs, RCTs provide thorough evidence of cause and effect [28]. The only over-lapping outcome measure between the two studies is strength increase of the untrained limb. Based on best evidence synthesis guidelines [29], the combination of the results included in this review suggest at least a moderate level of evidence (statistically significant findings in outcome measures in at least one high quality RCT) for the application of cross-education of strength in stroke rehabilitation. However, neither of the studies report long-term follow-up measurements, therefore the sustainability for strength improvements is unclear.

2.5 Discussion

The purpose of this literature review was to investigate the effects of cross-education of strength on the post-stroke hemiplegic patient and its role in rehabilitation and motor function recovery.

After a systematic literature search, 2 studies complied with the inclusion criteria and were therefore considered in this review. The first study included (Kim et al. [26]) was a high quality RCT. Even though the intervention was not strength specific, the results show a clear trend towards cross-educational strength transfer in post-stroke hemiplegic patients. Task–oriented training proved more effective than one leg standing

training with significantly more strength gain in 4 out of 6 measured muscle groups. In addition to the strength gain, gait performance improvements could be noted in both experimental groups compared to the control group. In 3 out of 5 gait characteristics the task–oriented training group scored significantly higher than the one-leg standing training group. The assumption can be made that strength gain translates into gait improvements.

The second study (Dragert & Zehr [27]) was a non-randomised one group controlled trial. The results of Dragert & Zehr's study give a strong indication that cross-education of strength exists in the post-stroke hemiplegic patient and are further supported by the previously mentioned findings of Kim et al. [26]. The strength gain achieved in the untrained, MA limb was 31.4% compared to baseline measurements. Furthermore, the significant improvement in Timed Up and Go (6.4%) and muscle activity measurements also suggest a possible translation of cross-educational strength transfer towards functional task improvements.

Comparison of the two studies indicates that task-oriented strength training [26] resulted in a higher overall (mean=39.5%) and dorsiflexor strength gain (45.5%) than a specific dorsiflexor isometric contraction programme (31.4%). The smaller strength increase might be due to the different training protocols used in the two trials. Dragert & Zehr [27] applied a mixed laboratory and home training programme, which might lead to less accurate performance of the intended exercise protocol. Participants conducted two sessions per week at home and one in the laboratory; this could lead to undertraining or poor training technique, which may negatively affect the magnitude of

strength gain. The participants of the trial by Kim et al. [26] were consistently supervised throughout all training sessions. In a comparison of a supervised clinical exercise programme with a home-based exercise programme to treat osteoarthritis in the knee, Deyle et al. [30] found that subjects in the clinic treatment group achieved approximately twice as much improvement compared to subjects who performed similar unsupervised exercises at home. Furthermore, the latter were training 5 days per week compared to 3 days per week in the dorsiflexor trial. Total intervention times given by the authors, indicates longer training periods in the trial by Dragert & Zehr [27] accumulating to 450 minutes compared to 300 minutes [26]. However, when actual times of repetitions, contractions and rest periods are considered, the three warm up sets plus the five sets of maximal dorsiflexor contractions [27] required approximately 5 minutes of training time per session, accumulating to 90 minutes of total intervention time. Even though there is no breakdown of the actual training time in the study by Kim et al. [26], the assumption can be made that total training time was greater than 90 minutes which may be a contributing factor to the higher strength gain.

The average dorsiflexor strength of the MA leg at pre-intervention was 3.4Nm in the trial by Kim et al. [26] compared to 9.18Nm for Dragert & Zehr [27]. This difference in baseline strength, combined with the fact that a more novel task-oriented training programme was used by Kim et al. [26], could be an influencing factor to the high variation of strength gains between the studies. It has been shown that a lower strength level at the beginning of a strengthening programme allows for higher and more rapid improvements [31]. Likewise the more novel or less familiar a training task is, the greater the potential strength transfer [9]. Furthermore, Dragert & Zehr [27] had no

inclusion/exclusion criteria regarding the Modified Ashworth Scale, 6 out of the 19 participants were graded 2 and higher. This is very much in contrast to the tilt table trial [26], which only included patients who were below 2 on the Modified Ashworth Scale, this may indicate that higher levels of spasticity reduce the ability for strength gain. A systematic review by Lieber et al. [32] reports that muscle tissue in patients presenting with spasticity is dramatically altered. Another factor contributing to higher training effects in the trial by Kim et al. [26] is the incorporation of a purposeful and task-oriented exercise protocol. For best outcomes exercise tasks need to be specific and should be practiced as meaningful tasks [33, 34].

Characteristics of participants in the trial by Dragert & Zehr [27] were very much heterogeneous, e.g. months post-stroke ranged from 6–284, whereas participants in Kim et al. [26] show more homogeneity in mean time after stroke of 6.71 ± 4.23 for the control group, 8.12 ± 4.95 for EG1 and 7.99 ± 3.85 for EG2. Such heterogeneity could be a possible influence on study results and make specific interpretations more challenging.

In the literature review by Carroll et al. [4] it is clearly stated that the strength increase in the untrained limb always corresponds to increases seen in the trained limb. Surprisingly, Kim et al. [26] reported no significant strength increase in the LA trained lower limb and there is no attempt to explain this finding. During our literature search we came across 2 studies which trained the MA side and reported strength outcome measures of the LA untrained side. This did not comply with the inclusion criteria (4 and 5 as outlined in Methodology 2.2.) for this literature review; however, the studies

describe the phenomenon of cross-education from the MA side to the LA side after stroke and therefore deserve a brief mentioning.

Clark & Patten [35] conducted a high intensity resistance training intervention for the MA lower extremity. After completion a significant increase in power in the LA untrained limb was reported. Results showed increased power in the eccentric strength training group (p = <0.0001) following resistance training, with the eccentric phase increase (+14%) being marginally larger than the concentric phase increase (+12%, p = 0.05). Whitall et al. [36] compared the rehabilitation effects of bilateral arm training with rhythmic auditory cueing (BATRAC) with dose-matched unilateral therapeutic exercises (DMTE). As part of the secondary outcome measures, isokinetic and isometric strength of both arms were reported. For this review, only results of the DMTE intervention were of interest. The unilateral exercises performed were weight bearing with the MA arm (elbow fixed), and opening the hand with finger extension. After completion there were significant isometric strength increases for the MA upper limb reported; however, this did not carry over to the LA untrained side. There were no significant isokinetic strength gains noted for the MA trained limb or for the LA untrained limb. It appears that cross-education of strength from the MA limb to the LA limb is possible, providing sufficient intensity and overload are applied. Even though these studies are not considered relevant to this review, which examines strength transfer from the LA limb to the MA limb, they support the theory that cross-education of strength is achievable after stroke.

2.6 Conclusion

Overall there is moderate to strong evidence [29] that the phenomenon of cross-education from the LA side to the MA side can be applied in stroke patients and has an impact on the recovery of muscle strength. Furthermore, there are indications that the improvement of strength following unilateral training of the LA limb also translates into motor function recovery. Following these findings, it is feasible to suggest that cross-education of strength should be implemented in post-stroke rehabilitation. However, due to the small number of studies with restricted numbers of participants and the trial's limitations, more high quality studies are needed to achieve a more satisfying conclusion regarding the effects of cross-education of strength on motor recovery after stroke. It is recommended that additional high quality randomised controlled trials are conducted to substantiate our findings and to further support the use of cross-education in stroke rehabilitation.

Authors and Contributors

DS and ME designed the search strategy and applied the same independently in different databases. The titles and abstracts resulting from the database search were screened for eligibility by DS and ME and final decisions regarding inclusion were made in discussion with PB and KM. DS and ME extracted data and equally contributed to the writing of this review which was critically revised with assistance from PB and KM.

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3.0 Peak Torque, Rate of Torque Development and Average Torque of Isometric Ankle and Elbow Contractions Show Excellent Test-Retest Reliability

Simpson, D., Ehrensberger, M., Broderick, P., Regan, J., Nulty, C., Monaghan, K. Peak torque, rate of torque development and average torque of isometric ankle and elbow contractions show excellent test-retest reliability. Hong Kong Journal of Physiotherapy 2018 October; 39 (1): 1-10.

3.1 Abstract

Background: Peak Torque (PT), Rate of Torque Development (RTD) and Average Torque over a single contraction (AT) assess the three components of muscle function during isometric contractions. Surprisingly, AT has never been reported or its reliability confirmed.

Objectives: This study aims to establish protocol reliability for ankle dorsiflexion and elbow extension isometric muscle function (PT, RTD, AT) in healthy participants using the Biodex System 3 Dynamometer.

Methods Twelve participants (6 male, 6 female, mean age 39.8± 16.0 years) performed four maximal isometric contractions on two occasions. Intraclass Correlation Coefficients (ICC), Typical Error (TE), and Coefficient of Variation (CV) for PT, RTD and AT were reported.

Results: The ICC for all strength parameters varied from 0.98 – 0.92. TE for ankle dorsiflexion PT was 1.38Nm, RTD 7.43Nm/s, and AT 1.33Nm, CV varied from 6.26± 6.25% to 11.72±8.27%. For elbow extension, TE was 3.36Nm for PT, 14.87Nm/s for RTD and 3.03Nm for AT, CV varied from 5.97± 4.52% to 18.46± 14.78%.

Conclusion: Maximal isometric ankle dorsiflexion and elbow extension PT, RTD and AT can be evaluated with excellent reliability when following the described protocol. This testing procedure, including the application of AT can be confidently applied in research, exercise or clinical settings.

3.2 Introduction

Muscular strength is defined as the production of maximal contractile force against a resistance in a single contraction [1]. To ensure regular functionality of the human body, muscle strength is a paramount requirement. Joint torque produced by muscle strength contributes to normal movement and athletic performance, assists in joint stability and posture control during activities of daily living and plays a vital role in the maintenance of functional independence during the aging process [2, 3].

The measurement of maximal muscular strength (Peak Torque) is often used to determine physical condition and the effects of training or rehabilitation programmes [4]. However, from a functional perspective, the ability to generate torque quickly (Rate of Torque Development) and to maintain torque (Work/Average Torque over a single contraction) may be more important than being able to generate high maximal force. Although Peak Torque is the universal standard parameter used to measure strength, changes in Rate of Torque Development, Work or Average Torque over a single contraction may represent the most important adaptations occurring from training or rehabilitation [5, 6]. A comprehensive muscle function assessment should include all three parameters [6, 7], however the parameter Average Torque over a single contraction has not previously been reported.

First introduced as a device for muscle strength measurement in 1967 by Thistle et al. [8], isokinetic dynamometry is the gold standard for assessing muscular functionality among athletic populations as well as populations engaging in rehabilitation programmes [9].

The application of isokinetic dynamometry for assessing muscular functionality in research and clinical practice requires testing procedures of high reliability, which refers to consistent reproduction of results when tests are performed multiple times under similar conditions [10]. Drouin et al. [11] report excellent 'mechanical reliability' (ICC 0.99) for the Biodex System 3 when using force applied by a weight on the dynamometer arm. However, potential for repeatability error increases when applying test protocols with live subjects.

Numerous studies have investigated protocol reliability with excellent results (ICC >0.75), primarily assessing in an isokinetic mode and focusing on knee extension or flexion [12-15]. However, isometric mode is regarded as a safer and more appropriate mode for maximal strength testing, particularly in populations who have restricted range of motion or are unable to comply with isokinetic procedures [16]. Currently, isometric reliability remains under-explored. Studies include Peak Torque and Rate of Torque Development only, Average Torque was not yet investigated [17, 18].

Peak Torque, the most widely reported muscle strength parameter, represents the maximum torque produced at a single point of contraction [19-22]. Rate of Torque Development or explosive muscular strength is key during movement performances, characterized by reduced contraction times such as sprinting or boxing [23-25]. In the older or clinical population, Rate of Torque Development can be an indicator for the risk of falls. After sudden postural perturbation, it is important to be able to generate contractile torque quickly to regain balance [6].

Average Torque over a single isometric contraction can replace the commonly used isokinetic parameter Work [5]. Work represents the capability to generate muscle torque throughout the full range of movement [22, 26], this parameter cannot be applied during isometric contractions as there is no movement or distance achieved. In isometric contractions, Average Torque over a single contraction represents the comparable capacity to maintain torque throughout the contraction time interval [5], which is an important factor when performing activities of daily living. Daily tasks generally do not require maximal strength output but the uphold of a lower torque over a period of time, e.g. lifting a glass of water to drink, putting the washing on the washing line etc. The ability to sustain a given level of torque production over time, is the most precise indicator of functional muscle rehabilitation [27]. It is possible for tested muscle groups to reach rehabilitation standards for maximal muscle strength without regaining the ability to sustain this standard over time, Peak Torque often returns to pre-injury levels before Average Torque or Work [7].

Considering the importance of the strength parameter Average Torque, for the evaluation of rehabilitation programmes and the appropriateness of isometric strength testing regarding safety and limited range of motion for patients, it is surprising that Average Torque over a single contraction was never before reported or its reliability established.

The current body of literature regarding isokinetic strength testing indicates that human joint actions such as ankle dorsiflexion and elbow extension have been investigated infrequently. Ankle dorsiflexion is a vital movement during the gait cycle and balance

control [28, 29]; likewise, elbow extension represents a movement of everyday function such as reaching [30]. The reliability of both movements has been investigated in an isometric mode in highly homogeneous populations, e.g. older women (mean age 73.3±4.7) or elite swimmers [17, 18]. These studies report excellent reliability (ICC 0.86-0.97) for isometric ankle dorsiflexion and elbow extension Peak Torque and Rate of Torque Development only.

To date no study has assessed the test-retest reliability of all three most important parameters for muscle function (Peak Torque, Rate of Torque Development, Average Torque) for isometric ankle dorsiflexion and isometric elbow extension using the Biodex System 3.

This study hypothesised excellent protocol reliability when measuring maximal isometric ankle dorsiflexion and elbow extension strength in healthy non-athletic participants using the Biodex System 3 Isokinetic Dynamometer, with particular focus on the currently unexplored parameter Average Torque over a single isometric contraction. Furthermore, this study set out to develop novel recommendations that ensure excellent reliability when assessing isometric Peak Torque, Rate of Torque Development and Average Torque using the Biodex System 3 Isokinetic Dynamometer with the Biodex advantage software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA).

3.3 Methods

Design

This study followed a study of repeated measures for test re-test reliability design. Each participant was familiarised in a separate session prior to the main testing at two time points. The same investigators conducted all tests and performed the verbal cueing in a consistent manner for all sessions and participants.

Participants

Twelve participants (Table 3.1), 6 male and 6 female (age 39.8± 16.0 years) (mean ± SD), height 1.68 ± 0.09m, weight 74.1 ± 11.1Kg) were recruited for this study. Both genders were recruited as previous studies using the Biodex System 3 for isometric strength use the same protocol for both males and females [31, 32]. Subjects were included if they 1) were aged between 18-65 years, 2) did not participate in strenuous exercise for 48 hours prior to testing and 3) were in good health with no reported musculoskeletal dysfunction or surgical intervention in the tested limb within the last 12 months. Subjects were excluded if they 1) suffered from cardiovascular, respiratory or neurological impairments that would prevent physical strengthening activity or if they 2) were pregnant. The Health Science and Physiology Ethics Committee, Department of Life Science, Institute of Technology Sligo granted ethical approval (Appendix A). Prior to recruitment all participants were provided with an information sheet (Appendix B) and were required to sign informed consent (Appendix C) according to the Declaration of Helsinki.

Table 3.1: Description of Participants

Subject ID	Sex	Age (yrs.)	Height (m)	Weight (Kg)
1	F	23	1.66	68.5
2	M	24	1.77	82.1
3	M	26	1.82	76.5
4	M	25	1.73	53.6
5	F	24	1.57	83.1
6	F	28	1.64	64.4
7	F	52	1.64	78.6
8	F	53	1.57	58.6
9	M	64	1.7	77.8
10	M	51	1.82	92.6
11	M	58	1.64	73.6
12	F	50	1.63	79.5
Mean		39.8	1.68	74.1
SD		16	0.09	11.1

Equipment

All tests were conducted on the Biodex System 3 Pro Isokinetic Dynamometer with the Biodex advantage software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA). The standard Biodex ankle unit attachment with limb support and the Biodex Velcro straps were used for ankle dorsiflexion (Figure 3.1). The standard shoulder/elbow unit attachment with limb support was used for elbow extension (Figure 3.2). Before testing each subject, the system was calibrated according to the procedure in the Biodex System 3 manual [33].

Figure 3.1: Participant Positioning for Ankle Dorsiflexion

Figure 3.2: Participant Positioning for Elbow Extension

Participant Positioning

Ankle dorsiflexion

Participants were positioned in stocking feet on the adjustable chair with the right leg elevated. The right foot was placed on the ankle unit footplate and the right knee was supported by the standard limb support, both were tightly secured with the Velcro straps provided (Figure 3.1). Maximal isometric ankle dorsiflexion strength was assessed at the ankle joint angle of 10° plantarflexion (anatomical reference of 0° was set with the tibia perpendicular to the sole of the foot), 120° knee flexion [34] and 75 ° hip flexion [33]. The axis of rotation was aligned with the body of talus, fibular malleolus, and through the tibial malleolus. The hip and knee angle were adjusted by changing the distance between the chair and the footplate and by altering the height of the knee support (Appendix D).

Elbow extension

Participants were positioned on the adjustable chair with their right upper arm supported by the standard limb support (Figure 3.2). Maximal isometric elbow extension strength was assessed at 85° elbow flexion (angle of most force production) [35], where 0° refers to full elbow extension, the shoulder joint was positioned at 45° shoulder flexion [30]. The axis of rotation was aligned with the centre of the trochlea and the capitulum, bisecting the longitudinal axis of the shaft of the humerus. Participants were instructed to hold the handle of the elbow/shoulder attachment with a closed grip. A 5cm space was consistently kept between the attachment and the anatomical axis of rotation; elbow and wrist joints were aligned with the wrist in neutral position by adjusting the chair, the dynamometer and the length of the arm/shoulder attachment.

The shoulder angle was achieved by altering the height of the limb support (Appendix E). All joint angles were measured with a hand-held goniometer; range of motion measurement followed the Biodex System 3 procedure. Participant positioning, e.g. chair height, dynamometer height, attachment length etc. was recorded during familiarisation to ensure consistent set-up for all testing sessions.

Test-Protocol

All testing was performed on the Biodex System 3 Isokinetic Dynamometer in the Health Science & Physiology Laboratory. The protocol was performed at three time points: **Familiarisation** (Pre-Test), **Test 1** (>48 hours post-familiarisation) and **Test 2** (at least 7 days post-test 1). For all participants, laboratory conditions were consistent and all testing was conducted on the right side only to facilitate data collection [36].

During all sessions, the lower limb was warmed up first and ankle dorsiflexion was assessed, the upper limb was then warmed up and elbow extension assessed. The warm-up consisted of 3 minutes of leg/arm cycling performed at a level of perceived exertion of 10-12 on the Borg scale [37] and 1 set of 5 repetitions of unilateral, submaximal (perceived 50% of MVC), isometric contractions held for 5 seconds, separated by 5 seconds of rest [38]. Following the warm-up maximal isometric strength was assessed using 4 maximal isometric contractions held for 5 seconds, separated by 45 seconds of rest [39]. Participants were blinded to the number of repetitions being recorded to avoid 'saving energy' for later contractions.

Verbal cues given by the investigator were consistent for all participants during all sessions. For each contraction participants were instructed to pull their toes towards their shin as 'hard and as fast as possible' for ankle dorsiflexion assessment and to push their fist towards the ground as 'hard and as fast as possible' for elbow extension assessment. Each participant was asked to give maximal strength each time and not to hold back. The starting sign given by the investigator was a count down from 3, 2, 1 followed by 'go'. During the 5-second contractions the principal investigator would loudly encourage the participant by using the verbal cues 'go, go, go, keep going, keep going, keep going and rest'.

Data Analysis

From each set of 4 contractions, assessors identified the contraction with 1) the highest Peak Torque in Nm, 2) the highest Rate of Torque Development in Nm/s within the first 0.20sec of a single contraction, and 3) the highest Average Torque in Nm of a single contraction. The time of contraction onset was identified manually (gold standard) [40-42], defined as the last trough before a sharp rise. Contractions were excluded if the participant performed an early contraction or counter movement before contraction onset. Counter movement refers to the lengthening of a muscle prior to contraction, resulting in a greater strength output and is indicated by a downward deviation of more than 10% of baseline torque in the resting position [43].

Statistical Analyses

Data were analysed using the statistical package for social sciences (SPSS) for Windows (Version X, Chicago, IL, USA). Mean Peak Torque, Rate of Torque Development and

Average Torque were compared using a paired samples t-test. The Intraclass Correlation Coefficient ($ICC_{2,1}$) was used to calculate relative reliability. The first subscript number represents the 'model' and the second subscript number signifies the 'form'. Model 2 was chosen as the appropriate model when each subject is measured by each assessor, and assessors are considered representatives of a larger population of similar assessors. Form 1 represents the use of a single score, in contrast to the use of a mean of multiple assessors' scores [44]. As a statistical measure of absolute reliability, Typical Error and the Coefficient of Variation (CV) were calculated. These values represent the expected random variability in measurement between two assessment time points [10].

Typical Error is expressed in the measurement unit it refers to, calculated as:
Typical Error = $SD_1/ \sqrt{2}$, where SD_1 is the standard deviation of the differences between the two measurements [10, 19].

CV is expressed as a percentage score. For a sample of individuals, it is recommended to calculate a mean CV from individual CV's.
CV= 100 * SD_2/ mean, SD_2 and the mean are calculated from the data of each individual [45].

3.4 Results

For ankle dorsiflexion 5 out of 96 (5.2%) contractions were excluded, for elbow extension 21 out of 96 (21.8%) were excluded.
Individual results for each strength parameter for Test 1 and Test 2 are given in Table 3.2. The means, standard deviations and reliability values for Peak Torque, Rate of

Torque Development and Average Torque are presented in Table 3.3. There were no significant differences between Test 1 and Test 2 for all measures for both ankle dorsiflexion and elbow extension (p = >0.05).

Table 3.2: Individual Results for Peak Torque, Rate of Torque Development and Average Torque for Each Test

	Ankle Dorsiflexion						Elbow Extension					
	Test 1			Test 2			Test 1			Test 2		
Subject ID	PT (Nm)	RTD (Nm/s)	AT (Nm)	PT (Nm)	RTD (Nm/s)	AT (Nm)	PT (Nm)	RTD (Nm/s)	AT (Nm)	PT (Nm)	RTD (Nm/s)	AT (Nm)
1	22.6	51.5	19.28	23.6	62.5	19.53	23.7	47.5	20.29	24.1	21.5	19.15
2	37.8	163.5	35.36	43.5	196	40.48	81.6	194	66.08	94.8	249	80.96
3	43.9	214	40.1	45.2	215	41.7	67.7	234.5	61	80.7	169.5	61.16
4	21.3	101.5	18.59	25.4	122	23.08	29.7	105.5	25.6	28.6	94	23.49
5	27.7	125	22.78	26.6	114.5	24.04	45	147	36.35	41.5	81.5	34.55
6	25.9	118	23.86	25.2	104.5	22.9	35.9	148	33.43	33	126	29.1
7	21.7	61.5	20.18	21.7	89.5	20.17	31.9	80.5	29.11	33.4	97.5	28.37
8	19.7	86	18.09	14.4	58.5	13.52	24.4	70.5	21.76	25.6	76.4	23.94
9	24.3	100.5	22.73	22	85	18.82	70.2	193	61.22	58.7	218.5	52.2
10	44.7	199.5	42.38	44.3	214	41.48	65.8	223.5	57.74	61.4	214	57.14
11	33.1	147	29.8	36.9	178.5	29.5	68.7	123.5	60.23	72.5	156.5	57.66
12	27.5	116	24.73	25.4	112	22.68	37	74	34.61	33.9	55.5	30.05

PT = Peak Torque, RTD = Rate of Torque Development, AT = Average Torque, Nm = Newton Metres, Nm/s = Newton Metres per second

Table 3.3: Means, Standard Deviations and Reliability Measures for Peak Torque, Rate of Torque Development and Average Torque

	Peak Torque (Nm)	Rate of Torque Development (Nm/s)	Average Torque (Nm)
Ankle Dorsiflexion			
Test 1 (n=12)	29.18 ± 8.73	123.67 ± 50.14	26.49 ± 8.47
Test2 (n=12)	29.52 ± 10.25	129.33 ± 56.89	26.49 ± 9.64
T1-T2 Difference (*p*)	0.72	0.35	1
Typical Error	1.38	7.43	1.33
ICC (95% CI)	0.98 (0.91-0.99)	0.96 (0.88-0.99)	0.98 (0.92-0.99)
CV (%)	6.26 ± 6.25	11.72 ± 8.27	6.44 ± 6.69
Elbow Extension			
Test 1 (n=12)	48.47 ± 20.83	136.79 ± 63.51	42.29 ± 17.49
Test 2 (n=12)	49.02 ± 23.807	129.99 ± 71.50	41.48 ± 19.54
T1-T2 Difference (*p*)	0.79	0.53	0.63
Typical Error	3.36	14.87	3.03
ICC (95% CI)	0.98 (0.92-0.99)	0.92 (0.74-0.98)	0.98 (0.92-0.99)
CV (%)	6.05 ± 3.82	18.46 ± 14.78	5.97 ± 4.52

The highest peak torque, the highest rate of torque development and the highest average torque of the 4 contractions of each individual in test 1 and test 2 were used to calculated means, standard deviations and for the reliability analyses. ICC = Intraclass correlation coefficient, CI=Confidence Interval, CV = Coefficient of variation, n = number of subjects, T1 = Test 1, T2 = Test 2, *p* = *p* -value.

Reliability Analysis

Relative reliability (ICC) was excellent [46] for ankle dorsiflexion (Peak Torque 0.98, Rate of Torque Development 0.96, Average Torque 0.98) and for elbow extension (Peak Torque 0.98, Rate of Torque Development 0.92, Average Torque 0.98).

Typical Error for ankle dorsiflexion Peak Torque was 1.38Nm, Rate of Torque Development 7.43Nm/s, and Average Torque 1.33Nm, CV was 6.26% for Peak Torque,

11.72% for Rate of Torque Development, and 6.44% for Average Torque. For elbow extension Typical Error was 3.36Nm for Peak Torque, 14.87Nm/s for Rate of Torque Development and 3.03Nm for Average Torque, CV was 6.05% for Peak Torque, 18.46% for Rate of Torque Development, and 5.97% for Average Torque.

3.5 Discussion

According to Fleiss [46], ICC's in the range of 0.5-0.6 = fair, 0.6-0.7 = good, and >0.75 = excellent test re-test reliability. When measuring Peak Torque, Rate of Torque Development and Average Torque for maximal isometric ankle dorsiflexion and elbow extension with the described protocol using the Biodex System 3 Isokinetic Dynamometer, this study established that the test re-test reliability was excellent (ICC 0.92 – 0.98). Excellent reliability implies high precision of measurement and allows confidence when assessing strength changes following exercise or rehabilitation programmes [10]. The combination of all three strength parameters offers a comprehensive analysis of muscle function or recovery [7].

Relative and absolute reliability established in this study is higher than previously reported values for ankle dorsiflexion and elbow extension [17, 18, 30, 38]. Previous reliability studies for ankle dorsiflexion and elbow extension have reported Peak Torque ICC values ranging from 0.80 to 0.97 [17, 18, 30, 38]. Contraction mode may be an influencing factor; joint movement during isokinetic testing appears to result in lower reliability values [30, 38]. Furthermore, it is important to record participant positioning to ensure exact replication of protocol [18]. It is not surprising that ICC values are slightly

lower due to potential positioning difficulties when assessing clinical populations, particularly if equipment modification is required [30].

Reliability (ICC, typical error and CV) for Rate of Torque Development in this study is generally lower than for Peak Torque and Average Torque. Participants were instructed to contract as hard and fast as possible. Although this is recommended practice, participant's attention may be more focussed on reaching highest peak values, with less emphasis on producing explosive muscular strength [47]. However, Rate of Torque Development ICC values in this study are higher than in previous similar studies (0.84 – 0.86) [17]. Variability in the methods for obtaining Rate of Torque Development values may be one reason for differing results. In this study, Rate of Torque Development was calculated using the manual procedure recommended by Biodex System 3 (initial contraction onset to 0.2sec) [33]. Rate of Torque Development has previously been reported for other time intervals, e.g. 0-50ms, 0-50% of Peak Torque and 40-80% of Peak Torque [17, 48]. Considering that Rate of Torque Development is an indicator of initial contraction torque [23-25], measurements should start at contraction onset. It is worth noting that the Biodex advantage software version 3.45 only allows time intervals of 200ms when analysing data using the curser function, or time intervals of 100ms when using the 'log to file' application. This limits the ability to analyse Rate of Torque Development at shorter time intervals.

This study is the first to include Average Torque over a single isometric contraction. The findings suggest the analysis of Average Torque is highly reliable for ankle dorsiflexion (ICC 0.98) and elbow extension (ICC 0.98) and should therefore be implemented in

future isometric strength testing studies. To assess a participant's torque generating capacity in all aspects, it is important to include all three of the aforementioned strength parameters, as one parameter alone does not provide a comprehensive insight into muscular function.

In this study, values for absolute reliability (typical error and CV) are lower than previously reported [17, 38]. Differences may be due to the lack of familiarisation with the testing equipment and procedure [17]. A lack of a familiarisation session may affect scores of the second testing session due to a learning effect [17]. Dynamic modes appear to result in lower absolute reliability [38], i.e. higher typical error and CV values.

Early contractions and counter movements occurred more frequently during elbow extension than ankle dorsiflexion. Observations during testing revealed that more efficient participant positioning could be achieved when performing ankle dorsiflexion compared to elbow extension. During ankle dorsiflexion all involved joints can be firmly stabilised. In comparison, during elbow extension the upper arm cannot be firmly strapped to the elbow support due to contraction restriction, potentially resulting in higher technique variability. It may be necessary to address this issue when giving verbal instructions.

Compared to other reliability studies, this study consists of a relatively small sample size (n = 12). However, it is advised to base sample size calculations for reliability studies on the ICC value and width of the confidence interval. The higher the ICC value and the narrower the width of the confidence interval, the smaller the sample size requirement

[49, 50]. With a z alpha/2 ($z_{\frac{\propto}{2}}$) score of 1.96 (a constant for studies with a 95% confidence interval) and based on the lowest ICC value (0.92) and its widest width of confidence interval (0.24) achieved in this study, the sample size of 12 participants is sufficient when calculated according to Shoukri et al. [51]:

$$k = \frac{8z^2_{\frac{\propto}{2}}(1-p)^2(1+(n-1)p)^2}{w^2\, n(n-1)}$$

k = number of subjects required, $z_{\frac{\propto}{2}}$ = 1.96, *n* = number of tests, *p* = ICC value, *w* = width of 95% confidence interval.

<u>Recommendations for achieving excellent reliability</u>

Assessor observation and comparison with previous studies has led to a number of recommendations resulting in excellent reliability when closely followed:

- Familiarisation session should take place prior to Test 1.
- Subject positioning should be carefully recorded and reproduced at each testing session.
- Participants should be blinded to the number of repetitions being recorded to avoid 'saving energy' for later contractions. Each participant should be instructed to give maximal strength each time and not to hold back.
- To ensure accurate curve analysis, the designed protocol should represent the desired number of repetitions as sets consisting of 1 repetition. For example, in this study 4 sets of 1 repetition were implemented rather than 1 set of 4 repetitions. When recording numerous repetitions per set, strength curves

cannot be viewed individually, this may compromise the accuracy of manual analysis.

- To reduce the number of excluded contractions, how to avoid counter movements should be explained to participants and the importance to wait for "go" before contracting should be emphasised.
- Calculation of the novel parameter Average Torque over a single contraction using the Biodex Software: select a specific contraction in the curve analysis programme, click on the 'log to file' application and save the data as a text document. The text document can then be opened in a spread sheet and calculations performed as normal.

Limitations

The inclusion criteria regarding age of participants in this study allowed for a wide age range to be recruited. Participation was voluntary and open to all staff and students of the Institute of Technology. This resulted in high age heterogeneity, which differs from other studies; however, this study did not aim to assess reliability according to age category and there are no obvious reasons why age in a healthy population should affect reliability. Although the relatively small sample size is sufficient for reliability testing, it does not allow for subgroup analysis, e.g. age categories, sex, dominant vs. non-dominant side.

3.6 Conclusion

This study is the first to establish excellent test-retest reliability for all three strength parameters (Peak Torque, Rate of Torque Development and Average Torque) for

isometric ankle dorsiflexion and elbow extension for the described protocol using the Biodex System 3 Isokinetic Dynamometer. Furthermore, this study has proven Average Torque to be a reliable strength parameter when testing in an isometric mode. When the aforementioned recommended procedures are closely followed, this testing protocol can be confidently applied in research, exercise science or clinical populations, in which impairments in ankle dorsiflexion and elbow extension are common.

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4.0 Cross-Education plus Mirror Therapy as a Post-Stroke Rehabilitation Intervention: A Case Study

Simpson, D., Ehrensberger, M., Broderick, P., Horgan, F., Blake, C., Roberts, D., Monaghan, K. Cross-education plus mirror therapy as a post-stroke rehabilitation intervention: A case study. Physiotherapy Practice and Research. 2019 February; 40 (1): 51-57.

4.1 Abstract

Background: A large proportion of patients with chronic stroke have permanent lower limb functional disability, leading to reduced levels of independent mobility. Individually, both cross-education of strength and mirror therapy have been shown to improve aspects of lower limb functioning in patients with stroke.

Objectives: This case report examined whether a new combination of both interventions would lead to improvements in lower limb functional disability for a patient with chronic stroke.

Methods: The participant was a 66-year-old male who had a first episode right hemisphere infarction (6 months post-stroke). Due to hemiparesis and spasticity, he had lower limb motor impairment. The participant engaged in a combination of cross-education strength training and mirror therapy 3 days per week, for 4 weeks. Outcome measures were chosen to cover the three levels of human functioning as outlined in the International Classification of Functioning, Disability and Health framework

Results: Maximal Voluntary Contraction increased in both limbs, Modified Ashworth Scale and the 10 Metre Walk Test demonstrated clinically meaningful change and Timed Up and Go showed substantial improvement. Improvements in function were reflected in a positive increase in self-perceived participation scores.

Conclusion: The positive outcomes from this new combination therapy for this participant are encouraging given the relatively small dose of training and indicate the potential benefit of mirror therapy as an adjunct to cross-education training for improving lower limb strength, spasticity and motor function in patients with chronic stroke.

4.2 Introduction

Stroke is the leading global cause of adult disability [1]. Of the fifteen million people who suffer a stroke annually, five million are permanently disabled [1]. Twelve months after stroke 35% of patients who presented with lower limb hemiparesis will still show reduced functional ability [2-4], associated with high levels of anxiety and poorer quality of life [5].

Hemiparesis, a one sided muscle weakness [6, 7], spasticity, an increased muscle tone due to stretch reflex disorder [8], and reduced motor function are the most commonly reported physical impairments post-stroke [9-12]. Hemiparesis following stroke is commonly more noticeable in distal muscle groups [13]. Maximal dorsiflexor torque of the most-affected (MA) limb can be reduced to as little as 38% of the less-affected (LA) limb [14]. Spasticity develops in 25%-30% of patients and in the lower limbs occurs predominantly in the ankle [10, 15]. Ankle dorsiflexion dysfunction is particularly common due to weakness and spasticity, contributing to walking impairment [16, 17]. Commonly performed rehabilitation techniques are based on repetitive methods, e.g. active assisted and passive manual movements, primarily addressing the MA limb directly [18]. In many cases, the impairment of the MA limb is too great to be engaged in active exercise, which denies the possibility of independent home training as therapist assistance is needed [19]. Therapy sessions mainly take place in acute or outpatient settings and prove to be expensive, labour intensive and require travel for patients [20]. Consequently, there is a need for community or home-based post-stroke rehabilitation techniques that are evidence based, cost effective, patient centred and allow for early supported discharge [9]. Innovative rehabilitation techniques that primarily engage the

LA limb, have been recommended [21] and may have potential to reduce the expense and labour required during traditional physical interventions.

Cross-education, the performance improvement in the untrained homologous muscle after unilateral exercise [22, 23], was first described by Scripture et al. in 1894 [24]. A meta-analysis of 31 cross-education studies [25] found definite evidence supporting the existence of the phenomenon of cross-education with the average degree of strength transfer being 11.9% of initial strength. To the healthy person there is no obvious relevance of the phenomenon as they usually strive to improve function and strength in both limbs simultaneously. From the perspective of rehabilitation, however, the relevance of cross-education emerges as a way to benefit the recovery of function after unilateral orthopaedic injury or neurological damage [26]. Exact mechanisms mediating cross-education are still up for debate. However, adaptations occur primarily on a neurological level rather than a muscular level and increased activation in the untrained M1 results in increased neural drive originating from the untrained motor cortex [27, 28].

The use of cross-education as a treatment option for the lower extremity in stroke rehabilitation is a relatively new concept. Dragert & Zehr [29] were the first to investigate the phenomenon in the stroke population, reporting strength increases of 34% in the trained (LA) limb and 31% in the untrained (MA) limb after 6 weeks of maximal isometric contractions. They also report a positive effect on motor function with significant improvements in Timed Up and Go (TUG) scores. Although the study did not find significant improvements in spasticity, previous studies have reported a

reduction in contralateral H-reflex excitability during unilateral training [30, 31]. A recent systematic literature review [32] supports the findings and concludes that neuromuscular cross–education effects can be effective in the lower extremity post-stroke.

It has been hypothesised that cross-education in the lower extremity may be further augmented by combining the strengthening therapy with mirror therapy (MT) [33, 34]; however, this has never been assessed in a stroke population. Mirror therapy, where a mirror is placed in the patient's mid-sagittal plane, reflecting the LA side as if it were the MA side [34], improves motor function and activities of daily living post-stroke [35]. When observing the mirror, movements of the LA limb create the illusion of normal movements of the MA limb. The therapeutic approach is based on visual stimulation, activating the Mirror Neuron System (MNS) [35]. Sutbeyaz et al [36] showed significant improvements in lower limb motor functioning with a 36% increase in Functional Independence Measure scores following dynamic ankle dorsiflexion movements with mirror visual feedback. Studies also indicate that MT can facilitate neuroplasticity by stabilising cortical activity within the primary motor cortex (M1) and consequently restore motor command execution and function [37, 38].

A recent study [21] has shown that the cross-education effect in a non-clinical population is indeed further augmented by combining cross-education with MT. The study concluded that untrained limb strength increased significantly in the mirror training group (61%) when compared to strength training only (34%). This combination of therapies has never been investigated in a chronic stroke population, therefore the

combined effects on hemiparesis, spasticity and motor function remain unexplored. This is the first study to investigate the potential of cross-education of strength plus MT for reducing spasticity and improving post-stroke motor function in the lower limb.

This case report explored the feasibility and effectiveness of the new combination therapy for the purpose of improving lower limb strength, spasticity and motor function for a person with chronic stroke. The authors hypothesised that this combination therapy would lead to clinically meaningful improvements as indicated by the minimal detectable change (MDC) and the minimal clinically important difference (MCID) for each outcome measure. The MDC indicates a clinically significant amount of change required to exceed measurement variability, the MCID indicates clinically meaningful change for the patient [39].

4.3 Methods

4.3.1 Participant

This case report examines an ambulatory 66-year-old male participant (Table 4.1) with first episode of right hemisphere infarction, six months prior to the beginning of the trial, with spastic hemiparesis in his dominant (left) lower limb. The participant lived independently in the community and was ambulatory but presented with residual strength, motor and gait impairment due to his stroke. By taking part in cross-education strength training and MT the participant hoped to improve the functioning of his MA limb. The participant was provided with an information sheet (Appendix F) and informed consent (Appendix G) to participate in the study was given based on procedures

approved by the Research Ethics Committee at Sligo University Hospital (Appendix H) and which complied with the Declaration of Helsinki.

Table 4.1: Participant Characteristics

Age (Years)	66
Gender	Male
Height (cm)	173
Weight (Kg)	70
Stroke Type	Ischemic
Side of stroke	Right
Time Since Stroke (months)	6
Dom Side	Left
MA Side	Left
Trained side	Right

4.3.2 Intervention

The intervention comprised of a home-based unilateral strength training and MT programme. The participant's LA lower limb was strapped into a custom designed ankle brace securing the ankle joint at a 100° angle (10° plantarflexion) [29]. The participant was seated in a chair with back support, with a knee joint angle at 120° (Figure 4.1). Following a warm-up consisting of unilateral submaximal isometric contractions [40], the main part of the training programme consisted of 4 sets of 5 maximal effort isometric ankle dorsiflexion contractions, performed with the LA limb only, held for 5 seconds with 5 seconds rest between repetitions and 3 minutes rest between sets. The same protocol was followed 3 times per week for 4 weeks (12 sessions).

Figure 4.1: Ankle Dorsiflexion Training Set-up

The participant is set up with the LA limb strapped into the isometric strengthening ankle brace with the reflection of the same limb in the mirror placed between the participant's legs. The MA limb is hidden behind the mirror in a relaxed position.

Maximal isometric contractions allow for strength training at the highest intensity which is associated with the greatest cross-education of strength effects [41]. Frequency and intensity were chosen according to maximal strength training guidelines [42, 43]. The participant was instructed to observe the reflection of the LA limb in the mirror while training. Verbal cues were given to "Go" and to "Rest" to ensure timely contractions and rest periods. Prompts to focus on the reflection in the mirror and consistent verbal cues to contract as hard and as fast as possible were given throughout each training session. All 12 sessions of the intervention were completed without adverse reactions.

4.3.3 Outcome Measures

Valid and reliable outcome measures were chosen to cover the three levels of human functioning as outlined in the International Classification of Functioning, Disability and Health framework (ICF) [44]:

Strength

Maximal Voluntary Isometric Contraction (MVIC) of dorsiflexion was assessed using the Biodex System 3 Isokinetic Dynamometer (Biodex Medical Systems, Shirley, NY, USA) according to the Biodex System 3 Pro Application/Operation Manual [45]. Three variables were collected for analysis: 1) Peak Torque (PT) 2) Rate of Torque Development (RTD) 3) Average Torque of a single contraction (AT). The procedure for assessing strength parameters was in accordance with the reliability study carried out as part of this thesis (detailed in Chapter 3.0).

Spasticity

Spasticity was assessed according to the Modified Ashworth Scale (MAS) (Appendix I), a 6-point (0, 1, 1+, 2, 3 and 4) rating scale with 0 representing “no increase in muscle tone” and 4 representing “affected part(s) rigid in flexion or extension”. The MAS is classed as the gold standard for assessment of spasticity with excellent reliability [46, 47]. This measure has a proposed MDC of a 1-point decrease but to the author's knowledge no MCID has been established [48].

Motor Function

Motor function was assessed with the Timed Up & Go (TUG) [49] (Appendix J) and the 10 Metre Walk Test (10MWT) [50, 51] (Appendix K).

The TUG was used to measure basic mobility and balance manoeuvres; the ability to perform sequential motor tasks relative to walking and turning. The TUG has high inter-reliability and intra-reliability, demonstrating consistent and reliable results [52]. To the author's knowledge, there is no MDC or MCID established for this measure to date.

The 10MWT was used to assess walking velocity in metres per second (m/s) over a short duration. The 10MWT has excellent interrater reliability [51] and excellent intrarater reliability [53]. For this measure MCID is reported as: Small meaningful change = 0.06m/s and Substantial meaningful change = 0.14m/s [54].

London Handicap Scale

London Handicap Scale (Appendix L) was used to assess self-perceived participation with excellent reliability [55, 56]. Again, to the author's knowledge, there is no MDC or MCID yet established for this measure.

Assessments were administered 1-day pre-intervention (baseline), 3 days post-intervention and 3 months post-intervention (3-month follow-up).

4.4 Results

Baseline assessment showed the participant to have noticeable strength deficit in the MA ankle dorsiflexors when compared to the LA limb. All joints in the MA limb (hip, knee and ankle) showed increased muscle tone, with highest muscle tone in the hip followed by the knee and ankle joints. The participant described the issues as affecting his mobility and a feeling of stiffness in the ankle. Assessment results are presented in Table 4.2. Baseline 10MWT and TUG scores were substantially below that of healthy aged matched males [50, 57] with an asymmetrical walking pattern apparent. These outcomes combined with the participant's subjective reports of lower limb motor impairment represented functional disability for the participant.

Table 4.2: Assessment Results

	Baseline	Post-Intervention	Follow-Up
Trained Ankle Strength			
PT (Nm)	33.0	34.2	33.0
RTD (Nm/s)	117.5	122	128
AT (Nm)	30.02	29.59	27.89
UnTrained Ankle Strength			
PT (Nm)	20.3	22.6	24.1
RTD (Nm/s)	59	64.5	64.5
AT (Nm)	12.46	16.13	14.84
MAS Hip mean	2.13	0.63	1.5
MAS Knee mean	1.75	0.5	1.25
MAS Ankle mean	1.63	0	1.13
10MWT (m/s)	0.85	1.06	0.8
TUG (s)	13.13	8.88	12.35
LHS	0.165	0.471	0.26

Nm = Newton Metre, Nm/s = Newton Metres per second, m/s = Metres per second, s = Seconds

4.4.1 Baseline

Baseline outcome assessments confirmed the presence of symptoms commonly associated with post-stroke recovery: LA ankle dorsiflexion PT = 33.0Nm, RTD = 117.5Nm/s, AT = 30.02Nm; MA ankle dorsiflexion PT = 20.3Nm, RTD = 59.0Nm/s, AT = 12.46Nm; Mean Hip MAS = 2.13; Mean knee MAS = 1.75; Mean ankle MAS = 1.63; 10MWT = 0.85m/s; TUG = 13.13s; LHS = 0.165.

4.4.2 Post-Intervention

Post-intervention assessment scores were as follows: LA ankle dorsiflexion PT = 34.2Nm, RTD = 122.0Nm/s, AT = 29.59Nm; MA ankle dorsiflexion PT = 22.6Nm, RTD = 64.5Nm/s, AT = 16.13Nm; Mean Hip MAS = 0.63; Mean knee MAS = 0.5; Mean ankle MAS = 0; 10MWT = 1.06m/s; TUG = 8.88s; LHS = 0.471.

4.4.3 Follow-Up

3-month follow-up assessment scores were as follows: LA ankle dorsiflexion PT = 33.0Nm, RTD = 128.0Nm/s, AT = 27.89Nm; MA ankle dorsiflexion PT = 24.1Nm, RTD = 64.5Nm/s, AT = 27.89Nm; Mean Hip MAS = 1.5; Mean knee MAS = 1.25; Mean ankle MAS = 1.13; 10MWT = 0.80m/s; TUG = 12.35s; LHS = 0.260.

Post-intervention subjective feedback from the participant consisted of reported improved mobility, stability, less stiffness in the MA limb. Additionally, the participant reported they had returned to partaking in hobbies with an ability to stand for longer durations whilst doing so.

4.5 Discussion

The authors of this case report hypothesised that cross-education strength training combined with MT would result in meaningful improvements in ankle dorsiflexion strength, lower limb spasticity and lower limb motor function. The results from this new combination therapy indicate positive findings in all outcomes. Ankle dorsiflexion strength increased in both the trained (LA) and untrained (MA) limbs. Spasticity improved in a clinically meaningful manner in all lower limb joints, with the greatest improvement noted for the ankle. There were clinically meaningful improvements in motor function (measured by the 10MWT and TUG). As a case report these results must be interpreted with caution, they do not provide conclusive evidence for the effectiveness of this intervention in all individuals with chronic stroke. Nonetheless, the results do indicate favourable outcomes and suggest that this combination therapy is feasible as an effective rehabilitation treatment for addressing post-stroke motor impairment.

Studies show that high intensity unilateral strength training can increase activation in the untrained M1 [27] and increase excitability in the untrained motor pathway [31, 58-63], leading to increased neural drive to the contralateral homologous muscle [28]. Furthermore, Dragert & Zehr [29] demonstrated that cross-education of strength is achievable post-stroke. Mirror visual feedback of a training limb has been shown to evoke adaptations in corticospinal excitability of the untrained side and enhance interhemispheric communication [33]. Additionally, mirror visual feedback overrides proprioception of the resting limb and increased attention towards the resting limb further enhances activation of the untrained hemisphere [64, 65]. The study by Zult et

al. [21] has shown the ability for MT to enhance the cross-education effect. With this in mind, it was not overly surprising to find post-intervention contralateral strength increases in this case study. Although clinically meaningful changes in strength are not fully established for this population, it is worth noting the substantial post-intervention increase in all three strength parameters for the untrained (MA) ankle (PT, RTD and AT). A PT increase of 3.6% and 11.3% was noted for the trained (LA) and untrained (MA) limbs respectively. Although these strength increases are lower than that reported by Dragert & Zehr (34 % in the trained (LA) limb, 31% in the untrained (MA) limb), they are in the realm of the average untrained limb strength gains of 11.9% reported in previous cross-education studies [25]. Typically PT is used to identify changes in strength; though, changes in RTD and AT over a single contraction may represent the most important adaptations occurring from training and be more meaningful indicators of strength improvements in a clinical population rather than PT alone [66, 67]. At post-intervention, untrained (MA) limb RTD had increased by 8.5% and more noticeably AT had increased by 29.5%. This is the first study to report RTD and AT in an individual with chronic stroke following a lower limb cross-education and MT intervention.

The underlying cause of spasticity is the hyperexcitability of the stretch reflex, resulting from abnormal processing in the spinal cord and the balance between excitatory and inhibitory signals being disrupted [8, 68]. Previous studies have reported a reduction in contralateral H-reflex excitability during unilateral training [30, 31]. Even though Dragert & Zehr [29] did not detect a reduction in spasticity, the study concluded that repeated bouts of high-intensity unilateral dorsiflexion strengthening could increase contralateral sensitivity of inhibitory interneurons and greater suppression of alpha-motoneuron

excitability [29, 69, 70]. Spasticity is just one component of muscle over-activity measured by the MAS [71]. Spastic co-contraction is another component of muscle over activity, described as an abnormal pattern of supraspinal descending drive, aggravated by abnormal reflex activity, causing simultaneous activity in the agonist and antagonist muscles [8, 72]. Mirror therapy has been suggested to reverse such neural reorganisation which can occur following a stroke [73]. The clinically meaningful reduction in spasticity seen in this case study may be attributed to improved motor output or firing pattern to the untrained limb, potentially reducing spastic co-contraction. It is, however, beyond the scope of this study to determine the neurophysiological mechanisms resulting in spasticity reduction.

Results of this case study show a clinically meaningful improvement [54] (0.21m/s) for post-intervention walking velocity measured by the 10MWT. Dragert & Zehr [29] reported no meaningful change in walking velocity but found a significant improvement (1.2s) in TUG scores following cross-education strength training. In this case study, TUG scores improved more (4.25s) than those reported by Dragert & Zehr [29]. Similarly, Sutbeyaz et al. [36] only report improvements in the Functional Independence Measure following a MT intervention. Improvements in motor function in this case may be attenuated to i) the increase in all three strength parameters of the MA ankle and ii) the substantial decrease in spasticity, potentially allowing for more push off strength and range of movement during gait. The findings of this case study indicate that the combination of lower limb cross-education training with MT may lead to more favourable outcomes than cross-education or MT alone.

The participant in this case study was also assessed for self-perceived participation in the following parameters; Activities of Daily Living, Functional Mobility, Life Participation, Occupational Performance, Quality of Life and Social Relationships. The fact that the participant rated themselves substantially better overall at post-intervention indicates that improvements in motor function had a direct impact on their self-perceived levels of participation.

Assessment at 3-month follow-up indicates a regression in most outcomes. It is normal to expect a reduction in strength gains following a continued period without training [74]. Nevertheless, strength in the untrained (MA) ankle remained greater at 3-month follow-up than at baseline. Spasticity had returned but again, not to baseline levels. The participant self-reported a prolonged feeling of positivity and a return to physical activity including walking and other hobbies for some time after the intervention. Potentially continued greater use of the MA limb post-intervention aided the maintenance of rehabilitation gains. However, at 3-month follow-up the participant stated that the limb had started to feel “weaker and stiffer” than immediately post-intervention, this was also reflected in LHS scores.

Due to this being a single case, results should be interpreted with caution. Potential placebo effects were not controlled for. A feasibility study which incorporates a larger sample size with randomised controlled trial design is needed for further robust evidence of the therapies benefits.

4.6 Conclusion

This case report is the first to investigate the combination of lower limb cross-education training with MT in a chronic stroke patient. Outcomes indicate that cross-education combined with MT substantially increases ankle dorsiflexion strength, reduces lower limb spasticity, increases motor function and improves self-perceived participation in a chronic stroke patient. This combination of therapies has shown to be time effective, easy to implement in an outpatient/community setting and without adverse effects.

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5.0 Cross-Education with Mirror Therapy to Improve Motor Function after Stroke: A Feasibility Randomised Pilot Study

5.1 Abstract

Background: A large proportion of patients with chronic stroke have permanent lower limb functional disability leading to reduced levels of independent mobility. Individually, both cross-education of strength and mirror therapy have been shown to improve aspects of lower limb functioning in patients with stroke. It is suggested that the inclusion of mirror visual feedback, by way of mirror therapy, in cross-education training can further augment the cross-education effect in healthy populations. However, little is known about the application of a combination of these therapies in a clinical setting. Therefore, a large gap remains in the literature regarding whether mirror visual feedback of the training limb can further augment the cross-education effect and enhance lower limb motor function post-stroke.

Objectives: This study examined the feasibility for applying a novel combination of cross-education and mirror therapy to chronic stroke patients and investigated whether the inclusion of mirror visual feedback in a cross-education intervention would further enhance rehabilitative improvements in the lower limb compared to cross-education alone.

Methods: Thirty-one participants (32 to 90 Years; 20 Male, 11 Female, 6 months post-stroke) completed either a unilateral strength training (ST) or unilateral strength training with mirror therapy (MST) intervention. Both groups strength trained the less-affected (LA) ankle dorsiflexors 3 times per week for 4 weeks. Only the MST group observed the reflection of the training limb in the mirror. Outcome measures included Maximal Voluntary Contraction (MVC) (Peak Torque, Rate of Torque Development and Average Torque), 10 Meter Walk Test (10MWT), Timed Up and Go (TUG), Modified Ashworth Scale (MAS) and the London Handicap Scale.

Results: No between group differences were identified for improvement in MVC, MAS, TUG or LHS. A trend to significant between group difference with medium effect (p = 0.055, d = 0.7) was shown for improvements in walking velocity (10MWT) in favour of the MST group. Treatment and assessments were well tolerated without adverse effects.

Conclusion: Cross-education plus mirror-therapy may have potential for improving motor function after stroke. Future studies with larger sample sizes are needed to further investigate the effectiveness of the combination treatment.

5.2 Introduction

A recent study [1] has shown that the cross-education training effect in a non-clinical population is further augmented by combining cross-education with mirror therapy (MT). After applying a unilateral strength training plus MT intervention that consisted of right sided 80% maximum voluntary wrist flexor contractions for 3 weeks (15 sessions), the study concluded that untrained limb strength increased significantly more in the mirror training group (61%) when compared to strength training only (34%). This thesis has presented a case report (Chapter 4.0) that examined the application of the combined therapy in a single stroke patient. The case study reported a substantial increase in more-affected (MA) limb strength, reduction in spasticity, increased walking velocity and improved self-perceived impact of stroke.

In summary; i) both cross-education and MT, as individual therapies, have been proven to produce significant strength and functional benefits after stroke [2, 3] ii) cross-education of strength has shown to be further enhanced with the inclusion of MT in a non-clinical population [1] iii) limited literature indicates positive rehabilitation outcomes in applying the combination of cross-education and MT to stroke patients (Chapter 4.0). With only one case study reporting an investigation into the application of the combined therapy after stroke, there remains a substantial gap in the literature. The effects of the combination therapy on strength, spasticity and motor function in comparison to cross-education alone remain underexplored.

This is the first randomised controlled study to investigate the potential of cross-education of strength plus MT for enhancing strength, reducing spasticity and improving

lower limb motor function in a cohort of participants with chronic stroke. The primary aim of this study was to investigate the feasibility of applying cross-education training with the inclusion of MT post-stroke. The authors hypothesised that the inclusion of MT during cross-education strength training would enhance rehabilitative outcomes in the lower limb more effectively than cross-education alone.

5.3 Methods

5.3.1 Participants

Thirty-six chronic (>6 months post-stroke) stroke patients were referred from local outpatient settings in the North West region of Ireland and contacted for eligibility. Of the 36 patients contacted, 31 (age 32 to 90 Years; 20 Male and 11 Female) participated in the study (Table 5.1). Inclusion criteria were: Adults presenting with lower limb post-stroke hemiparesis, at least 6 months post-stroke, discharged from formal rehabilitation services, not involved in any other type of lower limb strength training during the trial, cognition that allows participants to make informed consent (Mini Mental State Exam (MMSE) >24) (Appendix M). Exclusion criteria were: <6 months post-stroke, engagement in formal lower limb physiotherapy, other cardiovascular, neurological or musculoskeletal impairments not related to stroke that would prevent strength training, impaired cognition (MMSE <24) and vision impairments that would interfere with the ability to observe mirror images. All subjects were provided with an information sheet (Appendix F) and were required to sign informed consent (Appendix G). Sligo University Hospital Ethics Committee approved the study according to the Declaration of Helsinki (Appendix H). A flow diagram of participant enrolment is illustrated in Figure 5.1 below.

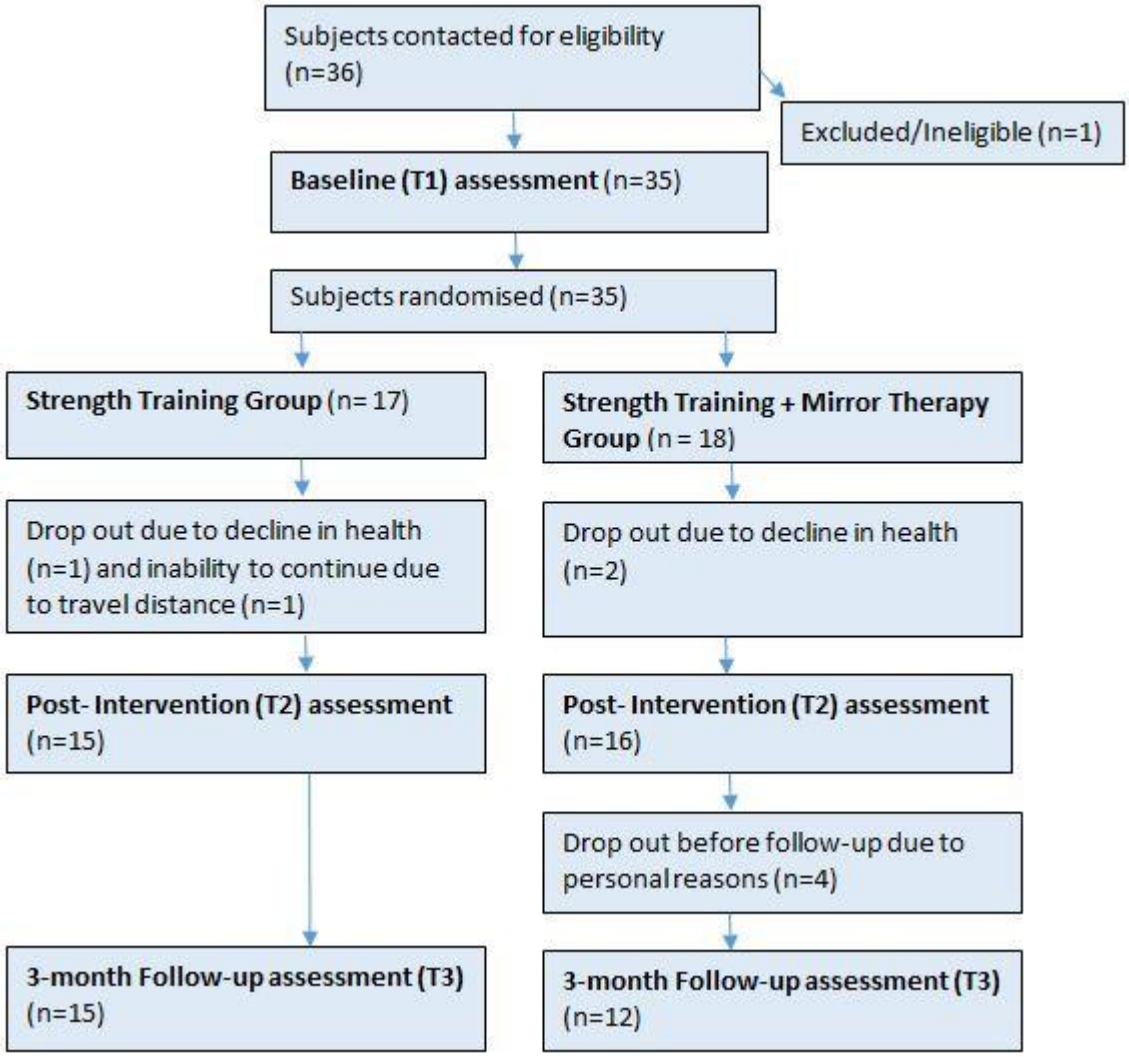

Figure 5.1: Participant Enrolment Flow Diagram

5.3.2 Design

This feasibility study followed a randomised controlled design with allocation concealment and blinding of the independent assessor. The same assessor, blinded to the treatment assignment, performed all assessments. After baseline measurements were obtained, subjects were randomly assigned to the Strength Training only group (ST) (n=17) or the combined Mirror + Strength Training group (MST) (n=18), using computer-generated block random numbers. An independent assistant, not otherwise involved in the trial, conducted the randomisation with notification delivered in opaque

sealed envelopes. Of the 35 participants randomised, 2 dropped out from the ST group and 2 dropped out from the MST group leaving a total of 31 participants to take part in the trial (ST: n = 15, MST: n = 16).

Table 5.1: Demographic Characteristics of Subjects at Baseline

mean ± SD (range)

	ST Group (n=15) Baseline (range)	MST Group (n=16) Baseline (range)	ST vs MST Differences (*p*)
Sex, M:F	11:4	9:7	0.54
Age (Years)	63.5±12 (36-80)	60±14.7 (32-90)	0.48
Type of Stroke Ischemic:hemorrhagic	9:6	11:5	
Time Since Stroke (Months)	90.1±83.3 (16-276)	78.7±75.2 (6-207)	0.48
MA Side Right:Left	8:7	6:10	0.6
Trained Side Dominant:Non-Dominant	7:8	9:7	0.87

MA = More-affected, n = number of subjects, *p* = *p* -value

5.3.3 Intervention

The intervention comprised of a home-based unilateral isometric strength training programme performed under supervision by two therapists. The participant's less-affected (LA) lower limb was strapped into an ankle brace securing the ankle joint at a 100° angle (10° plantarflexion) [2]. Participants were seated on a chair with back support, with a knee joint angle of 120° (Figure 5.2). Following a warm-up consisting of unilateral submaximal isometric contractions [4], the main part of the training programme consisted of 4 sets of 5 maximal effort isometric ankle dorsiflexion contractions, performed with the LA limb only, held for 5 seconds with 5 seconds rest

between repetitions and 3 minutes rest between sets. The same protocol was followed 3 times per week for 4 weeks (12 sessions).

Dorsiflexion was chosen due to the frequent pattern of lower limb spasticity in the MA ankle, resulting in plantarflexion and dorsiflexion dysfunction [5], and the important role of the ankle dorsiflexors during walking [6-9]. Maximal isometric contractions allow for training at the highest intensity which is associated with the greatest cross-education of strength effects [10]. Frequency and intensity were chosen according to maximal strength training guidelines [11, 12]. The ST group exercised without a mirror; the MST group observed the reflection of the LA lower limb in the mirror while training. Prompts to focus on the reflection in the mirror were given to the MST group only; other verbal cues were identical for all participants of both groups.

Figure 5.2: Ankle Dorsiflexion Training Set-up

The participant is set up with the LA limb strapped into the isometric strengthening ankle brace. For the MST group the reflection of the same limb is visible in the mirror placed between the participant's legs. The MA limb is hidden behind the mirror in a relaxed position. Set-up was the same for the ST group without the inclusion of the mirror.

5.3.4 Outcome Measures

This study explored the feasibility of applying the combination therapy of cross-education strength training and MT for the purpose of improving lower limb strength, spasticity and motor function for individuals with chronic stroke. Outcome measures were chosen in accordance to previous similar studies [2, 13] and, where possible, to detect clinically meaningful improvements as indicated by; Minimal Detectable Change

(MDC), Minimal Clinically Important Difference (MCID) or Smallest Real Difference (SRD). The MDC indicates a clinically significant amount of change required to exceed measurement variability, the MCID indicates clinically meaningful change for the participant [14] and the SRD represents the smallest change that indicates a real (clinical) improvement for a single individual [15]. Participants were familiarized with each outcome measure prior to assessment. Outcome measurements were assessed at baseline (T1), post-intervention (T2) and 3-month follow-up (T3) and were performed by the same assessor blinded to treatment allocation. Outcome measures cover the three levels of human functioning as outlined in the International Classification of Functioning, Disability and Health framework (ICF) [16]:

- *Function/body structure*
- *Activity*
- *Participation/involvement in life situations*

Strength

Maximal Voluntary Isometric Contraction (MVIC) of dorsiflexion was assessed using the Biodex System 3 Isokinetic Dynamometer (Biodex Medical Systems, Shirley, NY, USA). The procedure for assessing strength parameters was in accordance with the reliability study carried out as part of this thesis (detailed in Chapter 3.0). For MVIC assessment, participants were positioned in stocking feet with the foot placed on the ankle unit footplate and the knee securely supported by the standard limb support. Maximal isometric ankle dorsiflexion strength was assessed at the ankle joint angle of 10° plantarflexion (anatomical reference of 0° was set with the tibia perpendicular to the sole of the foot), 120° knee flexion [2] and 75° hip flexion [17]. The axis of rotation was

aligned with the body of talus, fibular malleolus, and through the tibial malleolus (Appendix D). Following familiarisation, 1 set of 4 MVCs were performed by both the LA and MA limbs. Three variables were collected for analysis: 1) Peak Torque (PT) in Nm 2) highest Rate of Torque Development (RTD) in Nm/s within the first 0.20s of a single contraction 3) highest Average Torque (AT) in Nm of a single contraction. The highest PT was obtained using the Biodex Software curve analysis. For RTD measurements, cursor A was placed at contraction onset; cursor B was placed at 0.20s from contraction onset (RTD (Nm/s) = (Torque (Nm) at 0.2s – Torque (Nm) at contraction onset)/0.2s). To calculate AT, torque values were obtained every 0.1s from contraction onset using the Biodex Software. The time of contraction onset was identified manually (gold standard) [18-20], defined as the last trough before a sharp rise or 2.5% of peak torque - baseline torque [21, 22]. For the aforementioned strength parameters, no MDC, MCID or SRD is yet established.

Spasticity

Spasticity was assessed according to the Modified Ashworth Scale (MAS). The MAS measures spasticity in patients with lesions of the Central Nervous System and is considered gold standard for the assessment of spasticity with excellent reliability [23, 24]. This measure has a proposed MDC of a 1-point decrease [25]. The MAS (Appendix I) is a scaled scoring measure as indicated below [26]:

0 = No increase in muscle tone.

1 = Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension.

1+ = Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of motion.

2 = More marked increase in muscle tone through most of the range of motion, but affected part(s) easily moved.

3 = Considerable increase in muscle tone, passive movement difficult.

4 = Affected part(s) rigid in flexion or extension.

Motor Function

Motor function was assessed with the Timed Up & Go (TUG) and the 10 Metre Walk Test (10MWT). The TUG was used to measure basic mobility and balance manoeuvres, i.e. the ability to perform sequential motor tasks relative to walking and turning. The TUG has high inter- and intra-reliability, demonstrating consistent and reliable results [27]. For a chronic stroke population the TUG has a MDC of 2.9 seconds and a smallest real difference (SRD%), representing the smallest change that indicates a real (clinical) improvement for a single individual, of 23% [15]. Assessment protocol for the TUG [28] is outlined in Appendix J.

The 10MWT was used to assess walking speed in metres per second (m/s) over a short duration. The 10MWT has excellent inter-rater reliability [29] and excellent intra-rater reliability [30]. For this measure MCID is reported as; Small meaningful change = 0.06m/s and Substantial meaningful change = 0.14m/s [31]. Assessment protocol for the 10MWT [29, 32] is outlined in Appendix K.

London Handicap Scale

The London Handicap Scale (LHS) questionnaire is frequently used in the assessment of self-perceived participation of stroke patients and shows favourable psychometric results with excellent reliability [33, 34]. There is currently no MDC, MCID or SRD yet established for this measure. The LHS (Appendix L) consists of a scale that generates a profile of handicaps on six different dimensions:

- Mobility
- Physical independence
- Occupation
- Social integration
- Orientation
- Economic self-sufficiency
- Overall handicap severity score

5.3.5 Statistical Analysis

Data was analysed using IBM SPSS for Windows (Version 20, Chicago, IL, USA). All variables were tested for normal distribution using the Shapiro-Wilk test [35]. Sample demographics (Table 1) and outcome measures (Table 2) are described in Mean±Standard Deviation (SD). Between group differences for demographic characteristics were tested for using the Independent t-test, the Mann-Whiteny U test and the Chi-Square test. Within group means (T1 v T2 and T1 v T3) were analysed using the Paired-Samples t-test for normally distributed data and the Wilcoxon Signed Rank test for non-normally distributed data. Between group differences (ST v MST) in change over the intervention were tested for using the independent-sample t-test (normal

distribution) and the Mann-Whitney U test (non-normal distribution or non-continuous scale). A *p*-value <0.05 was considered statistically significant and effect sizes expressed as either Cohen's d [36] or *r*. Effect sizes for within group differences were calculated as follows:

Paired differences effect size = $\frac{mean}{Sd}$ or $r = Z/\sqrt{n}$. Effect sizes for between group differences for the independent-samples t-test were calculated using an online effect size calculator [37] and expressed as Cohen's d. For the Mann-Whitney U test, between group differences were calculated as $r = Z/\sqrt{n}$.

5.4 Results

There were no baseline demographic or characteristic differences between the ST and the MST groups (Table 5.1). ST group results are presented in Table 5.2 and MST group results presented in Table 5.3. Within group mean change, within group differences and between group differences for T1-T2 and T1-T3 are presented in Table 5.4.

5.4.1 Strength

MVIC Peak Torque

Peak Torque (PT) was not normally distributed for both ST and MST groups for all time points.

T1-T2

There was no significant change in PT for the trained (0.01Nm, *p* = 0.99) or the untrained side (-0.08Nm, *p* = 0.76) in the ST group. Likewise, the MST group showed no significant change in the trained (-0.76Nm, *p* = 0.44) or untrained (0.81Nm, *p* = 0.16) side, with no

significant differences between the ST and MST groups for the trained (U = 106.0, z = -0.250, *p* = 0.80) or untrained side (U = 104.0, z = 0.044, *p* = 0.97).

T1-T3

There was no significant change in PT for the trained (0.04Nm, *p* = 0.97) or the untrained side (2.01Nm, *p* = 1.55) in the ST group between baseline (T1) and 3-month follow-up (T3). The MST group showed a significant increase of 2.17Nm in the untrained side ($t^{(11)}$ = -2.530, *p* = 0.028) with medium effect size (Cohen's d = 0.7) between baseline (T1) and follow-up (T3) with no significant change in the trained side (1.43Nm, *p* = 0.26). Between group analysis showed no significant differences between the ST and MST groups for the trained (U = 73.0, z = -0.566, *p* = 0.58) or untrained side (U = 73.5, z = -0.54, *p* = 0.59).

MVIC Rate of Torque Development

Rate of Torque Development (RTD) was not normally distributed for both ST and MST groups for all time points.

T1-T2

There was no significant change in RTD for the trained (0.0Nm/s, *p* = 1.00) or the untrained side (10.54Nm/s, *p* = 0.14) in the ST group. The MST group showed an approaching significant increase in RTD between baseline (T1) and post-intervention (T2) in the untrained side (4.71Nm/s, $t^{(14)}$ = -2.001, *p* = 0.065) with medium effect size (Cohen's d = 0.5). There was no change in RTD in the trained side for the MST group (1.81Nm/s, *p* = 0.61). Between group analysis showed no significant differences in RTD between the ST and MST groups for the trained (U = 107.5, z = -0.187, *p* = 0.86) or untrained sides (U = 94.50, z = -0.460, *p* = 0.65).

T1-T3

There was no significant change in RTD for the trained (1.2Nm/s, p = 0.89) or the untrained side (7.32Nm/s, p = 0.24) in the ST group between baseline (T1) and 3-month follow-up (T3). Likewise, the MST group showed no significant change in the trained (7.79Nm/s, p = 0.09) or untrained (3.58Nm/s, p = 0.21) side, with no significant differences between the ST and MST groups for the trained (U = 71.5, z = -0.903, p = 0.44) or untrained side (U = 76.0, z = -0.414, p = 0.68).

MVIC Average Torque

Average Torque (AT) was not normally distributed for both ST and MST groups for all time points.

T1-T2

There was no significant change in AT for the trained (0.36Nm, p = 0.63) or the untrained side (-0.05Nm, p = 0.98) in the ST group. The MST group showed an approaching significant change in AT between baseline (T1) and post-intervention (T2) in the untrained side (1.35Nm, z = -1.805 p = 0.071) with medium effect size (r = 0.33). There was no significant change in AT for the trained side in the MST group (0.04Nm, p = 0.97). Between group analysis showed no significant differences between the ST and MST groups for the trained (U = 110.5, z = -0.062, p = 0.95) or untrained side (U = 95.50, z = -0.416, p = 0.66).

T1-T3

There was no significant change in AT for the trained (0.49Nm, p = 0.60) or the untrained side (1.56Nm, p = 0.2) in the ST group. The MST group showed a significant increase of

1.95Nm (z = -2.547, *p* = 0.011) in AT between baseline (T1) and 3-month follow-up (T3) in the untrained side with large effect size (*r* = 0.52). There was no significant change in the trained side for the MST group (1.77Nm, *p* = 0.21) and no significant differences between the ST and MST groups for the trained (U = 77.0, z = -0.360, *p* = 0.72) or untrained side (U = 63.500, z = -0.289, *p* = 0.29).

5.4.2 Spasticity

Spasticity was measured with the Modified Ashworth Scale (a non-continuous scale).

T1-T2

There were significant reductions in spasticity for the hip, knee, and ankle in both the ST and MST groups. For the ST group mean hip MAS decreased by 0.50 (z = - 2.62, *p* = 0.009) with a large effect size (*r* = 0.48), mean knee MAS decreased by 0.73 (z = -3.20, *p* = 0.001) with a large effect size (*r* = 0.58), and mean ankle MAS decreased by from 0.77 (z = -3.21, *p* = 0.001) with a large effect size (*r* = 0.59). For the MST group, mean hip MAS decreased by 0.38 (z = -2.08, *p* = 0.038) with a large effect size (*r* = 0.38), mean knee MAS decreased by 0.77 (z = -3.46, *p* = 0.001) with a large effect size (*r* = 0.61), and mean ankle MAS decreased by 0.58 (z = -3.08, *p* = 0.002) with a large effect size (*r* = 0.54). There were no significant differences in MAS reduction between groups for hip (U = 94.50, z = -1.012, *p* = 0.31), knee (U = 112.50, z = -0.302, *p* = 0.76) or ankle (U = 104.500, z = -0.615, *p* = 0.54).

T1-T3

For the ST group mean hip MAS significantly decreased by 0.41 (z = - 3.276, *p* = 0.001) with a large effect size (*r* = 0.60) between baseline (T1) and 3-month follow-up (T3).

There was no difference between baseline (T1) and 3-month follow-up (T3) for mean knee MAS (p = 0.12) or mean ankle MAS (p = 0.13) in the ST group. For the MST group, mean hip MAS significantly decreased by 0.33 (z = -2.145, p = 0.032) with a large effect size (r = 0.44), mean knee MAS significantly decreased by 0.42 (z = -2.420, p = 0.016) with a large effect size (r = 0.49). There was no significant difference in mean ankle MAS (p = 0.44) between baseline (T1) and 3-month follow-up (T3) in the MST group. However, between group analysis showed an approaching significant difference in MAS reduction between groups for the ankle (U = 53.0, z = -1.81, p = 0.07) with a medium effect size (r = 0.35). There were no between group differences for MAS reduction for the hip (U = 76.5, z = -0.661, p = 0.51) or knee (U = 80.0, z = -0.493, p = 0.62).

5.4.3 Motor Function

10 Metre Walk Test

The 10 Metre Walk Test (10MWT) scores (m/s) were normally distributed for both the ST and MST groups across all time points.

T1-T2

There was no significant change in walking speed for the ST group (0.03m/s, p = 0.12). There was a significant increase in walking speed of 0.09m/s ($t^{(15)}$ = -4.808, p = <0.001) for the MST group between baseline (T1) and post-intervention (T2) with a large effect size (Cohen's d = 1.1). Between group analysis showed a near significant between group difference for the change in 10MWT scores in favour of the MST group ($t^{(28)}$ = -1.999, p = 0.055) with a medium effect size (Cohen's d = 0.7).

T1-T3

There was no significant change in walking speed for the ST group (-0.06m/s, $p = 0.36$) or the MST group (0.02m/s, $p = 0.63$) between baseline (T1) and 3-month follow-up (T3). There were also no significant between group differences ($t^{(24)} = -1.029$, $p = 0.31$).

Timed Up & Go

Timed Up & Go (TUG) scores (s) were not normally distributed for the ST and MST groups.

T1-T2

There was no significant change in TUG scores for the ST group (-0.73s, $p = 0.12$). The MST group showed an approaching significant improvement of 0.84s ($z = -1.758$, $p = 0.079$) between baseline (T1) and post-intervention (T2) with a medium effect size ($r = 0.31$). Between group analysis showed no differences in change in TUG scores ($U = 102.0$, $z = -0.416$, $p = 0.68$).

T1-T3

There were no significant changes in TUG scores for both the ST (-1.26s, $p = 0.20$) and MST (2.03s, $p = 0.27$) groups. Between group analysis showed no differences in change in TUG scores ($U = 71.0$, $z = -0.669$, $p = 0.50$).

5.4.4 London Handicap Scale

London Handicap Scores were normally distributed for both the ST and MST groups.

T1-T2

There was no significant change for the ST group (1%, $p = 0.79$). The MST group showed a significant improvement in LHS assessment scores of 8% ($t^{(15)} = -2.392$, $p = 0.03$) with a medium effect size (Cohen's d = 0.6) between baseline (T1) and post-intervention (T2). There were no significant differences in LHS score change between the groups ($t^{(29)} = -1.149$, $p = 0.26$).

T1-T3

There was no significant change in LHS assessment scores for the ST group (2%, $p = 0.73$). The MST group showed a significant improvement in LHS scores of 6% ($t^{(11)} = -2.214$, $p = 0.049$) with a medium effect size (Cohen's d = 0.6) between baseline (T1) and 3-month follow-up (T3). Between group analysis showed no significant differences in LHS score change between the groups ($t^{(18.8)} = -0.547$, $p = 0.59$).

Table 5.2: ST Group Results

ST Group	T1 mean±SD	T2 mean±SD	Within Group T1-T2 Difference (*p*) (ES)	T3 mean±SD	Within Group T1-T3 Difference (*p*) (ES)
Trained Ankle Strength (MVIC)					
PT (Nm)	30.01±7.91 (n=14)*	30.01±9.31 (n=14)*	0.99 (0.0)^{d}	30.05±9.47(n=14)*	0.97(0.0)^{d}
RTD (Nm/s)	87.75±41.11 (n=14)*	87.75±45.59 (n=14)*	1.00 (0.0)^{d}	88.95±49.40(n=14)*	0.89 (0.0)^{d}
AT (Nm)	26.42±7.57 (n=14)*	26.79±8.55 (n=14)*	0.63 (0.1)^{d}	26.92±8.95(n=14)*	0.60(0.1)^{d}
UnTrained Ankle Strength (MVIC)					
PT (Nm)	15.86±15.61 (n=14)*	15.79±16.15 (n=14)*	0.76 (0.06)^{r}	17.88±15.07(n=14)*	1.55 (0.27)^{r}
RTD (Nm/s)	39.35±43.05 (n=14)*	49.89±52.63 (n=14)*	0.14 (0.3)^{d}	46.67±45.90(n=14)*	0.24 (0.3)^{d}
AT (Nm)	13.10±13.80 (n=14)*	13.05±14.08 (n=14)*	0.98 (0.0)^{d}	14.66±13.42(n=14)*	0.20 (0.4)^{d}
MAS Hip mean	1.64±0.42 (n=15)	1.14±0.60 (n=15)	**0.009 (0.48)^{r}**	1.23±0.44(n=15)	**0.001 (0.60)^{r}**
MAS Knee mean	1.63±0.51 (n=15)	0.90±0.57 (n=15)	**0.001 (0.58)^{r}**	1.10±0.54(n=15)	0.12 (0.46)^{r}
MAS Ankle mean	1.83±0.65 (n=15)	1.07±0.64 (n=15)	**0.001 (0.59)^{r}**	1.29±1.02(n=15)	0.13 (0.45)^{r}
10MWT (m/s)	0.78±0.45 (n=14)*	0.81±0.45 (n=14)*	0.12 (0.4)^{d}	0.73±0.43(n=14)*	0.36 (0.3)^{d}
TUG (s)	18.68±15.02 (n=14)*	17.95±14.09 (n=14)*	0.12 (0.29)^{r}	17.42±14.08(n=14)*	0.20 (0.24)^{r}
LHS	0.52±0.23 (n=15)	0.53±0.27 (n=15)	0.79 (0.1)^{d}	0.54±0.27(n=15)	0.73 (0.1)^{d}

PT = Peak Torque, RTD = Rate of Torque Development, AT = Average Torque, MVIC = Maximal Voluntary Isometric Contraction, Nm = Newton Metres, Nm/s = Newton Metres per second, m/s = metres per second, s = seconds, *p* = *p*-value, (n) = Number of subjects, ES = Effect size, * = subject unable to be assessed due to discomfort, ^{r}= Effect size expressed as r, ^{d}= Effect size expressed as Cohen's d

Table 5.3: MST Group Results

MST Group	T1 mean±SD	T2 mean±SD	Within Group T1-T2 Difference (*p*) (ES)	T3 mean±SD	Within Group T1-T3 Difference (*p*) (ES)
Trained Ankle Strength (MVIC)					
PT (Nm)	24.63±10.57 (n=16)	23.87±11.59 (n=16)	0.44 (0.2)[d]	26.82±12.37(n=12)†	0.26 (0.3)[d]
RTD (Nm/s)	84.63±42.59 (n=16)	86.44±45.53 (n=16)	0.61 (0.09)[r]	95.46±43.91(n=12)†	0.09 (0.34)[r]
AT (Nm)	20.91±10.48 (n=16)	20.96±10.74 (n=16)	0.97 (0.0)[d]	23.70±11.65(n=12)†	0.21 (0.4)[d]
UnTrained Ankle Strength (MVIC)					
PT (Nm)	14.56±11.93 (n=15)*	15.37±12.26 (n=15)*	0.16(0.4)[d]	16.62±14.97(n=12)†	**0.028 (0.7)[d]**
RTD (Nm/s)	50.27±40.39 (n=15)*	54.97±42.36 (n=15)*	**0.065 (0.5)[d]**	54.21±44.56(n=12)†	0.21 (0.4)[d]
AT (Nm)	11.27±10.56 (n=15)*	12.62±10.83 (n=15)*	**0.071 (0.33)[r]**	13.42±13.07(n=12)†	**0.011 (0.52)[r]**
MAS Hip mean	1.50±0.40 (n=16)	1.13±0.57 (n=16)	**0.038 (0.38)[r]**	1.11±0.37(n=12)†	**0.032 (0.44)[r]**
MAS Knee mean	1.50±0.34 (n=16)	0.73±0.57 (n=16)	**0.001 (0.61)[r]**	1.04±0.56(n=12)†	**0.016 (0.49)[r]**
MAS Ankle mean	1.80±0.80 (n=16)	1.22±0.87 (n=16)	**0.002 (0.54)[r]**	1.56±0.65(n=12)†	0.44 (0.16)[r]
10MWT (m/s)	0.82±0.50 (n=16)	0.91±0.52 (n=16)	**0.000 (1.1)[d]**	0.90±0.50(n=12)†	0.63 (0.1)[d]
TUG (s)	28.05±43.95 (n=16)	27.22±46.63 (n=16)	**0.079 (0.31)[r]**	31.42±59.72(n=12)†	0.27 (0.27)[r]
LHS	0.44±0.23 (n=16)	0.53±0.19 (n=16)	**0.03 (0.6)[d]**	0.53±0.23(n=12)†	**0.049 (0.6)[d]**

PT = Peak Torque, RTD = Rate of Torque Development, AT = Average Torque, MVIC = Maximal Voluntary Isometric Contraction, Nm = Newton Metres, Nm/s = Newton Metres per second, m/s = metres per second, s = seconds, *p* = *p*-value, (n) = Number of subjects, ES = Effect size, * = subject unable to be assessed due to discomfort, † = Subject dropouts at follow-up (n=4), [r]= Effect size expressed as r, [d]= Effect size expressed as Cohen's d

Table 5.4: ST and MST Group Mean Change, Within and Between Group Differences

	ST Group		MST Group		Between Group Difference (T1-T2) (*p*) (ES)	Between Group Difference (T1-T3) (*p*) (ES)
	T1-T2 Change mean±SD	T1-T3 Change mean±SD	T1-T2 Change mean±SD	T1-T3 Change mean±SD		
Trained Ankle Strength (MVIC)						
PT (Nm)	0.01±2.89 (n=14)*	0.04±3.72 (n=14)*	-0.76±3.80 (n=16)	1.43±4.15 (n=12)†	0.80 (0.05)^{r}	0.58 (0.11)^{r}
RTD (Nm/s)	0.00±20.68 (n=14)*	1.20±30.74 (n=14)*	1.81±20.93 (n=16)	7.79±14.56 (n=12)†	0.86 (0.03)^{r}	0.44 (0.18)^{r}
AT (Nm)	0.36±2.78 (n=14)*	0.49±3.44 (n=14)*	0.04±3.83 (n=16)	1.77±4.63 (n=12)†	0.95 (0.01)^{r}	0.72 (0.07)^{r}
UnTrained Ankle Strength (MVIC)						
PT (Nm)	-0.08±8.44 (n=14)*	2.01±4.94 (n=14)*	0.81±2.11 (n=15)	2.17±2.97 (n=12)†	0.97 (0.01)^{r}	0.59 (0.11)^{r}
RTD (Nm/s)	10.54±33.88 (n=14)*	7.32±22.0 (n=14)*	4.71±9.11 (n=15)*	3.58±9.38 (n=12)†	0.65(0.08)^{r}	0.68 (0.08)^{r}
AT (Nm)	-0.05±7.01 (n=14)*	1.56±4.28 (n=14)*	1.35±2.66 (n=15)*	1.95±2.78 (n=12)†	0.66 (0.08)^{r}	0.29(0.21)^{r}
MAS Hip mean	-0.50±0.54 (n=15)	-0.41±0.32 (n=15)	-0.38±0.66 (n=16)	-0.33±0.47 (n=12)†	0.31 (0.18)^{r}	0.51 (0.13)^{r}
MAS Knee mean	-0.73±0.46 (n=15)	-0.53±0.62 (n=15)	-0.77±0.40 (n=16)	-0.42±0.43 (n=12)†	0.76 (0.05)^{r}	0.62 (0.09)^{r}
MAS Ankle mean	-0.77±0.65 (n=15)	-0.54±0.81 (n=15)	-0.58±0.52 (n=16)	-0.19±0.76 (n=12)†	0.54 (0.11)^{r}	**0.07 (0.35)^{r}**
10MWT (m/s)	0.03±0.08 (n=14)*	-0.06±0.21 (n=14)*	0.09±0.07 (n=16)	0.02±0.12 (n=12)†	**0.055 (0.7)^{d}**	0.31 (0.4)^{d}
TUG (s)	-0.73±2.28 (n=14)*	-1.26±4.77 (n=14)*	-0.84±4.43 (n=16)	2.03±9.73 (n=12)†	0.68 (0.08)^{r}	0.50 (0.13)^{r}
LHS	0.01±0.19 (n=15)	0.02±0.22 (n=15)	0.08±0.14 (n=16)	0.06±0.09 (n=12)†	0.26 (0.4)^{d}	0.59 (0.2)^{d}

PT = Peak Torque, RTD = Rate of Torque Development, AT = Average Torque, MVIC = Maximal Voluntary Isometric Contraction, Nm = Newton Metres, Nm/s = Newton Metres per second, m/s = metres per second, s = seconds, *p* = *p*-value, (n) = Number of subjects, ES = Effect size, * = subject unable to be assessed due to discomfort, † = Subject dropouts at follow-up (n=4), ^{r}= Effect size expressed as r, ^{d} = Effect size expressed as Cohen's d

5.5 Discussion

This study provides the first evidence that unilateral strength training of the LA lower limb with mirror visual feedback has potential to achieve therapeutic effects in the MA lower limb post-stroke and that a fully powered trial to investigate the effectiveness of the treatment is feasible. This study is the first to show that unilateral strength training combined with MT in the lower limbs has potential to improve strength outcomes, reduce spasticity, increase motor function and improve self-perceived participation in a chronic stroke population. It is also the first to demonstrate a significant reduction in spasticity in the lower limb using cross-education only. To date, no other study has investigated the combination of cross-education with MT in the lower limb following stroke. Additionally, no previous similar studies have included follow-up assessment. For the purpose of comparison in this section, the most relevant previous cross-education studies are described in Table 5.5.

5.5.1 Strength

In this study, only the MST group showed post-intervention contralateral (MA limb) strength improvements with approaching significant increases in RTD (9.3%, $p = 0.065$) and AT (12%, $p = 0.071$) and a non-significant increase in PT (5.6%, $p = 0.160$). There were no strength gains in the untrained (MA) limb in the ST group and, contrary to expectation, no strength gain was detected for the trained (LA) limb for both groups.

The trend in this study is in agreement with Zult et al. [1] who report a greater untrained limb strength gain in the mirror training group (61%) when compared to strength training only (34%). The study by Zult et al. [1], which tested 23 healthy participants

randomised into a mirror training group (n = 12 mean age 25 ± 4) or a non-mirror training group (n = 12 mean age 29 ± 9) and strength trained the right wrist flexors (6 sets of 8 dynamic reps, 80% MVC, 5 times per week for 3 weeks), attributed the strength gains to a cross-education effect mediated by neural substrates that promote the M1 to increase neural output to the untrained limb.

It is known that an injury can alter cortical structure and function [38-40], which has been suggested to potentially reduce the ability of the brain to induce cross-education [41]. However, Dragert & Zehr [2] report significant PT strength increases in the LA trained (34%) and MA untrained (31%) limbs after 6 weeks of high-intensity unilateral strength training in post-stroke subjects (n = 19, mean age 58.3 ± 12.2, 3 sets of 5 reps, maximal isometric dorsiflexion contractions, 3 times per week for 6 weeks), without the inclusion of mirror visual feedback. These results indicate that cross-education is indeed achievable following neurological injury due to stroke. Although, a strength increase of 31% in the untrained limb is a relatively high magnitude. To put this into context, a meta-analysis of 31 cross-education studies in healthy participants [42] reports a mean untrained limb strength increase of 11.9% (9.4% in the upper limb and 16.4% in the lower limb). Furthermore, numerous previous studies have indicated no significant change in untrained limb strength whatsoever [43-47]. Dragert & Zehr [2] suggest that the cross-education effect in their study may be linked to increased sensitivity to descending motor commands and modulation of inhibitory pathways associated with voluntary movement. Furthermore, the study suggests that the high magnitude of cross-education may be partly explained by the reduced pre-intervention capacity in people with stroke, who are detrained, compared to healthy participants.

A plausible explanation for such differing results in this present study may be linked to the shorter intervention duration. Intervention duration in this study was 4 weeks, which when compared to Dragert & Zehr [2] (6 weeks) is a short intervention. Previously, healthy subjects have achieved significant cross-education strength gains in 3-4 weeks [1, 10, 48, 49]. Although, a recent study on patients with Multiple Sclerosis reported a linear response to unilateral strength training, requiring 6 weeks to reach significant cross-education strength gains in the untrained dorsiflexors [50], which may support the need for a longer training intervention duration in neurologically impaired subjects. Intervention duration in this study does compare to that of Zult et al. [1] (3 weeks) and to a study by Urbin et al. [51], who implemented 4 weeks of unilateral dynamic wrist extension strengthening (2 sets of 6 repetitions, 50-80% 1-RM, 4 times per week for 4 weeks) in healthy (n = 7, mean age 50 ± 11.8) and post-stroke (n = 6, mean age 55 ± 14) subjects. However, these studies achieved a treatment dose of 15 and 16 sessions respectively, meaning that the overall treatment dose in this study (12 sessions) was lower, again suggesting the need for increased intervention duration and ultimately increased treatment dose.

The training mode in this study was isometric which has previously shown to induce significant cross-education strength gains in the untrained limb [2, 10, 49, 52] and is a safe training mode that is easily implemented, allowing for contractions at a maximal level. However, since the implementation of this study, a recent meta-analysis [42] has reported an isometric mode to be less effective for mediating cross-education when compared to concentric and eccentric modes [42]. Implementing a dynamic unilateral

strength training intervention may therefore have potential to achieve greater cross-education effects post-stroke.

Studies show that high-intensity unilateral strength training can increase activation in the untrained M1 [53] and increase excitability in the untrained motor pathway, leading to increased neural drive to the contralateral homologous muscle [54-60]. Previous research in healthy subjects suggests that strength gains in the untrained limb are related to strength gains in the trained limb [42, 53], i.e. approximately 52% of the strength increase of the trained limb [53]. Interestingly, recent findings report a significant correlation between the magnitude of trained and untrained limb strength gains for concentric and eccentric modes only, no correlation between the trained and untrained gains was found for an isometric mode [42]. In line with this, the findings of this present study indicate that strength gains may indeed be possible for the untrained (MA) limb even in the absence of such gains in the trained (LA) limb when training isometrically. Additionally, cross-education gains in RTD and AT are achievable without gains in PT. One other study, in healthy subjects, also reports a greater strength gain in the untrained limb compared to the trained limb (untrained PT: 17.9% - 27.5%; trained PT: 15% - 16.3%) [61]. Furthermore, similar to this study, a higher magnitude in the cross-education of Work (W) than PT was reported for the untrained limb (untrained W: 30 - 37%). Such findings in this present study are of particular interest, especially as changes in RTD, W and AT represent the most important adaptations occurring from training [22, 62] and may therefore be more meaningful indicators of strength improvements in a clinical population, rather than PT alone. This is the first study to

report RTD and AT, in a chronic stroke population following a lower limb cross-education and MT intervention.

The high variability in day to day physical ability of stroke patients may have been an influencing factor for both training capacity and performance during assessment [63]. In an attempt to control for these factors, subjects were asked to not attend training or assessments if they were not feeling well. During training, subjects were verbally encouraged to put as much effort as possible in to each contraction, yet effort was not objectively measured during training sessions. Therefore, it is possible that subjects did not consistently reach a high enough training intensity (80-100% MVC) needed to elicit PT strength gains and PT strength transfer [10]. With this in mind, favourable strength results (RTD and AT) in the MST group indicate that submaximal effort contractions, with the inclusion of mirror visual feedback, could be sufficient to cause some strength transfer and rehabilitative effect.

Assessment at 3-month follow-up (T3) showed that untrained limb PT and AT were both significantly greater (PT $p = 0.028$, AT $p = 0.011$) compared to baseline levels for the MST group. Cross-education effects have been reported to last up to 12 weeks in healthy participants [64] and up to 26 weeks in patients with wrist fracture [65]. Exact reasons for the increase in untrained limb PT between baseline (T1) and 3-month follow-up (T3) with no baseline (T1) to post-intervention (T2) increase is difficult to quantify. Perhaps post-intervention gains in RTD and AT, combined with spasticity reduction and functional improvement, allowed for increased daily use of the MA untrained limb for some time after the intervention, thus continuing some rehabilitation effect. It must also

be noted that although participants were instructed to refrain from strength training activity between post-intervention and 3-month follow-up, it was impossible to control for continued training. Although, it seems unlikely participants would have continued maximal dorsiflexion strength training without access to similar equipment utilised in the intervention in this study.

5.5.2 Spasticity

In this study, spasticity significantly reduced (p = <0.05) with large effect size (r = 0.38 – 0.61) for all lower limb joints (Hip, Knee, Ankle) between baseline and post-intervention assessment, for both the ST and the MST groups. There were no significant between group differences in baseline to post-intervention changes, suggesting that mirror visual feedback does not further augment spasticity reduction compared to cross-education strength training alone.

Even though the reduction in spasticity did not reach the clinical significance of 1 point decrease in MAS score [25] for either group in this study, it contradicts findings by Dragert & Zehr [2] who report no change in MAS scores following cross-education strength training. With the training protocol in this study similar to that of Dragert & Zehr [2], it is difficult to give reason for the differing result. A difference in participant's baseline spasticity levels may be one explanation for the contrasting findings. Dragert & Zehr [2] report a mean pre-intervention MAS score of 1.3 for the leg, which is not substantially different to the overall leg MAS means reported in this present study (ST group = 1.7, MST group = 1.6). However, 5 out of the 19 participants (26%) in the study by Dragert & Zehr [2] were reported to have a pre-intervention MAS score of 0,

indicating no spasticity. Therefore, it is reasonable to suggest that 26% of participants in their study would not have made measurable improvements in spasticity. In this present study, no participants had a pre-intervention MAS score of 0, meaning all participants had potential to improve.

Additionally, many of the participants in this study, and within both the ST and MST groups, subjectively reported 'more awareness' or 'new sensations' felt in the MA limb after training. It may be possible that experiencing such positive effects motivated participants to use the MA limb during daily activities. More regular use of the MA limb may have encouraged flexibility in tissues that had become contracted or rigid due to long-term non-use after stroke, thus improving range of motion which may have been detected in MAS assessment.

The underlying cause of spasticity is the hyperexcitability of the stretch reflex resulting from abnormal processing in the spinal cord and the balance between excitatory and inhibitory signals being disrupted [66, 67]. Previous studies have reported a reduction in contralateral H-reflex excitability during unilateral training [13, 57, 68]. Even though Dragert & Zehr [2] did not detect a reduction in spasticity, they conclude that repeated bouts of high-intensity unilateral dorsiflexion strengthening could increase contralateral sensitivity of inhibitory interneurons and greater suppression of alpha-motoneuron excitability [2, 69, 70]. Earlier work in healthy populations [13] suggests that unilateral dorsiflexion strengthening reduced H-reflex excitability of the antagonist muscles.

Urbin et al. [51] reported a significant increase in active range of motion (AROM) (100%) of the untrained MA wrist extensors. Although AROM is not a direct measurement of

spasticity, such findings may reinforce the notion that unilateral strength training could help to re-organise the disrupted motor pathway, allowing for improved agonist/antagonist synergy.

It is worth mentioning that spasticity is just one component of muscle over-activity measured by the MAS [71]. Spastic co-contraction is another component of muscle over activity, described as an abnormal pattern of supraspinal descending drive, aggravated by abnormal reflex activity, causing simultaneous activity in the agonist and antagonist muscles [66, 72]. The reduction in spasticity observed in participants of this study may be further attributed to an improved motor output or firing pattern to the untrained limb, potentially reducing spastic co-contraction.

Modified Ashworth Scale scores at 3-month follow-up were lower for all joints for both groups when compared to baseline MAS scores. The ST group maintained a significant reduction in spasticity in the hip (p = 0.001), while the MST group maintained a significant reduction in spasticity in the hip (p = 0.032) and the knee (p = 0.016) joints. These findings demonstrate long-term positive effects of both cross-education and cross-education plus MT for reducing post-stroke spasticity in the lower limb.

5.5.3 Motor Function

Post-intervention results indicate that a significant reduction in spasticity, coupled with a trend to significant increase in RTD for the untrained limb, in the MST group resulted in a significant meaningful change (>0.06m/s) [31] in walking speed (10MWT) (0.09m/s, p = <0.001) and a trend to significant improvement in TUG scores for the MST group

(0.84s, $p = 0.079$). Despite a significant reduction in spasticity in the ST group, there were no improvements in motor function outcomes. While cross-education has previously been shown to improve TUG scores after stroke [2], no study reports significant improvements for walking speed. Similar to unilateral strength training, mirror visual feedback of a training limb has been shown to evoke adaptations in corticospinal excitability [73] and corticomotor activity [74] of the untrained M1. Additionally, mirror visual feedback overrides proprioception of the resting limb and increased attention towards the resting limb further enhances activation of the untrained hemisphere [75, 76]. The results of this study indicate an approaching significant between group difference ($p = 0.055$) with medium effect size (Cohen's d = 0.7), in favour of the MST group, in pre- to post-intervention walking speed, suggesting that the combination of cross-education training with the inclusion of mirror visual feedback may increase the ability to achieve motor function improvements. However, further studies are needed to substantiate the effectiveness of this combination treatment. Contradictory to previous findings [2], this study found no significant improvement in TUG scores for the ST group. As described earlier, reasons for such differing findings could be training intensity or intervention duration.

In this study, the trend to more favourable motor function gains in the MST group may indicate the possibility of achieving both strength and functional gains if mirror visual feedback is included, even when strength training isometrically at a submaximal intensity for a relatively short intervention duration.

Results in this study show that walking speed for the MST group at 3-month follow-up was not significantly different to that of baseline measures but had significantly increased at post-intervention (T2). Similarly, there was no significant difference between baseline and 3-month follow-up RTD in the MST group, whereas RTD had significantly increased at post-intervention (T2). These findings support the idea that an increase in RTD for the untrained (MA) ankle dorsiflexors, along with a reduction in spasticity, may have influenced an improvement in post-intervention (T2) walking speed for the MST group. Previous research has confirmed that ankle movement during gait is adversely affected due to ankle dorsiflexor weakness, particularly in clinical populations [9, 77]. After stroke, dorsiflexor strength and control of the affected side has been reported as the primary determinant for gait velocity [9]. Insufficient dorsiflexion control increases the swing time of the MA leg, resulting in temporal asymmetry and slower gait velocity [78]. Therefore, an increase in the rate of dorsiflexion contractile torque (i.e. RTD), as demonstrated by the MST group in this study, may have resulted in a more effective gait pattern and increased gait velocity. The findings of this study reinforce previous recommendations that an emphasis on strengthening the MA ankle dorsiflexors (either directly or indirectly via cross-education and MT) should be considered in order to achieve improvements in gait velocity and restore gait symmetry [9].

5.5.4 London Handicap Scale

When measured by the LHS, participants in the MST group reported a significant improvement of 8% (p = 0.03) in their self-perceived impact of stroke on mobility, physical independence, occupation, social integration, orientation, and economic self-

sufficiency [33]. Although the ST group reported no change, there were no between group differences for change in LHS scores over the intervention.

Assessment at 3-month follow-up (T3) showed that the MST group had maintained a significant 8% improvement in LHS scores (p = 0.049) compared to baseline (T1) levels, with no change in the ST group. Again there were no between group differences for change in LHS scores at 3-month follow-up. However, the results indicate the potential for lasting effects of rehabilitation gains on the self-perceived impact of stroke following the combination treatment intervention. This is the first lower limb study to investigate and report the beneficial influence of cross-education with MT on the self-perceived impact of stroke.

Table 5.5: Previous Studies Relevant for Comparison of Outcomes

Reference	Subjects	Muscle group	Training Mode	Intervention / Duration	Post-intervention Outcomes (p <0.05)			
					Trained limb strength increase	Untrained limb strength increase	Spasticity	Functional change
Zult et al (2016)	23 Healthy adults	Dominant (right) wrist flexors	Dynamic Concentric	Unilateral strength training only (n = 12), Unilateral strength training plus mirror (n = 11). 5 times per week for 3 weeks	Strength training only group 72%, Strength training plus mirror group 72%	Strength training only group 34%, Strength training plus mirror group 61%	N/A	N/A
Dragert & Zehr (2013)	19 chronic stroke adults	Dorsiflexors	Isometric	Less-affected side only maximal strength training. 3 times per week for 6 weeks	34%	31%	No change	Timed up & Go improved by 1.2 seconds
Urbin (2015)	7 Healthy adults (control) and 6 adults post stroke	Wrist extensors	Dynamic Concentric	Control (n = 7): Unilateral strength training, Stroke (n = 6): Less-affected side strength training. 4 times per week for 4 weeks	% gain in 1-RM: Control 38%, Stroke 29%	% gain in 1-RM: Control approx 19%, Stroke: Not reported	Not reported	Increase in Active Range of Motion of more-affected wrist extensors

1-RM = 1 Repetition Max, n = number of subjects, p = p -value

5.5.5 Feasibility

The purpose of a feasibility pilot study is to establish important parameters that are needed in order to design a larger scale main study, i.e. a fully powered randomised controlled trial (RCT) [79].

Such important parameters include:

- Availability of eligible participants and willingness of clinicians to recruit participants
- Adherence/compliance/follow-up rates
- Characteristics and suitability of proposed outcome measures
- Effect size of the main outcome measure, needed to estimate sample size
- Time needed to collect data and statistical analysis of data

A pilot study is a smaller version of the main study which sets out to test the components of the main study [79]. A pilot study focusses on the processes of the larger scale main study to determine whether recruitment, treatment, pre, post, and follow-up assessments run as planned. The main outcome measures will be assessed during a pilot study. Often a larger scale study may incorporate a pilot study as the first phase allowing data to be included in the final analysis [79].

This study assessed the feasibility and efficacy of a home-based unilateral strength training and unilateral strength training plus MT intervention in chronic stroke participants. Based on the described purpose of both feasibility and a pilot studies, this study has explored the parameters necessary for a fully powered RCT. These parameters will be discussed in detail within this section.

Availability of eligible participants and willingness of clinicians to recruit

This study achieved a 97% eligibility rate (1 participant excluded out of the 36 patients referred), indicating that the inclusion/exclusion criteria were designed appropriately. However, a number of potential barriers to recruitment were identified in the initial stages of this study. The training intervention in this study was designed to take place within the exercise laboratory at the Institute of Technology Sligo (IT Sligo). This required participants to visit the laboratory 3 times per week for 4 weeks. Feedback from participants during the recruitment process suggested that there were difficulties with travel to and from the laboratory, potentially disrupting adherence to the intervention. For this reason, the intervention was altered to a supervised home-based training programme. An application to Sligo University Hospital Ethics Committee, to amend the intervention location for this study, was submitted and subsequently granted (Appendix G).

The amendment to the intervention procedure required two therapists to travel to participant's homes for each training session. Given the rural geographical location of the North West region of Ireland this proved to be time consuming, presenting a potential limitation to achieving a larger sample size in a fully powered RCT. However, as a feasibility study that set out to assess the concept of applying the principles of cross-education and MT in chronic stroke, the sample size is considered sufficient.

Through the development of this feasibility study, the IT Sligo Neuroplasticity Research Group has established a comprehensive nationwide network of clinicians with access to the Health Services Executive (HSE) database of all stroke related hospital admissions

within the North West region of Ireland. Collaboration with clinicians and therapists in the North West region has allowed access to, and recruitment of, chronic stroke patients in the immediate area. More recently, nationwide media coverage (Appendix N) of the IT Sligo Neuroplasticity Research Group has given rise to increased interest from other regions of Ireland outside of the North West. The IT Sligo Neuroplasticity Research Group has received expressed interest from a large number of chronic stroke patients wishing to volunteer for future studies. With an extensive database of potentially eligible participants, the IT Sligo Neuroplasticity Research Group is confident that a fully powered RCT sample size can be achieved in future studies.

Adherence and compliance rates

The feasibility of this study was partly assessed by tracking adherence, retention and safety. Training sessions were recorded daily by the principal researcher implementing the therapy sessions. If participants were unable to attend training sessions, sessions were re-arranged to ensure all participants were exposed to the same dose of treatment. Any adverse reactions or adverse events (e.g. pain, fatigue or falls) were also recorded.

An attrition rate of <15% is considered acceptable for a high quality RCT according to the PEDro Scale [80]. Out of the 35 participants recruited, assessed at baseline (T1) and randomised for this study, a total 11% (n=4) dropped out before post-intervention assessment (T2). Between post-intervention (T2) and follow-up (T3) a further 4 participants dropped out, equating to a 23% attrition rate between T1 – T3. For a fully powered RCT which includes 3-month follow-up, particular attention to participant

retention is needed between T2 – T3. Of the 31 participants that attended for post-intervention (T2) assessment, 22 completed 100% of the intervention (12 training sessions), 8 completed 92% (11 training sessions) and 1 completed 83% (10 training sessions). Therefore, adherence to the intervention was >70%, which is considered a sufficient adherence rate in previous studies involving adults with physical impairment as a result of stroke [81, 82]. There were no injuries, adverse reactions or events reported during this intervention, therefore the intervention was considered safe.

Suitability of outcome measures

As previously discussed, outcome measures for this study were chosen in accordance with the three levels of human functioning as outlined in the International Classification of Functioning, Disability and Health framework (ICF) [16]. The suitability of each outcome measure will be discussed in this section:

Strength: *Maximal Voluntary Isometric Contraction (MVIC)*

The primary principle underpinning the therapy applied during this study was cross-education of strength. The measurement of maximal muscular strength is often used to determine physical condition and the effects of training or rehabilitation programmes [83]. As previously mentioned, an isometric mode of training was applied during this intervention. Therefore, as in a previous similar study [2], the primary outcome measure was MVIC. As isokinetic dynamometry is considered gold standard for measuring strength parameters, the Biodex System 3 Isokinetic Dynamometer was chosen for strength assessment [84]. The reliability study within this thesis (Chapter 3.0) assessed the strength measuring protocol for this study, showing excellent reliability for all three

strength parameters assessed; PT, RTD, and AT. There were a number of limitations noted while using the Biodex System 3 Isokinetic Dynamometer during this study:

- A number of participants had difficulty positioning themselves onto the chair. Even with assistance and at its lowest setting the chair was often too high for the participant to be easily transferred. This may have been stressful and intimidating for some participants, potentially affecting strength performance.
- To avoid limb counter movement or the weight of the attachment initiating the dynamometer, initiation threshold of the dynamometer was set to 3Nm. As a result, the threshold may have been too high to detect very weak MA limb dorsiflexion contractions. Some participants were able to dorsiflex the MA ankle without resistance but were unable to initiate the dynamometer to achieve a MVIC recording. This may have resulted in minimal strength gains below the 3Nm threshold being undetected.

In a similar unilateral strength training study [2], ankle dorsiflexion MVIC force was measured via a load cell and then converted to ankle PT. The use of a load cell to measure MVIC may have allowed for more comfortable positioning of participants and may have enabled detection of minimal strength gains. While Dragert and Zehr [2] report PT, they do not report data for RTD or AT. From a functional perspective, the ability to generate torque quickly (RTD) and to maintain torque (AT) may be more important than being able to generate high maximal force (PT). Although PT is the universal standard parameter used to measure strength, changes in RTD or AT over a single contraction may represent the most important adaptations occurring from training or rehabilitation [22, 62]. A comprehensive muscle function assessment should

include all three strength parameters [22, 85]. With this in mind, future studies utilising an isokinetic dynamometer for assessing strength outcomes might consider the ability to achieve the pre-set dynamometer threshold as a participant inclusion criterion.

Spasticity: *Modified Ashworth Scale (MAS)*

The validity of the MAS in measuring spasticity has previously been questioned. The MAS scale produces a global assessment of the resistance to passive movement of an extremity, not just stretch-reflex hyperexcitability. Specifically, the MAS score is likely to be influenced by non-contractile soft tissue properties, by persistent muscle activity (dystonia), by intrinsic joint stiffness, and by stretch reflex responses [86]. It has been argued that the MAS is a description of resistance to passive movement and therefore measures only one aspect of spasticity, and is not a comprehensive assessment [87]. Furthermore, it has been put forward that the MAS does not comply with the concept of spasticity (a velocity-dependent increase in muscle tone) and measures muscle tone intensity at one, unspecified, velocity which can make comparisons difficult [88]. While the aforementioned limitations should be considered, the MAS is easily administered and remains the most widely reported assessment of spasticity in the chronic stroke population [89]. Inclusion of this outcome measure allows for comparison of outcomes from different studies which is paramount for determining the effectiveness of an intervention.

Motor Function:

Timed Up and Go (TUG)

The TUG is widely used to assess mobility, balance and locomotor performance in elderly people with balance disturbances [90]. This outcome measure requires minimal equipment and assessor training, is quick and easy to administer with minimal limitations when performed correctly. Previous lower limb cross-education studies in stroke report TUG outcomes [2], again allowing for direct comparison of interventions across studies. Based on the results of this feasibility pilot study, it is recommended that the TUG is included as an outcome measure in a fully powered RCT.

10 Metre Walk Test (10MWT)

The 10MWT is used in previous lower limb cross-education studies in stroke [2] to assess functional mobility and gait velocity by measuring walking speed in metres per second over a short duration. Again, this outcome measure is easily administered with minimal equipment and assessor training. Although this measure may not be appropriate for individuals that require assistance to ambulate, in this study all participants were able to complete the test either with assistive walking devices or without any assistance whatsoever. With its use widely reported and clearly defined Minimal Detectable Change and Minimal Clinically Important Difference, this measure was deemed suitable for this current study and is recommended for inclusion in a larger trial.

London Handicap Scale (LHS)

As in other stroke studies [91, 92], the LHS was used in this study to assess self-perceived participation and self-perceived impact of stroke. Measurement tools with good

psychometric properties are essential in documenting the effects or impacts of any clinical intervention [93] and measurement of participation, one of the major outcomes of stroke rehabilitation, is essential [33]. This assessment tool has been reported to have good reliability and validity and is deemed suitable for measuring self-perceived participation in stroke patients [33]. In this study, the questionnaire was easy and quick to administer with little assessor training required. Therefore, it is recommended that the LHS is implemented in a similar larger scale trial.

Effect size of the main outcome measure needed to estimate sample size

The main purpose of this study was to investigate the concept of using 2 neuroplastic principles in stroke patients, to test the use of outcome measures, assess for adverse effects and to explore the evidence for the benefit of cross-education plus MT over cross-education alone. Evidence for such benefits would be detected via outcome measures, with particular attention to clinically significant changes observed as a result of either treatment. Ultimately, the aim of any rehabilitation intervention is to bring about clinically important improvements in functional ability for the patient as a result of the treatment. In this study, such improvements were clearly noted for walking speed in the MST group, measured by the 10MWT.

One of the objectives of a feasibility study is to establish a) if there is a potential benefit of one treatment over another, b) establish the effect size of the difference between the treatments, and c) recommend an appropriate sample size for a future fully powered RCT based on these effect sizes.

With the above in mind, this study has established that the combination treatment of cross-education with MT shows a trend to greater therapeutic outcomes than cross-education alone. The results indicate a near significant difference between the two treatments, in favour of the MST therapy, for improving walking speed (p = 0.055) with a medium effect size (Cohen's d = 0.7). Based on sample size calculation in the literature [94], it is therefore recommended that a future fully powered trial consists of a total sample size of 68 participants (34 in each group) [95].

Time needed to collect data and statistical analysis of data

In this study, data was collected over three separate assessment sessions; baseline, post-intervention and 3-month follow-up. Each assessment session took place at the IT Sligo exercise physiology laboratory and required a duration of approximately 30 minutes per participant. Assessments required at least 2 assessors, blinded to treatment allocation, to be present. All assessments proved to be easily managed with minimal stress to the participant. After each assessment time point, strength data was extracted from the Biodex Isokinetic Dynamometer System 3 Advantage software (version 3.45) by the principal researcher. Strength data extraction took approximately 20 minutes per participant for each strength assessment time point. All assessment data was then entered manually into IBM SPSS for Windows (Version 20, Chicago, IL, USA) and statistically analysed. Overall, data collection and analysis proved efficient therefore the same process is recommended for future research based on this feasibility study.

Finally, in feasibility studies the emphasis is not strictly on hypothesis testing, but to estimate important parameters needed for fully powered trials [96]. For that reason, in

this study all *p*-values <0.05 were considered statistically significant [96]. For a fully powered trial, significant *p*-values could be adjusted to <0.025 when analysing 2 priori hypotheses (i.e. change T1-T2 and change T1-T3) to compensate for the Family Wise Error (FWE) inflation [97]. When using analysis of variance (ANOVA) over the three time points, only data sets of participants completing all three assessments (T1, T2 and T3) are included. Four participants were lost to follow-up assessment (T3) in this feasibility study, therefore using multiple statistical tests instead of ANOVA in this study permitted inclusion of all complete data sets when analysing pre-intervention (T1) to post-intervention (T2). When analysing pre-intervention (T1) to 3-month follow-up (T3), only complete data sets for both time points were included.

5.6 Limitations

Recruitment and participation in this study were influenced by geographical location, resulting in a limited sample size and wide demographic characteristics and baseline measures of subjects. Due to the nature of the intervention and the fact that the principal researcher of this study was also the therapist administering the treatment, blinding of both the participants and the therapist to the treatment was not achieved. It must be noted that although participants were instructed to refrain from lower limb strength training activity between post-intervention and 3-month follow-up, it was impossible to eliminate the potential for continued training. Also, this study did not objectively measure training intensity or control for placebo effects, therefore the results of this study must be interpreted with caution.

As previously described, isometric contractions were used as the training mode in this study. Previous studies have reported that the magnitude of cross-education is dependent on training mode and training intensity [42, 64, 98], suggesting that a dynamic mode focussing on muscle lengthening rather than shortening may achieve greater cross-education effects [64]. With this in mind, future studies may consider including a high resistance dynamic training mode rather than training isometrically.

Previous research has attempted to identify exact mechanisms that result in contralateral performance improvements following unilateral training by using brain imaging [99]; however, it was not possible to include such techniques during this feasibility study. Studies that include brain imaging during performance of the combined cross-education and MT training would provide valuable information regarding the mechanisms by which mirror visual feedback enhances the cross-education effect post-stroke. Future high quality RCT's with larger sample sizes are required to further investigate the effects of these therapies and to substantiate the findings of this feasibility study.

5.7 Recommendations

Based on the findings of this pilot study, a fully powered trial is feasible. Future research may consider implementing a cross-education and MT intervention in a stroke population that maximises the potential for rehabilitative outcomes. Ideally, a longer intervention duration (>6 weeks) should be applied that allows for a greater overall treatment dose. As previously described, the magnitude of cross-education seems to be influenced by training mode [42, 64, 98]. Therefore, future studies may consider including a high resistance dynamic training mode rather than training isometrically.

5.8 Conclusion

This study presents new evidence that cross-education combined with MT may have the potential to reduce lower limb spasticity, increase motor function and improve self-perceived participation in chronic stroke patients. The findings of this research also add weight to existing evidence [1] that mirror visual feedback during unilateral strength training may achieve more favourable rehabilitative gains than unilateral strength training alone. This combination of therapies has shown to be time effective, easy to implement in an outpatient/community setting and without adverse effects. This feasibility study has established effect sizes for appropriate clinical measures which can be further implemented when calculating sample sizes for fully powered trials. In summary, this study provides important and not previously investigated information that viewing the LA lower limb in a mirror while strength training may have the ability to enhance rehabilitation of a paretic lower limb post-stroke.

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6.0 A Cross-Education and Mirror Therapy Strength Training Device

6.1 Outline

Previous research [1] has established the benefits for mirror therapy (MT) to enhance the cross-education effect in healthy subjects. Chapters 4.0 and 5.0 of this thesis applied the combined principles of cross-education of strength and MT to chronic stroke patients, with positive outcomes reported for reducing lower limb spasticity, increasing strength, improving motor function and improving self-perceived participation.

As previously discussed, initial recruitment of participants for the case study (Chapter 4.0) and the randomised controlled feasibility pilot study (Chapter 5.0) within this thesis, proved difficult due to the need for participants to travel to and from the Institute of Technology Sligo (IT Sligo) exercise physiology laboratory to take part in the intervention training sessions. With this in mind, it was decided to amend the methods of the study to include a home-based cross-education and MT intervention. Previously, all intervention training was planned to take place using the Biodex System 3 isokinetic dynamometer in the IT Sligo exercise physiology laboratory. However, this equipment is not portable and not suitable for a home-based intervention. Therefore, the need arose for a portable ankle dorsiflexion strength training device.

After extensive research for a suitable portable strength training device, it became apparent that no such device that allowed for the specific combination of cross-education and MT was available for purchase. This led the IT Sligo Neuroplasticity Research Group to collaborate with the Creative Design Department at IT Sligo, to design a suitable ankle dorsiflexion strength training device that could be used in the participants own home with or without the addition of mirror visual feedback.

6.2 Design

The device was designed in accordance with previously established isometric strength training [2] and reliable assessment criteria (as detailed in Chapters 3.0 of this thesis) (i.e ankle joint angle of 100^{o}). The strength training device was designed to fit a wide range of foot/leg sizes and to be used both left and right sided. It made sense that the shell of the device would be transparent to allow for viewing of contracting muscles and ligaments when observing the mirror reflection of the training limb. A number of prototypes were created and trialled on healthy volunteers before trialling on stroke patients. The final device was used in the unilateral strength training intervention implemented in the case study (Chapter 4.0) and the randomised controlled feasibility pilot study (Chapter 5.0) within this thesis.

6.3 Commercialisation

With positive subjective feedback from participants, expressing wishes to keep or purchase the device after the trial, the IT Sligo Neuroplasticity Research Group investigated the possibility of bringing the device to commercialisation. Since then, a number of stages have been successfully completed with IT Sligo Research and Innovation Centre confirming the device patentable. Based on the findings within this thesis and findings of a similar upper limb study (currently under review) conducted by the IT Sligo Neuroplasticity Research Group, Enterprise Ireland have funded a Commercialisation Feasibility Project. The IT Sligo Neuroplasticity Research Group are now finalising an application for further Enterprise Ireland funding to bring a lower and

upper limb mirror strength training product to commercialisation. Prototypes of devices are illustrated in Figure 6.1 (lower limb) and Figure 6.2 (upper limb).

Figure 6.1: Lower Limb Mirror Strength Training Device

Figure 6.2: Upper Limb Mirror Strength Training Device

6.4 Summary

Rehabilitation for chronic stroke patients is currently time consuming and expensive. The findings of this thesis indicate that the principles of cross-education combined with MT can significantly improve post-stroke motor function in a low risk, cost effective way. The new mirror strength training device utilises these principles allowing for independent and inexpensive therapy.

Further to findings discussed, this thesis has established:

- The development of a new innovative cost effective 'Mirror Strength Training Device' prototype that can be used in home settings.

- The beneficial effects of the device/therapies on strength, spasticity and motor function with no increase in asymmetry deficits or adverse effects.
- Subjective enthusiasm and motivational benefits of using both principles when function has already plateaued.

6.5 References

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7.0 General Discussion and Conclusions

7.1 Summary of Main Findings

The main aims of this thesis were to: 1) investigate the feasibility for applying the combination of cross-education strength training with mirror therapy (MT) in a chronic stroke population and 2) compare the combination therapy to cross-education alone, exploring the hypothesis that MT influences the cross-education effect and improves lower limb motor function in chronic stroke patients. This section summarises the main findings of this thesis and suggests potential areas for future research.

7.1.1 Evidence for Cross-Education with and without Mirror Therapy for Post-Stroke Rehabilitation

Chapter 1.0 describes the theoretical background to both cross-education and MT and offers evidence that a) both therapies have proven effective singularly as rehabilitation techniques for conditions with unilateral deficit, b) the combination therapy has shown more favourable outcomes than cross-education alone in a healthy population [1] and c) both therapies seem to evoke increased activity in the untrained M1 resulting in cortical and spinal adaptations that create a more effective motor pathway to the untrained limb.

Chapter 2.0 reviews existing literature and provides moderate to strong evidence that cross-education of strength can induce rehabilitative effects in a chronic stroke population [2, 3]. Together, Chapters 1.0 and 2.0 identify the positive effects of cross-education and MT and describe the substantial gap in the literature exploring the previously untested hypothesised theory that MT may have the potential to augment the cross-education effect and further enhance motor recovery after stroke.

7.1.2 A Reliable Strength Testing Protocol

Chapter 3.0 outlines and tests the reliability of a strength testing protocol for assessing the three important parameters of isometric strength; Peak Torque (PT), Rate of Torque Development (RTD) and the previously unexplored parameter of Average Torque (AT). This chapter describes that RTD and AT may be more meaningful strength parameters than PT alone, particularly when assessing isometric strength in clinical populations. The study in Chapter 3.0 reports excellent reliability for all three strength parameters and provides novel guidance for implementing the testing protocol on the Biodex System 3 Isokinetic Dynamometer. The study concludes that the reliable testing protocol is applicable for assessing ankle dorsiflexion and elbow extension strength in both exercise science and clinical settings and forms the basis for assessing ankle dorsiflexion strength in the proceeding chapters (4.0 and 5.0) of this thesis.

7.1.3 The Application of Cross-Education and Mirror Therapy for Post-Stroke Recovery

Chapter 4.0 presents a case study that explores the application of cross-education combined with MT as a rehabilitation treatment for a chronic stroke patient. This case study is the first to investigate the novel combination therapy in the lower limb after stroke. It is also the first to develop and implement the use of a custom lower limb isometric mirror strength training device that can be used in a patient's own home, requiring minimal therapist assistance. The results of this case study indicate that cross-education combined with MT has the potential to substantially increase contralateral more-affected (MA) ankle dorsiflexion strength, reduce lower limb spasticity, increase motor function and improve self-perceived participation post-stroke. Furthermore, the

therapy has shown to be time effective, easy to implement in an outpatient/community setting and without adverse effects. The findings provided new positive evidence for implementing the combination therapy and suggested the need for a larger study which incorporates a randomised controlled trial design to further explore the feasibility of applying the treatment to chronic stroke patients.

Chapter 5.0 details a randomised controlled feasibility study to explore the concept that viewing the training less-affected (LA) lower limb in the mirror may augment the cross-education effect and enhance post-stroke motor recovery more favourably than cross-education alone. Chapter 5.0 also further demonstrates the implementation of the training protocol and outcome measures used in the case study presented in Chapter 4.0. Clinical evaluation of motor function was assessed as well as psychometric evaluation of self-perceived participation. Results at post-intervention indicated that a significant reduction in spasticity was achieved in both the non-mirror and the mirror training group. However, the mirror training group showed near significant gains in untrained (MA) dorsiflexion strength and significant improvements in motor function and self-perceived participation. The findings of the feasibility study suggest that a fully powered trial is both feasible and necessary to further establish whether mirror visual feedback of the training (LA) limb may induce more favourable rehabilitative effects on motor function than cross-education alone.

The feasibility study has implemented a reliable strength testing protocol that allows the three major strength parameters (PT, RTD and AT) to be assessed in a clinical population. This project has also demonstrated the use of a practical mirror strength training device

that has potential to be accessible to clinical populations for use in their own home, allowing for reduced patient–therapist contact time. This feasibility study has established a rehabilitation intervention that has shown to be easy to implement in outpatient/community settings and without adverse effects. It has also identified suitable outcome measures that are in-line with the three levels of human functioning as outlined in the International Classification of Functioning, Disability and Health framework (ICF) [4]. Finally, the feasibility study has established an effect size that can be used to calculate sample sizes for future similar research. The results indicate a near significant difference between the two treatments in favour of cross-education with mirror visual feedback, for improving walking speed (p = 0.055) with a medium effect size (Cohen's d = 0.7), recommending that a future fully powered trial consists of a total sample size of 68 participants (34 in each group).

7.1.4 A Cross-Education Mirror Strength Training Device

Chapter 6.0 offers a brief description of the development of a novel 'mirror strength training device'. Use of this device was implemented in the home-based rehabilitation interventions outlined in chapters 4.0 and 5.0 of this thesis. As discussed in Chapter 6.0, patient subjective feedback on the use of the device was extremely positive. With no such device currently available worldwide for purchase, the Institute of Technology Sligo (IT Sligo) Neuroplasticity Research Group have been successful in being awarded Enterprise Ireland funds to complete a Commercialisation Feasibility Project (currently ongoing). The development of an ankle dorsiflexion mirror strength training device has enabled this thesis to investigate the potentially positive rehabilitative effects of cross-education and MT in the lower limb after stroke. Similarly, an upper limb mirror strength

training device has been developed by the IT Sligo Neuroplasticity Research Group and implemented in a similar upper limb study. Together, these devices will offer stroke patients the chance to engage in an effective, affordable, home-based rehabilitation therapy that addresses post-stroke deficits of the MA limb by training the LA limb. Furthermore, the therapy can be applied without the need for constant therapist supervision, potentially reducing costs to health services.

7.1.5 Mechanisms of Cross-Education and Mirror Therapy

This thesis did not set out to measure or identify the specific mechanisms of cross-education and MT post-stroke. Nevertheless, it is important to consider existing literature and at least speculate on the possible adaptations that result in reduced spasticity, cross-education of strength, and improved motor function.

The underlying cause of spasticity is the hyperexcitability of the stretch reflex resulting from abnormal processing in the spinal cord and the balance between excitatory and inhibitory signals being disrupted [5]. As previously discussed the Modified Ashworth Scale (MAS), used in this thesis, produces a global assessment of the resistance to passive movement which is influenced by non-contractile soft tissue properties, persistent muscle activity (dystonia), intrinsic joint stiffness, and stretch reflex responses [6]. Therefore, the specific adaptations underlying the improvements in MAS scores cannot be quantified here. However, cross-education training has been shown to increase activity in the untrained M1 [7, 8], decrease interhemispheric inhibition [1, 9], reduce H-reflex excitability [10, 11], reduce antagonist co-activation [12] and increase

active range of motion in the untrained limb [13]. A combination of such adaptations may be responsible for the reduction in spasticity observed in this thesis.

Cross-education of strength is further associated with reductions in contralateral silent period (cSP) duration [1, 14]. Interestingly, silent period has been shown to lengthen in the contralateral hemisphere to the paretic side after stroke [15]. Following unilateral strength training with mirror visual feedback, Zult et al. [1] found a 15% decrease in cSP in the mirror training group, with no decrease in the non-mirror training group, which also coincided with a higher magnitude of strength transfer in the mirror group (61%) compared to the non-mirror group (34%). These findings emphasise the importance of the modulation of this inhibitory path in evoking cross-education. In line with Zult et al. [1], a trend to more favourable motor function outcomes were observed in the mirror training group in this thesis. It is therefore plausible that mirror visual feedback of the training limb has resulted in greater cross-education adaptations, further reducing inhibitory mechanisms, enhancing untrained M1 activity, decreasing stretch reflex excitability and increasing agonist/antagonist synergy in the MA limb. Additionally, mirror visual feedback may have influenced a restored congruent afferent feedback, leading to a reversing of learned paralysis after a long period of non-use, resulting in more effective motor output and ultimately improving motor performance. To date, no study has attempted to identify the specific mechanisms underlying the combination of cross-education and MT in a stroke setting. It would make sense that mechanisms are similar to that of non-clinical populations, i.e. primarily on cortical and corticospinal levels; however, future research needs to focus on confirming these speculations.

7.2 Clinical Implications

This thesis has established the need for a fully powered trial to further investigate the combination of cross-education and MT as a post-stroke rehabilitation treatment. Intervention and assessments protocols are presented in this body of work along with effect sizes for calculating fully powered sample sizes. This thesis also presents new evidence that cross-education combined with MT may have potential to significantly reduce lower limb spasticity, increase motor function and improve self-perceived participation in chronic stroke patients. Furthermore, it offers valuable evidence that a novel home-based unilateral strength training intervention achieves positive therapeutic outcomes with the potential to reduce patient–therapist contact time, offering a patient centred treatment in-line with early supported discharge services [16].

7.3 Limitations

This thesis has several limitations. The case study (Chapter 4.0) reports substantial positive outcomes for a single stroke patient after a cross-education and MT intervention. Findings of this case study simply offer an insight into the application of the combination therapy for stroke recovery. However, as with any single case report, findings must be interpreted with caution and cannot be generalised for the wider population. Due to the nature of the intervention, it was impossible to blind both the participants and therapists to treatment. It was also difficult to control for participant's engagement in additional training/rehabilitation exercise outside of the intervention sessions. Similarly, such limitations exist within the randomised controlled feasibility study (Chapter 5.0). This study consisted of two training experimental groups (a cross-

education training group and a cross-education with mirror training group), without a non-treatment control group. The primary aim of the study was to investigate whether mirror visual feedback of the training limb can further enhance the cross-education effect and result in rehabilitative outcomes in the MA lower limb after stroke. A more extensive investigation of the therapies might include a non-training group to allow comparison of intervention outcomes. Furthermore, this study did not control for a placebo effect. Previous MT studies have included a sham therapy, i.e. the non-reflective side or an obstructed view of the mirror [1, 17, 18]. With this in mind, the influence of a training placebo on the positive findings in this study cannot be ruled out.

Unilateral strength training intensity (i.e. % of MVC) has been shown to affect the magnitude of cross-education [19, 20]. Participants in the studies within this thesis were instructed to contract as hard as possible in an effort to achieve maximal cross-education gains. Without measuring individual training intensity, it is impossible to gauge if participants were actually training at a maximal level. Therefore, one potential reason for the lack of cross-education of strength observed in the cross-education only group may be due to not training at a high enough intensity. For a more comprehensive investigation, training intensity should be monitored.

This thesis did not directly investigate the physiological mechanisms underlying the cross-education or MT effects post-stroke. Therefore, no concluding inferences can be made for the specific sites of physiological adaptation following the training interventions. Similarly, this thesis cannot give direct evidence that physiological

adaptations occurring for stroke patients is comparable to adaptations identified in healthy subjects of previous cross-education and MT studies.

One major limitation of this thesis is sample size. The protocol reliability study (Chapter 3.0) consisted of 12 participants. Although the sample size is considered sufficient for testing reliability [21], it does not allow for sub-group analysis of age categories, sex or dominant vs. non-dominant side.

Recruitment for the randomised controlled feasibility study (Chapter 5.0) was heavily influenced by rural geographical location. This resulted in a relatively small sample size of 31 participants with broad variability in demographic characteristics. Sample size calculation based on motor function effect sizes of this feasibility study identified a requirement of 68 participants (34 in each group) for a fully powered trial. A larger sample size would have again permitted more detailed analysis and comparison of sub-groups. Even so, the fact that this study is a feasibility study, the relatively small sample size is justified. Furthermore, this study is the first to carry out a lower limb cross-education with MT intervention in a stroke population and to compare the combination therapy to cross-education alone. Therefore, the findings of this thesis are novel and offer new knowledge on the application of these therapies.

7.4 Future Research

This project has identified a number of questions in relation to the therapies applied that are yet to be resolved. Questions of particular interest are:

When strength training with mirror visual feedback, what are the minimum and optimum training intensities/durations required to achieve therapeutic effects for a chronic stroke population?

Is this combination of therapies more effective in stroke patients if dynamic resistance training is applied rather than isometric?

Can the principles of cross-education and MT be combined with other neuroplasticity principles with beneficial outcomes? (e.g. virtual reality/augmented reality, constraint induced therapy and mental practice).

Can the combinations of cross-education and MT be applied effectively to acute/sub-acute stroke patients to accelerate early stage recovery?

What are the specific cortical or corticospinal adaptations occurring in chronic stroke patients that result in spasticity reduction and motor function improvement following unilateral strength training with and without mirror visual feedback?

Finally, this thesis presents new evidence that cross-education combined with MT can induce therapeutic effects that ultimately improve motor function. Therefore, a natural progression would be to explore whether such rehabilitation improvements can be achieved in other neurological or orthopaedic conditions that result in a one sided weakness.

In summary, future high quality clinical trials should focus on exploring variations of training intensity, duration and contraction type to identify the optimum training mode and dose for achieving clinical improvements after stroke.

7.5 Conclusion

This thesis provides novel and not previously investigated information that viewing the LA lower limb in a mirror, while unilaterally strength training, may have potential to enhance the rehabilitation of the MA lower limb post-stroke. The findings offer new evidence that the combination therapy of cross-education and MT could be beneficial to neurological injury rehabilitation and that a fully powered trial is necessary to further substantiate the effectiveness of the treatment. This thesis also adds weight to existing evidence [1] that mirror visual feedback during unilateral strength training is associated with more favourable outcomes than unilateral strength training alone.

7.6 References

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Appendices

Appendix A: Ethical Approval - *Reliability of Isometric Ankle Dorsiflexion and Elbow Extension Measured with Biodex System 3 Isokinetic Dynamometer.*

IT Sligo
An Institiúid Teicneolaíochta, Sligeach

Daniel Simpson
School of Science
IT Sligo
Ash Lane
Sligo

March 20th 2016

Re. Research Ethics Application

Dear Mr Simpson,

The Research Ethics Committee (REC) at IT Sligo Health Science Programme Board has received your revised submission of the study "*Reliability of Isometric Ankle Dorsiflexion and Elbow Extension Measured with Biodex System 3 Isokinetic Dynamometer*". The revisions / clarifications meet the requirements of the REC and the REC Chairman has given a favourable ethical opinion for the above study.

Documents reviewed:
- REC Application Form
- Consent Form
- Invitation letters
- Information Sheet
- PI CV

The REC requires that approved studies submit an annual report to the REC. The annual report for the above study is due on March 20th 2017.

Yours sincerely,

Dr Kenneth Monaghan
Chairman

Appendix B: Participant Information Sheet - *Reliability of Isometric Ankle Dorsiflexion and Elbow Extension Measured with Biodex System 3 Isokinetic Dynamometer*.

Re: Test-retest reliability study for ankle dorsiflexion and elbow extension on the Biodex System 3 Isokinetic Dynamometer

Thank you for expressing an interest in the above mentioned study.

If you choose to take part, you will be required to follow a maximal isometric strength testing protocol for the right dorsiflexor and right triceps. Isometric means you will contract muscles without initiating movement like clenching a tight fist. The dorsiflexor enables you to pull your toes towards your shin; the triceps muscle is activated when you straighten your arm. The testing will take place in IT Sligo Physiology Laboratory with the Biodex System 3 Isokinetic Dynamometer.

If you decide to take part in the study you will be asked to perform the maximal isometric strength testing protocol at three different dates. The first time (familiarization) will approximately take 60min; the second and third session will only take 30min. Participants cannot partake in any strenuous exercise for 48hours prior to testing.
Two principal researchers (Daniel & Monika) will be present during each assessment and will explain the protocol thoroughly.
The protocol consists of:

- Warm – up: 3 minutes on an exercise/hand bike & 5 submaximal contractions.
- Strength testing: 4 maximal isometric contractions held for 5s with a 45s break

Please feel free to contact us with any questions that you may have.

Kindest regards

Mr Daniel Simpson & Ms Monika Ehrensberger

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Appendix C: Participant Consent Form - *Reliability of Isometric Ankle Dorsiflexion and Elbow Extension Measured with Biodex System 3 Isokinetic Dynamometer.*

Participation Consent Form

<u>Test-retest reliability study for triceps extension and dorsiflexion on Biodex System 3</u>

1. I confirm that I have received a copy of the Information Sheet for the above study. I have read it and I understand it. I have received an explanation of the nature and purpose of the study and what my involvement will be.

2. I have had time to consider whether to take part in this study and I have had the opportunity to ask questions.

3. I understand that my participation is voluntary and that I can decide to opt out of the research at any time.

4. I understand that all information gathered about me during this study will be treated with full confidentiality.

5. I agree to take part in the above study.

_____ _____ _____

Appendix D: Biodex System 3 Isokinetic Dynamometer Application/Operation Manual – *Ankle Dorsiflexion*

ANKLE: PLANTAR/DORSIFLEXION (SEATED)

Figure 3.4.

Figure 3.5.

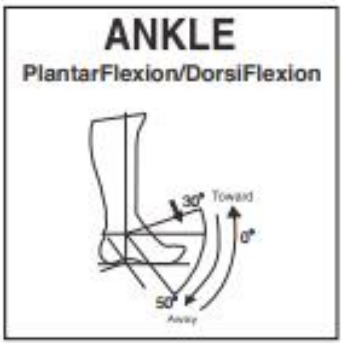


Figure 3.6.

Quick Reference

Dynamometer Orientation:	90°
Dynamometer Tilt:	0°
Seat Orientation:	90°
Seatback Tilt:	70 - 85°
Footplate Tilt:	0°
Footplate Code:	Red dot to P/D
Knee Flexion:	20 - 30°
Axis of Rotation:	In neutral position, axis passes through the body of talus, fibular malleolus, and through or just below the tibial malleolus.
Ready Position:	Full Plantarflexion

Parts Needed

Dynamometer:	Ankle Attachment
Positioning Chair:	Limb-Support Pad, T-Bar, Footrest (optional)

ANKLE: PLANTAR/DORSIFLEXION (SEATED)

The ankle joint or talocrural joint is really three joints (tibiotalar, fibulotalar, and tibiofibular) formed by the superior portion of the body of the talus fitting within the cavity created by the combined distal ends of the tibia and fibula. The subtalar joint is the articulation between the talus and calcaneus.

Motions of the ankle are rarely true single plane motions. This holds for dorsiflexion/plantarflexion, which usually occurs in conjunction with other movements.

Setup and Positioning

(Starting Movement: Toward/Dorsiflexion)

NOTE: For both ankles, the limb support pad is positioned in the positioning chair front right receiving tube.

1. Seat patient on chair.
2. Rotate chair to 90 degrees.
3. Set seat back tilt to 70 - 85 degrees.
4. Install Limb Support Pad (with T-Bar) in the positioning chair front right receiving tube. Angle support toward chair. Place pad under distal femur and secure with strap. The pad should be positioned under the calf (distal to the knee) allowing for approximately 20° to 30° of knee flexion.

   NOTE: Because the origin of insertion of the gastrocnemius is above the knee, the extent of ankle dorsiflexion will generally increase with increased knee flexion and decrease with knee extension. Positioning should be recorded for valid comparisons and reproducibility.

   NOTE: For exercise, the footrest may be inserted in the left chair front receiving tube if desired. Use of the footrest provides a stable base for the patient to push off and may cause the system to record artificial peak torques.

5. Rotate dynamometer to 90 degrees.
6. Set dynamometer tilt to 0 degrees.
7. Attach Ankle Attachment dynamometer.
   - Place Ankle Attachment input tube on dynamometer so that P/D engraving faces outward then rotate footplate so that P/D aligns with the dynamometer shaft red dot.
   - With attachment tube horizontal, press Hold.
8. Raise dynamometer to align axis of rotation.
9. Move patient into position and align patient ankle axis of rotation with dynamometer shaft.
10. Strap foot to footplate.
11. Stabilize patient with appropriate straps.
12. Set ROM stops

Opposite Side

1. Press Hold to retain dynamometer shaft position.
2. Unstrap patient's ankle and leg.
3. With patient remaining in chair, slide chair away from dynamometer.
4. Place limb support in the opposite receiving tube .
   Angle limb support toward patient (switch with footrest if needed).
5. Place limb support pad under distal femur and secure with strap.
6. Slide dynamometer in front of ankle to be tested.
7. Move patient forward and secure leg in limb support with foot on footplate.
8. Align patient ankle axis of rotation with dynamometer shaft.
9. Strap foot to footplate.
10. Stabilize patient with appropriate straps.
11. Reset ROM Stops as needed.

Appendix E: Biodex System 3 Isokinetic Dynamometer Application/Operation Manual – *Elbow Extension*

ELBOW: EXTENSION/FLEXION (SEATED)

Figure 3.34

Figure 3.35.

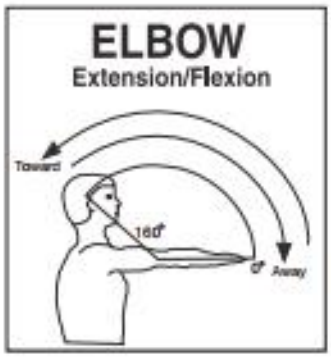


Figure 3.36.

Quick Reference

Dynamometer Orientation:	30°
Dynamometer Tilt:	0°
Positioning Chair Orientation:	0°
Seatback Tilt:	85°
Axis of Rotation:	Passes through the center of the trochlea and the capitulum, bisecting the longitudinal axis of the shaft of the humerus.
Ready Position:	Full Flexion

Parts Needed

Dynamometer:	Elbow/Shoulder Attachment
Positioning Chair:	Limb-Support Pad, Footrest (optional)

ELBOW: EXTENSION/FLEXION

The elbow joint consists of the articulation between the trochlea of the humerus and the trochlear notch of the ulna, the capitulum of the humerus and the facet on the head of the radius and the circumference of the head of the radius and the radial notch of the ulna. Any bony malalignment (such as a fracture) interferes with the critical angles of these articulations making normal movement impossible.

Of special note at the elbow are the tendinous origins of the wrist musculature. The flexor/pronator muscles of the wrist originate at the medial epicondyle of the humerus and wrist extensor group at the lateral epicondyle. These are areas that frequently become inflamed with overuse.

Setup and Positioning

(Starting Movement: Away/Extension)

1. Seat patient on chair
2. Place Elbow/Shoulder attachment onto shaft (remove cuff). Align shaft dot with either R or L. Bring attachment to vertical. Press Hold.
3. Install limb support (angled toward patient) in chair side receiving tube for side to be tested or exercised.
4. Rest elbow on limb support. Limb support pad should be angled back with pad angled slightly downward, allowing full extension. Securing strap may not be necessary.
5. Rotate chair to 0 degrees.
6. Rotate dynamometer to 30 degrees.
7. Tilt dynamometer to 0 degrees.
8. Move patient into position. Slide dynamometer along travel and raise to align axis of rotation.
9. Stabilize patient with shoulder, waist and thigh straps.
10. Allow handgrip to rotate as patient goes through motion.
11. Set ROM Stops.

Opposite Side

1. Press Hold.
2. Unstrap patient from support pad. With patient remaining in chair, slide chair back away from dynamometer.
3. Place limb support in opposite side chair receiving tube.
4. Remove attachment and rotate it 180 degrees opposite. Align shaft dot with R or L. Place attachment back onto shaft and secure with locking knob.
5. Rotate dynamometer to 30 degrees on opposite side.
6. Rotate chair to 0 degrees on opposite side.
7. Move patient into position. Slide dynamometer along travel to align axis of rotation.
8. Allow handgrip to rotate as patient goes through motion.
9. Stabilize patient with shoulder, waist and thigh straps.
10. Reset ROM stops

Appendix F: Participant Information Sheet - *Mirror Therapy and Unilateral Strength Training for Enhancing Motor Function after Stroke in the Lower Extremity*

Participant Information Sheet

Mirror Therapy and Unilateral Strength Training for Enhancing Motor Function after Stroke

Introduction

Hello, thank you for expressing your interest in taking part in our study. You have been invited to take part in a research study on a new and emerging stroke rehabilitation therapy called 'Mirror Therapy and Unilateral Strength Training'. This information sheet has been written for you, to clearly explain what those terms mean, how and where the study will take place and why we are conducting this research. Please read the sheet carefully to ensure that you understand all the information. If there are any questions, please feel free to contact us at any time. All contact details are provided at the bottom of the page.

The study is being conducted by the Institute of Technology Sligo (IT Sligo).

Mirror therapy

Mirror therapy is based on visual stimulation or visual illusion. Basically, it is tricking the brain into thinking it is seeing something it is not. During mirror therapy, a mirror is placed in the centre of a person's line of vision. The affected (weakened) limb is placed behind the mirror out of sight and the unaffected limb is placed in front of the mirror so as you can see its reflection. As we mentioned, this is now tricking the brain, as when you look in the mirror you do not see your weakened arm or leg but the reflection of your unaffected limb. It now appears that both legs or both arms are working perfectly. This then causes your brain to increase the amount of signals it sends to the hidden and affected limb, helping to increase its movement. It has been suggested that mirror therapy is a simple, inexpensive method and, most importantly, can be done by the patient themselves to improve upper and lower limb function.

Unilateral Strength Training

Unilateral strength training is strength training of one side of the body only, in this case your less-affected side only. Evidence shows that strength improvements shown in the trained limb can also be transferred into the untrained limb, this is known as cross-education.

The combination of mirror therapy and unilateral strength training means that the training of the less-affected lower limb will take place while you watch its reflection in a mirror.

Study

This study is being conducted as part of a research masters and PhD qualification by postgraduate student Daniel Simpson. He has attained a BSc Degree in Health Science & Physiology, and BSc Honors degree in Public Health & Health Promotion. Daniel has previously worked with the North-Western Rheumatology unit at Our Ladys Hospital, Manorhamilton. Daniel's supervisor is Dr Kenneth Monaghan, who lectures in IT Sligo. Dr Kenneth Monaghan is a chartered Physiotherapist who specialises in stroke rehabilitation and he has attained a PhD in this area from Trinity College Dublin.

You will be required to attend the Institute of Technology Sligo Health Science & Exercise Physiology Lab for assessment. The training sessions will take place in your own home for 30 minutes, 3-days per week, for 4 weeks. At each session, you will be required to perform voluntary isometric contractions of a muscle in the lower limb of your less-affected side, i.e. dorsiflexion (lifting your toes in an upward direction), while seated comfortably in a chair. The lead researcher (Mr. Daniel Simpson) will be present at all times during your training sessions. You will be formally assessed by a chartered physiotherapist (Dr. Kenneth Monaghan) at the beginning of the study, directly after the study has finished and 3 months after its completion. This is to accurately gauge any progress made during the study period. This study comprises of two separate groups. The first will receive mirror therapy and unilateral strength training and the second will receive unilateral strength training only. It is necessary to have two groups within this study to clearly see the effects of mirror therapy and unilateral strength training. However, no matter what group you are assigned to, you will receive the proven benefits of strength training rehabilitation for a 4-week period.

Location

All rehabilitation/training sessions will take place in your own home.

Assessments

Assessments will take place on Institute of Technology Sligo (IT Sligo) campus in the Health Science & Physiology Exercise Laboratory. IT Sligo is located directly behind Sligo Regional Hospital and is easily accessible from anywhere in the Sligo area. All assessments will be carried out by a chartered physiotherapist. The assessments will take place at the beginning of the study, 4 weeks later upon study completion and 3 months after you have completed the therapy. Three assessments are necessary to accurately track progress made throughout the therapy. The first assessment identifies levels of functioning before you begin. The second identifies progress made directly

after the therapy and the third assessment is necessary to see how the improvements have been maintained over the 3-month gap.

Confidentiality

All personal information and results from the study are treated as highly confidential. All final results are anonymised; this means that names or any other information that could identify you as a participant are removed after the initial testing period. All personal information collected is legally protected under both the Data Protection Act and the IT Sligo confidentiality agreement. You have the right to access all personal information at any time throughout the study and after its completion. All information is stored securely on the IT Sligo campus and access to this information is given only to those directly involved in the study. All hard copy (written) information is kept securely in a locked filing cabinet in a secure office and all electronic data (computer) is password protected. No information is taken off the IT Sligo campus. Results may potentially be published in scientific journals or be presented at medical conferences, however, no participant can be identified as all data is anonymised at this stage.

Do I have the right to opt out of the study?

Yes. Your participation is entirely voluntary. You have to right to cease involvement in the study at any time you wish, without having to provide a reason.

Potential benefit of the study

Unilateral strength training has already been proven to benefit functional recovery post-stroke. In addition, Mirror therapy is a new therapeutic intervention for stroke rehabilitation, which aims to improve stroke health care and rehabilitation. Thus, for these improvements to happen, it is vital that research studies such as this one take place. Very little research has taken place involving unilateral strength training and mirror therapy following stroke and so, results from this study stand to benefit those who have decreased lower limb functioning.

Personal benefit

Previous studies from around the world involving mirror therapy/unilateral strength training have shown a direct benefit to those who participated, with both upper and lower limb functioning improving and these improvements were also found to remain

after the therapy has finished. Thus, it is hoped that individual levels of lower limb functioning and walking ability will improve following the 4 weeks of mirror therapy and unilateral strength training in the present study. However, it must be stated, that as a study of this exact nature has never taken place, the improvements seen in other studies cannot be guaranteed.

Potential risks

No adverse effects or harm has been reported in all previous studies involving unilateral strength training or mirror therapy. The study has a rigorous design to ensure that all potential risks are kept to a minimum. Participants will be monitored at all times during the therapy sessions. Any unlikely problem which participants may have during the therapy sessions will be dealt with immediately, with the utmost professionalism and confidentiality.

Results

Upon completion of the study, all results will be sent to you by letter or by email.

Contact details

Mr. Daniel Simpson

Job Title: Principal Researcher

Phone number: 087 0531507

Email: daniel.simpson@mail.itsligo.ie

Address: Room B2208, Institute of Technology Sligo, Ash Lane, Sligo.

Appendix G: Participant Consent Form – *Mirror Therapy and Unilateral Strength Training for Enhancing Motor Function after Stroke in the Lower Extremity*

Participation Consent Form

Mirror Therapy and Unilateral Strength Training for Enhancing Motor Function after Stroke

1. I confirm that I have received a copy of the Information Sheet for the above study. I have read it and I understand it. I have received an explanation of the nature and purpose of the study and what my involvement will be.

2. I have had time to consider whether to take part in this study and I have had the opportunity to ask questions.

3. I understand that my participation is voluntary and that I can decide to opt out of the research at any time.

4. I understand that all information gathered about me during this study will be treated with full confidentiality.

5. I agree to the video recording of training sessions and understand that all recordings will be kept confidential.

6. I agree to take part in the above study.

_____ _____

Name of patient Date Signature

Appendix H: Ethical Approval - *Mirror Therapy and Unilateral Strength Training for Enhancing Motor Function after Stroke in the Lower Extremity*

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Research Ethics Committee
Sligo Regional Hospital
The Mall
Sligo
Chairman Dr. John Williams
Adm. Mette Jensen Kavanagh

Daniel Simpson
IT Sligo
Ash Lane
Sligo

March 18 2015

Re. Research Ethics Application

Dear Mr. Simpson,

The Research Ethics Committee (REC) at Sligo General Hospital has reviewed your submission for ethical review of the study "*Mirror therapy and unilateral strength training for enhancing motor function after stroke in the lower extremity: A pilot randomised controlled trial* " at its meeting March 18 2015. The REC has granted the study **provisional approval**.

The REC requested that you clarify/address the following:

a. Please outline how patient safety will be protected during the intervention.
b. In the letter to health professionals who will be involved in the recruitment, add a statement to say that consent will be sought from patients at the assessment.
c. Clarify anonymisation of data: In the application it states that data will be irrevocably anonymised at some point. However, it also states that patients will have access to their own data. Will this be for a limited time period?
d. Information Sheet: Describe in further detail what isometric strength training involves.

Please submit revised relevant document(s) to the REC administrator.

Yours sincerely,

Dr John Williams
Chairman

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Research Ethics Committee
Sligo Regional Hospital
The Mall
Sligo
Chairman Dr. John Williams
Adm. Mette Jensen Kavanagh

Daniel Simpson
IT Sligo
Ash Lane
Sligo

July 10th 2015

Re. Research Ethics Application

Dear Mr. Simpson,

The Research Ethics Committee (REC) at Sligo General Hospital has received your application for an amendment of the study "*Mirror therapy and unilateral strength training for enhancing motor function after stroke in the lower extremity: A pilot randomised controlled trial* ". The REC Chairman has granted favourable opinion on the amendment proposed.

Documents reviewed:

- Amendment application form
- Revised protocol
- Revised Information Sheets
- Revised Health Professional Request Letter
- Certificate of Indemnity

The approval is granted on the basis that the terms outlined in the email from K Monaghan to Mette Jensen dated July 8 2015 are adhered to.

Yours sincerely,

Dr John Williams
Chairman

Appendix I: Modified Ashworth Scale Instructions

Modified Ashworth Scale Instructions

General Information (derived Bohannon and Smith, 1987):

- Place the patient in a supine position
- If testing a muscle that primarily flexes a joint, place the joint in a maximally flexed position and move to a position of maximal extension over one second (count "one thousand one")
- If testing a muscle that primarily extends a joint, place the joint in a maximally extended position and move to a position of maximal flexion over one second (count "one thousand one")
- Score based on the classification below

Scoring (taken from Bohannon and Smith, 1987):

0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part(s) rigid in flexion or extension

Patient Instructions:

The patient should be instructed to relax.

Modified Ashworth Scale Testing Form

Name:_____ Date:_____

Muscle Tested	Score
_____	____
_____	____
_____	____
_____	____
_____	____
_____	____
_____	____
_____	____
_____	____

Reference for test instructions:

Bohannon, R. and Smith, M. (1987). "Interrater reliability of a modified Ashworth scale of muscle spasticity." Physical Therapy 67(2): 206.

Appendix J: Timed Up & Go Instructions

Timed Up and Go Instructions

General Information (derived from Podsiadlo and Richardson, 1991):

- The patient should sit on a standard armchair, placing his/her back against the chair and resting his/her arms chair's arms. Any assistive device used for walking should be nearby.
- Regular footwear and customary walking aids should be used.
- The patient should walk to a line that is 3 meters (9.8 feet) away, turn around at the line, walk back to the chair, and sit down.
- The test ends when the patient's buttocks touch the seat.
- Patients should be instructed to use a comfortable and safe walking speed.
- A stopwatch should be used to time the test (in seconds).

Set-up:

- Measure and mark a 3 meter (9.8 feet) walkway
- Place a standard height chair (seat height 46cm, arm height 67cm) at the beginning of the walkway

Patient Instructions (derived from Podsiadlo and Richardson, 1991):

- Instruct the patient to sit on the chair and place his/her back against the chair and rest his/her arms chair's arms.
- The upper extremities should not be on the assistive device (if used for walking), but it should be nearby.
- Demonstrate the test to the patient.
- When the patient is ready, say "Go"
- The stopwatch should start when you say go, and should be stopped with the patient's buttocks touch the seat.

Timed Up and Go Testing Form

Name:_____

Assistive Device and/or Bracing Used:_____

Date:_____

TUG Time:_____

Date:_____

TUG Time:_____

Date:_____

TUG Time:_____

Date:_____

TUG Time:_____

Date:_____

TUG Time:_____

Reference:

Podsiadlo, D. and Richardson, S. (1991). "The timed "Up & Go": a test of basic functional mobility for frail elderly persons." J Am Geriatr Soc 39(2): 142-148.

Appendix K: 10 Metre Walk Test Instructions

Timed 10-Meter Walk Test

General Information:

- individual walks without assistance 10 meters (32.8 feet) and the time is measured for the intermediate 6 meters (19.7 feet) to allow for acceleration and deceleration
  - start timing when the toes of the leading foot crosses the 2-meter mark
  - stop timing when the toes of the leading foot crosses the 8-meter mark
  - assistive devices can be used but should be kept consistent and documented from test to test
  - if physical assistance is required to walk, this should not be performed
- can be performed at preferred walking speed or fastest speed possible
  - documentation should include the speed tested (preferred vs. fast)
- collect three trials and calculate the average of the three trials

Set-up (derived from the reference articles):

- measure and mark a 10-meter walkway
- add a mark at 2-meters
- add a mark at 8-meters

Patient Instructions (derived from the reference articles):

- Normal comfortable speed: *"I will say ready, set, go. When I say go, walk at your normal comfortable speed until I say stop"*
- Maximum speed trials: *"I will say ready, set, go. When I say go, walk as fast as you safely can until I say stop"*

10 Meter Walk Testing Form

Name:_____

Assistive Device and/or Bracing Used:_____

Date:_____

Seconds to ambulate 10 meters (only the middle 6 meters are timed)

Self-Selected Velocity: Trial 1_____sec.___ Fast Velocity: Trial 1_____sec.___

Self-Selected Velocity: Trial 2_____sec.___ Fast Velocity: Trial 2_____sec.___

Self-Selected Velocity: Trial 3 _____sec.___ Fast Velocity: Trial 3_____sec.___

Self-Selected Velocity: Average time___sec.__ Fast Velocity: Average time___sec.__

Actual velocity: Divide 6 by the average seconds

Average Self-Selected Velocity:_____m/s

Average Fast-Velocity:_____m/s

Date:_____

Seconds to ambulate 10 meters (only the middle 6 meters are timed)

Self-Selected Velocity: Trial 1_____sec.___ Fast Velocity: Trial 1_____sec.___

Self-Selected Velocity: Trial 2_____sec.___ Fast Velocity: Trial 2_____sec.___

Self-Selected Velocity: Trial 3 _____sec.___ Fast Velocity: Trial 3_____sec.___

Self-Selected Velocity: Average time___sec.__ Fast Velocity: Average time___sec.__

Actual velocity: Divide 6 by the average seconds

Average Self-Selected Velocity:_____m/s

Average Fast-Velocity:_____m/s

References:

Bohannon, R. W. Comfortable and maximum walking speed of adults aged 20-79 years: reference values and determinants." *Age Ageing*. 1997;26(1): 15-9.

Bohannon RW, Andrews AW, Thomas MW. Walking speed: reference values and correlates for older adults. *J Orthop Sports Phys Ther*. 1996;24(2):86-90.

Wolf SL, Catlin PA, Gage K, Gurucharri K, Robertson R, Stephen K. Establishing the reliability and validity of measurements of walking time using the Emory Functional Ambulation Profile. *Phys Ther*. 1999;79(12):1122-33.

Appendix L: London Handicap Scale Instructions

The London Handicap Scale

Overview: The London Handicap Scale can be used to determine the effect of chronic disorders on a person's functional ability using a self-completion questionnaire. The authors are from the Royal Free Hospital in London.

Development:

- Each degree of handicap along a 6-point interval was assigned a scale weight.
- The scale weights were assigned using conjoint analysis with the derivation process described on page 12.

Parameters:

(1) mobility: "getting around"

(2) physical independence: "looking after yourself"

(3) occupation: "work and leisure activities"

(4) social integration: "getting on with people"

(5) orientation: "awareness of your surroundings"

(6) economic self-sufficiency: "affording the things you need"

Parameter	Finding	Value
mobility	no disadvantage	0.071
	minimal disadvantage	0.038
	mild disadvantage	0.000
	moderate disadvantage	-0.036
	severe disadvantage	-0.072
	most severe disadvantage	-0.108
physical independence	no disadvantage	0.102
	minimal disadvantage	0.011
	mild disadvantage	-0.021
	moderate disadvantage	-0.053
	severe disadvantage	-0.057
	most severe disadvantage	-0.061
occupation	no disadvantage	0.099

	minimal disadvantage	-0.004
	mild disadvantage	-0.014
	moderate disadvantage	-0.024
	severe disadvantage	-0.035
	most severe disadvantage	-0.060
social integration	no disadvantage	0.063
	minimal disadvantage	0.035
	mild disadvantage	0.007
	moderate disadvantage	-0.022
	severe disadvantage	-0.029
	most severe disadvantage	-0.041
orientation	no disadvantage	0.109
	minimal disadvantage	-0.008
	mild disadvantage	-0.038
	moderate disadvantage	-0.051
	severe disadvantage	-0.063
	most severe disadvantage	-0.075
economic self sufficiency	no disadvantage	0.100
	minimal disadvantage	0.067
	mild disadvantage	0.033
	moderate disadvantage	-0.023
	severe disadvantage	-0.067
	most severe disadvantage	-0.111

from Table 1 page 13

London handicap scale = SUM(all 6 utility values) + 0.456

where:

- The sum of all "no disadvantage" values is 0.544 which when added to 0.456 gives 1.00.
- The sum of all "most severe disadvantage" values is –0.456 which when added to 0.456 gives 0.00.

Interpretation:

- minimum scale value: 0
- maximum scale value: 1.00
- The scale value corresponds to residual function with 1.00 indicating normal function and 0.00 indicating total disability.

Performance:

- Pearson's correlation coefficient between predicted and measured values: 0.98
- Kendall's coefficient of concordance (tau): 1.00

References:

Harwood RH Rogers A et al. Measuring handicap: the London handicap scale a new outcome measure for chronic disease. Quality in Health Care. 1994; 3: 11-16.

Appendix M: Mini Mental State Examination Instructions

Mini-Mental State Examination (MMSE)

Patient's Name: _____ Date: _____

Instructions: Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

Interpretation of the MMSE:

Method	Score	Interpretation
Single Cutoff	<24	Abnormal
Range	<21	Increased odds of dementia
	>25	Decreased odds of dementia
Education	21	Abnormal for 8th grade education
	<23	Abnormal for high school education
	<24	Abnormal for college education
Severity	24-30	No cognitive impairment
	18-23	Mild cognitive impairment
	0-17	Severe cognitive impairment

Interpretation of MMSE Scores:

Score	Degree of Impairment	Formal Psychometric Assessment	Day-to-Day Functioning
25-30	Questionably significant	If clinical signs of cognitive impairment are present, formal assessment of cognition may be valuable.	May have clinically significant but mild deficits. Likely to affect only most demanding activities of daily living.
20-25	Mild	Formal assessment may be helpful to better determine pattern and extent of deficits.	Significant effect. May require some supervision, support and assistance.
10-20	Moderate	Formal assessment may be helpful if there are specific clinical indications.	Clear impairment. May require 24-hour supervision.
0-10	Severe	Patient not likely to be testable.	Marked impairment. Likely to require 24-hour supervision and assistance with ADL.

Source:

- Folstein MF, Folstein SE, McHugh PR: "Mini-mental state: A practical method for grading the cognitive state of patients for the clinician." *J Psychiatr Res* 1975;12:189-198.

Appendix N: Media Coverage

Magazine Article: Irish Independent STEM supplement 2017

IT Sligo researchers using mirrors to help patients recover from stroke

A team of researchers at Institute of Technology, Sligo is using mirror therapy to help stroke patients improve the strength and mobility of affected limbs. The Stroke Research Group, led by Institute lecturer and chartered physiotherapist Dr Kenneth Monaghan, uses mirrors to 'trick' the brain into believing that a weak limb is functioning properly, thus kick-starting a recovery process.

Following clinical trials on more than 60 patients, Enterprise Ireland granted the team €15,000 in August to investigate the feasibility of developing the product commercially.

Dr Monaghan says 40pc of patients reported 'a significant life-changing improvement' after undergoing the trials. The researchers use a treadmill with a mirror attached, and alternatively a brace for strengthening arms and legs, which incorporates the mirror therapy. Both devices were created by Dave Roberts, a lecturer in Creative Design at IT Sligo.

"I think it's good news for people who have had a stroke and who have limited function as a result. This therapy can improve dexterity and strength for a significant proportion," says Dr Monaghan.

Two of the researchers, PhD students Monika Ehrensberger and Daniel Simpson, presented a paper on their findings at the European Stroke Conference in Berlin during the summer, while Irish and international experts have expressed an interest in collaborating with them.

"We have seen strength gains as well as improvement in function, which has an impact on quality of life," says Mr Simpson, who has spent two years travelling to patients' homes with Ms Ehrensberger to provide the therapy three times a week over a four-week period.

PhD student Patrick Broderick, who specialises in the treadmill-with-mirror-therapy, says it has the potential to transform lives.

Dr Monaghan says: "This has never been done before. The mirror on the treadmill helps people to walk more symmetrically. In other words, they lose that stroke gait."

The team, which operates within the Clinical Health & Nutrition Centre at IT Sligo, has been awarded more than €230,000 in grants over the last two years, including funding from the college, the Northwest Stroke Support Group and Enterprise Ireland.

Many of those participating in the trials were referred by local medical experts from Sligo University Hospital (SUH) and St John's Community Hospital, Sligo.

Dr Paula Hickey, consultant geriatrician at SUH, says more than 30,000 people in Ireland live with disability due to stroke.

"Through our collaboration with this research group, we are seeing substantial benefits in a group of patients that traditionally might have been viewed as having 'finished' their treatment and even felt to be beyond help."

Ms Ehrensberger says recovery appeared to be more marked in 'moderate' patients, while Dr Monaghan acknowledged that patients might not benefit several years after having had a stroke.

"After several years, the muscle and tissue tighten up if not moved."

The Enterprise Ireland grant will be used for market research into the potential of the brace.

"If the results are good, which they should be, we will apply for a full commercial grant to make the product which people could bring into their own homes. It all ties into the idea of getting people out of hospital," says Dr Monaghan.

Visit *www.itsligo.ie*

Magazine Article: Spectrum September 2017

Reflective therapy for stroke patients

A team of researchers at IT Sligo is using mirror therapy to help stroke patients improve the strength and mobility of affected limbs, and the researchers claim the results of clinical trials are 'very significant'.

The Stroke Research Group, led by college lecturer and chartered physiotherapist, Dr Kenneth Monaghan, uses mirrors to 'influence' the brain into believing that a weak limb is functioning properly, thus kick-starting a recovery process.

The Irish Times reported that, following clinical trials on more than 60 patients, Enterprise Ireland has granted the team €15k to investigate the feasibility of developing the product commercially.

Dr Monaghan said 40% of patients reported "a significant life-changing improvement" after undergoing the trials.

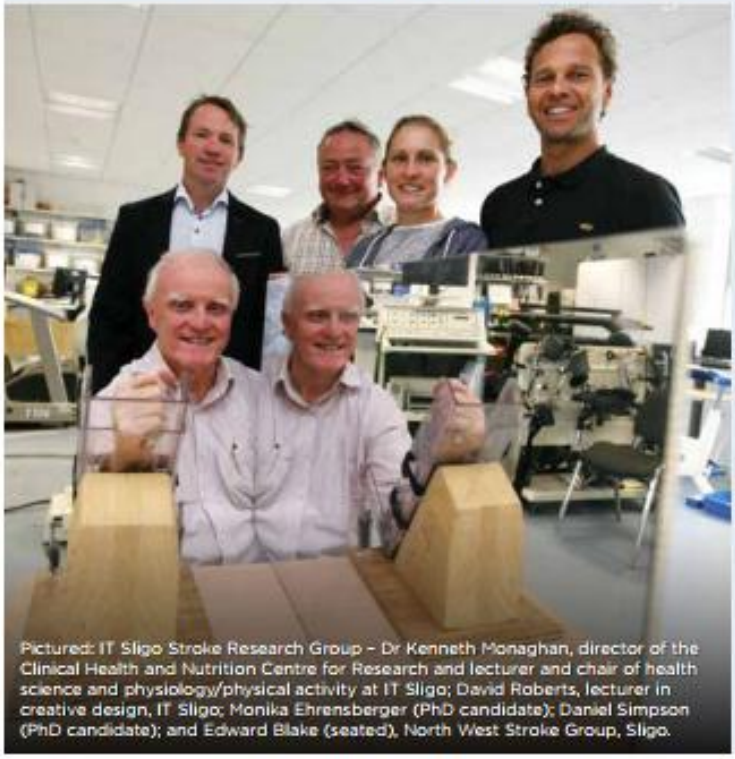
The researchers use a treadmill with mirror attached, and alternatively a brace for strengthening arms and legs, which incorporates the mirror therapy.

Both devices were created by Dave Roberts, creative design lecturer in the college. "I think it's good news for people who have had a stroke and who have limited function as a result. This therapy can improve dexterity and strength for a significant proportion," he said.

Two of the researchers, PhD students, Monika Ehrensberger and Daniel Simpson, presented a paper on their findings at the European Stroke Conference in Berlin this summer, while Irish and international experts have expressed an interest in collaborating with the team.

"We have seen strength gains as well as improvement in function, which has an impact on quality of life," said Daniel, who has spent two years travelling to patients' homes with his research colleague, to provide the therapy three times a week over a four-week stretch.

PhD student Patrick Broderick, who specialises in the treadmill-with-mirror therapy, said it has the potential to transform lives. The team, which operates within the clinical health and nutrition centre at IT Sligo, has been awarded over €230k in grants over the last two years, including funding from the college, the Irish Research Council, the Northwest Stroke Support Group and Enterprise Ireland.



Pictured: IT Sligo Stroke Research Group – Dr Kenneth Monaghan, director of the Clinical Health and Nutrition Centre for Research and lecturer and chair of health science and physiology/physical activity at IT Sligo; David Roberts, lecturer in creative design, IT Sligo; Monika Ehrensberger (PhD candidate); Daniel Simpson (PhD candidate); and Edward Blake (seated), North West Stroke Group, Sligo.

Lower limb therapy has shown positive outcomes in trials. The device is shown being used during therapy by a patient. The team also have a mirror device designed for treadmill walking, which is showing positive results.

Magazine Article: Healthy Ireland September 2017

IT Sligo Stroke Research Group – Dr Kenneth Monaghan, director of the Clinical Health and Nutrition Centre for research and lecturer and chair of health science and physiology/physical activity at IT Sligo; David Roberts, lecturer in creative design, IT Sligo; Monika Ehrensberger (PhD candidate); Daniel Simpson (PhD candidate); and Edward Blake (seated), North West Stroke Group, Sligo.

Stroke of innovation

Can you remember when we believed that the brain was incapable of change? Well, scientific evidence now disputes this, **Shauna Rahman** speaks to Sligo native, **Kenneth Monaghan**, who, along with his Neuroplasticity Research Group in IT Sligo, are finding excellent benefits to new innovative rehabilitation treatments for patients with chronic stroke

Research is now showing that brain-damaged patients are making full recoveries and there is definite proof that the idea that the brain is a 'glorious machine', is redundant.

Since qualifying as a chartered physiotherapist from University College Dublin 25 years ago, Kenneth Monaghan has always been fascinated with neurological rehabilitation. Having worked in Florida for four years, he experienced ground-breaking rehabilitation techniques and first heard of 'mirror therapy' when it was being used to treat phantom limb pain. On returning to Ireland, he

Around 7,000 people suffer a stroke annually in Ireland, with almost half of these suffering anxiety, depression or severe psychological distress.

THREE-PRONGED APPROACH TO STROKE:

Mirror therapy

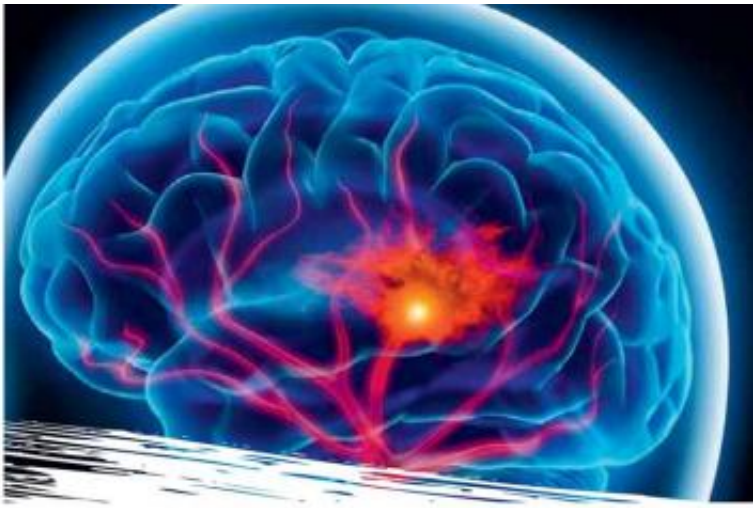
This involves covering a weak limb with a mirror, observing movement of the strong limb and fooling the brain into believing that the weak limb is working. These principles involve getting both hemispheres of the brain to work 'in sync', and together more efficiently, and it is this action that is believed to repair symmetrical gait patterns, enhance motor recovery and reduce spasticity in a weak or paretic limb following stroke.

Treadmill therapy

This is simply using treadmills to allow gait training at various speeds.

Cross-education of strength

The aim is to strengthen one side of the body and observe up to 50 per cent strength changes occurring on the opposite side of the body, despite no work being done on that side.



worked in various rehabilitation settings. "It was during this time that I was able to create videos of limbs moving that my patients could observe, and I saw incredible results from using mirrors," Kenneth says.

Since then, he became health science lecturer and clinical director for the Clinical Health & Nutrition Centre (CHANCE) in IT Sligo, School of Science and has successfully been awarded €230k in research grants from organisations including IT Sligo President's Bursary's, Irish Research Council, Enterprise Ireland, and the Northwest Stroke Volunteer Group, to investigate if different combinations of neuroplastic (changes in the brain) treatments can work together. Now, five years later, Kenneth and his neuroplasticity team are beginning to see the benefits of these investigations for chronic stroke patients.

Global first in stroke breakthrough

"Like most family members that have witnessed stroke first hand, I wanted to understand how to stimulate neuroplasticity and, being a scientist, I wanted to help to find new treatments," says Kenneth. Patrick Broderick, neuropsychologist, Sligo; Monika Ehrensberger, exercise specialist, Germany; Daniel Simpson, health promotion expert, Wales; Irish and Norwegian industrial designers David Roberts and Jostein Robstad, and commercial expert, Irish BioInnovate alumni, Rhona Hunt, make up Kenneth's neuroplasticity team. "Our focus is to find innovative avenues to stimulate neuroplasticity post-stroke. We work very closely with consultant geriatrician, Dr Paula Hickey's, Stroke Network in Sligo University Hospital, as well as researchers from several European and non-European countries.

"Our clinical trials are the first to be performed in a stroke population in the world and have been advocated and recommended by the top researchers investigating neuroplasticity. This may not seem very important at first glance, but new treatments that use the good side of the body allow patients to independently rehabilitate in their home environment and save exhaustive therapy sessions. This, in turn, has led to the development of a new medical device the 'mirror strengthening brace', which Enterprise Ireland has targeted for commercial funding. We are linked to Dr Tjerk Zult from Anglia Ruskin University in Cambridge, who is the world's leading expert in this area and we are making plans for him to join our research group next year."

Future trials

"Our trials show very clearly that mirror therapy increases the benefits of both treadmill training and cross-education of strength. The use of these treatments is still in its infancy and we now need to establish the 'dose required' of these treatments. However, there are good reasons to be optimistic. Further trials are soon starting to combine our new mirror strengthening brace with augmented reality environments (a live direct or indirect view of a physical, real-world environment whose elements are augmented by computer-generation).

"Another treatment that shows promise is mental practice and preparations are underway to bring in another postdoctoral researcher to our group to investigate its potential for stroke rehabilitation. It is important to establish the efficacy of new innovative treatments in stroke but we must not get carried away with our progress because it can be slow to convince professionals to adopt these new treatments into rehabilitation clinics," Kenneth says. "However, the team, our research colleagues and I, personally believe that if our current momentum continues, we may soon see that establishment of these innovative treatments to rehabilitation settings worldwide. Ultimately, we will see reduced impairments in chronic stroke patients."

What is a stroke?

A stroke happens when there is a blockage or leakage in a blood vessel in the brain. Since this blood vessel is no longer able to carry oxygen and blood to a particular part of the brain, that part of the brain dies. As a result, the part of your body that is controlled by that section of the brain can no longer function properly. Typically, strokes are haemorrhagic (bleeding on the blood tissue) or ischaemic stroke where a blood clot is preventing blood from flowing properly to the brain. Broadly speaking, one third of stroke sufferers are left with the chronic symptoms of hemiplegia (weakness), spasticity, poor coordination, reduced function, and reduced quality of life

Newspaper Article: Sligo Champion June 2017

Mirror therapy for stroke patients getting results

IT RESEARCHERS HAVE BEEN FUNDED FOR FRESH TRIALS AND MARKET RESEARCH INTO DEVICE

BY SORCHA CROWLEY

Researchers from IT Sligo are gaining ground internationally with their exciting new mirror therapy for stroke patients.

They've received funding for fresh trials in September and a grant from Enterprise Ireland to further develop a new medical device.

Their clinical trials used mirrors in conjunction with exercises on the device to trick the brain into thinking a stroke-affected limb was working again.

Participants' arms and legs got stronger as a result.

Director of the Clinical Health & Nutrition Centre (CHANCE) at the IT, Dr Ken Monaghan set up the Stroke Research Group which includes PhD students Monika Ehrensberger, Daniel Simpson and Patrick Broderick.

"Monica and Dan got very positive feedback when they presented their research at the Irish Stroke Conference in Dublin," he said.

Some of the world's top experts in neurology attended the Dublin conference.

"Following on from that, Dan and Monica presented at the European Stroke Conference in Berlin and again it was very well received," he said.

"They asked us what kind of participants we had, what were the outcomes, what they benefited from, the mechanics, how mirror-therapy works," said Monica.

"We had a really positive response. Some stroke experts from the States, Holland and from Germany were there, it was really well received," added Daniel.

The Centre has received €30,000 to pay for another post-graduate researcher to come on board and start fresh clinical trials in the autumn.

The three researchers worked with Creative Design Lecturer, Dave Roberts to invent a device that patients could use in their own homes.

The prototype is so well developed Enterprise Ireland have signalled their approval by granting them €15,000 towards doing some market research into the area.

"They think that the device has good potential," said Ken.

"We know now how the exercises work so we'll design trials that should show better effects," he said.

"The case now is that we've tried and shown there is merits in these principles so now we want to find out the right 'dose patients need to use," he said.

If the market research provides evidence there is a market for their device, they can apply for further funding from Enterprise Ireland to manufacture it.

However Ken sees a physical device as just the start - he believes the future of stroke rehabilitation should involve both limbs in a virtual reality environment.

An Irish professor at John Hopkins University in America is pioneering robotic equipment for stroke patients.

"We should be talking to people like that, funding somebody to come in here, use our device and put it into some kind of a game or virtual reality. I think that's the next stage we move on to," he said, "We've reached our tipping point."

Dr Ken Monaghan with researchers Monika Ehrensberger and Daniel Simpson.

Ankle got stronger

Claire McCusker was the youngest participant in the IT mirror therapy trials on stroke patients.

She didn't have a stroke however. A haemorrhage at 18 in 2004 affected her left side and balance but she didn't let that stop her, going on to qualify as a speech therapist.

Ironically, Claire works with stroke patients but didn't think Dan and Monica's trial would help her.

"I thought it was for old people but rosiness got the better of me. I went to the IT three days a week on my lunch or after work," she told The Sligo Champion.

"I would have had a weakness in my left leg and have to wear flats for my balance," she said.

Quite quickly, her ankle felt stronger. "I didn't expect it. I was only going for the craic. I was surprised as I didn't expect any improvement," she said.

Claire gained a 10 per cent improvement in her strength which when living with long term affects, is a good outcome in anyone's book.

"The principle is fascinating. I'm continuing with my own normal exercises. I haven't noticed any deterioration," she said.

Her positive attitude helps many stroke patients: "I tell them to quit feeling sorry for themselves and be positive," she said.

PJ felt "on top of the world" after stroke trial

PJ Wymbs was "on top of the world" after his participation in the IT trials.

He had a stroke on 1st April 2016 and it affected his left side, his arm and leg being significantly weakened.

This is his story:

"One of the physiotherapists at the hospital asked me would I take part in this experiment with Daniel and Monica.

"So they came out to my house six months after the stroke, last November. They came three times a week for four weeks. Each session lasted 45 minutes and involved mirror therapy with strength training.

"You sit at the table and you put your right arm into the device, do their exercises and focus on the mirror.

"The mirror is tricking your brain into thinking that your left hand is working. I did the same with my leg.

"I could find my left side improve after three treatments.

"I was hoping the HSE would get involved in follow-up strength training – if something like that could be going it would be great for people with stroke.

"Before the treatment I couldn't lift a full cup of tea, I'd be afraid it would fall. After the treatment, I had so much control I could lift a cup and lift on and off the hand break in my car perfectly after it," he told The Sligo Champion.

Has he continued doing exercises himself since the experiment finished?

"It's not as simple as just looking in the mirror," said PJ.

"Some people would say you would make it worse if you didn't know what you were at," he said.

He was checked three months after the trial finished. While everything was 'OK' but he claims he has noticed some weakness returning.

"I would go anywhere to do it again if I got the option. I would have a bit of a limp in my leg, dragging it, I can walk 50m at a time. It has a little bit of weakness in it again," he said.

"Immediately after the experiment, it probably wasn't at full strength but it felt like nothing had happened to me, it was that good," he added.

PJ Wymbs from Kinlough. Pic: Donal Hackett.

Tongue Tie and conflicting advice affect breastfeeding

CONFLICTING advice from midwives and tongue tie in newborns have emerged as big issues for new mothers at Sligo University Hospital.

A new study has also found that the majority of new mothers in Sligo breastfed for longer than six weeks if they felt they used the support provided by a Breastfeeding Preparation Class.

Third Year Health Sciences student Eleanor Loftus made the findings after studying 165 new mums at Sligo hospital earlier this year.

"I found that tongue tie was a big issue, it wasn't really checked according to the mothers. Before they left the hospital they might have asked but it wasn't necessarily checked and they had to go back and pay for it to be snipped," Eleanor told The Sligo Champion.

"Lactation consultants are needed in Sligo University Hospital, they're definitely needed. There were a lot of differences in attitudes among the midwives and the nurses towards breastfeeding. Some of them would leave a bottle at the end of the bed, some of them would be very supportive but they mightn't necessarily have time, some of them just had no time, there was a lot going on," she said.

Research Supervisor Margaret McLoone with 3rd Year Student Eleanor Loftus presenting her findings on breastfeeding in Sligo.

"There were also differences between day and night staff in what they'd be telling the woman, which is kind of confusing if you're a new mother.

"If they were all saying the same thing it would make breastfeeding more successful," said Eleanor.

Research supervisor Margaret McLoone said: "I hear that these have been approved nationally - that every hospital would get a lactation consultant. Conflicting advice from health professionals was one of the reasons women said they needed lactation consultants."

Newspaper Article: Sligo Champion January 2017

FACE TO FACE WITH STROKE RESEARCHERS AT IT SLIGO

SECOND LEASE OF LIFE

DR KEN MONAGHAN AND HIS TEAM OF THREE PHD RESEARCHERS TELL SORCHA CROWLEY ABOUT GIVING STROKE PATIENTS FRESH HOPE AND MOBILITY

L-R: PhD researcher Patrick Broderick, Director Clinical Health and Nutrition Centre Dr Ken Monaghan and PhD researchers Monika Ehrenberger and Daniel Simpson in their lab at IT Sligo. Pic: Donal Hackett.

A QUIET miracle is happening in homes around Sligo since 2015. A team of researchers at IT Sligo are helping stroke patients to move again - by using mirrors to trick their brains.

"If you train one side of your body in the gym for six weeks, that side of your body will get stronger, but amazingly the other untrained side gets stronger as well, by maybe 40-50 per cent," he tells The Sligo Champion in his lab.

The Rathcormac native first came into contact with mirror therapy while working as a clinical specialist musculoskeletal physiotherapist in rehab centres in Ireland and the US.

Then, when treating a friend who had a stroke, he had a lightbulb moment.

"I saw some great improvements in treating him and saw the potential in it. That was my spark to wanting to do this," he says.

Now the Director of the Recognised Research Group at the IT, Ken has a team of three PhD researchers dedicated to stroke rehabilitation as he saw the room for bringing on new treatments.

The common perception of strokes are that once you hit six months post-stroke rehabilitation, that's it. You're sent on your merry way to live with whatever restrictions you're left with.

Dr Ken Monaghan and his team are changing all that, however.

Ordinarily, your brain sees that your affected limb isn't working and so effectively, 'ignores' that part of the body.

If however, you watch a reflection of your mobile limb in a mirror, something happens in your brain, as researcher and neuro-psychologist Patrick Broderick explains:

"It appears as if I'm moving my good hand, so I'm getting a positive visual feedback telling my brain that I have two fully functioning and moving hands.

"It effectively tricks the brain into believing that your hand is working again. Or it's tricking the brain into believing that I'm walking in a proper pattern again and that my weak leg is now working properly," he says.

The result is that it stimulates the motor function areas of the brain, prompting it to send energy and to activate that damaged hemisphere.

"It creates new pathways in your brain. It can re-ignite old pathways or establish new ones that help your limb function," he says.

The mirrors work for arms and legs and it's surprising how quickly - after just 30 seconds - that the brain can be fooled into thinking both limbs are functioning again.

Patrick is another Sligo native who is qualified in the assessment of head injuries or a stroke and designs interventions for them.

He was working with Acquired Brain Injury Ireland when he first became interested in the area.

"The first time I saw mirror therapy I saw instantly the effects that it had, bringing movement to limbs which had no movement whatsoever for years. For me that was startling. And the fact that very little research was being done on it," he says.

"We're seeing a lot of increases in people's overall ability to walk on a day to day basis, increases in walking speed, in their endurance and big increases in their overall motor function.

"When people have increased mobility then they can do all the other activities in their lives a lot easier. It creates a lot of independence. It's giving chronic stroke patients a second lease of life. A patient told me yesterday that for the first time since she had her stroke she felt like a normal person. She felt like she didn't have a stroke anymore, she could get on with her life. We're seeing this in all our patients. It's transforming," he says.

> "I SAW INSTANTLY THE EFFECTS IT HAD, BRINGING MOVEMENT TO LIMBS WHICH HAD NOT MOVED FOR YEARS"

What this form of therapy is offering is a new approach to rehabilitation. Traditional physiotherapy gets people to a point. Mirror therapy comes in afterwards and brings people a step further.

"The beauty of mirror therapy is that it cuts down on expense. You don't need a therapist, you can use it yourself at home. You can put this device onto your treadmill at home and you can start walking and do it. You lead the way. That's the beauty of it," adds Patrick.

Sports Science specialist Monika Ehrenberger and Health Promotion Officer Daniel Simpson are the other two phD researchers working with Ken.

They are working on strength training in chronic stroke patients but their first obstacle turned out to be their most opportune.

"We initially tried to get all the stroke patients to come here but it's very difficult to get stroke patients to come here because they need someone to bring them and it's a big commitment to come here for four weeks of the exercises," says Ken.

As the proverb goes, "If the mountain won't come to Muhammad then Muhammad must go to the mountain", Ken and his team had to devise a way of bringing the therapy out to patients.

Monica and Daniel devised a portable medical device that allows them to go out to patients houses and allows them to do exercises and use the mirrors.

They've had such good results, they're now in talks with Enterprise Ireland to see about developing it as an official medical device.

"We think there's great potential in it and they're very interested in it. It's kind of like an offspring of what's happened. It's very good for your soul," says Ken.

"They do all the training on their good side so that the other side will benefit," says Monika.

"The strength increases and stiffness decreases, it relaxes in nearly every patient we've seen," she says, adding that "significant improvements" have been seen, with patients able to open a jar of coffee or button up a coat.

Industrial Designer David Roberts from the IT's Creative Design Department is tasked with developing the new devices and is currently building a portable treadmill for Patrick's patients.

"It's always exciting to work in a new area, particularly with people who are enthusiastic about what they are doing," he says.

"I'm really excited by this because it could have a huge benefit to people."

Ken and his team are in touch with the five or six people in the world that see potential in this kind of therapy. It's the only research of its kind going on in Ireland at the moment.

They have high hopes for the future of both the therapy and the device.

"When a person sees a little bit of an improvement, that's a great motivator. It encourages people to do more. In the early stages it was difficult to get people involved in trials.

"What's lovely now is for the first time the word is out there and people are starting to contact us now looking to be involved in the trials.

"You don't need much supervision. It's completely safe. Imagine somebody using it every day for a week? Surely there's benefit for acute patients in hospitals," he says.

"My hopes are that we could inject some virtual reality into this. That would be the next stage," says Ken.

"In ten years time that device will be used in hospitals worldwide - that would be the hope."

FACT FILE

A stroke destroys two million brain cells every minute. If you suspect that someone is having a stroke call 999 immediately.

When stroke strikes, act F.A.S.T.

F.A.S.T. stands for:

F – Face – has their face fallen on one side? Can they smile?

A – Arms – Can they raise both arms and keep them there?

S – Speech – is their speech slurred?

T – Time to call 999 if you spot any single one of these signs.

'FOR THE FIRST TIME I COULD RUN AGAIN WITHOUT THINKING'

Helen Cassells was four years post-stroke when she heard about Dr Monaghan and the work he was doing with his team at IT Sligo.

She'd had a stroke in 2011 and while she wasn't confined to a wheelchair or a stick, she felt much slower than normal in walking.

"I felt I needed a little bit extra so I joined the IT team and found the mirror therapy very good," she said. "I had a weakness on the right side but I was mobile."

Helen completed a four week trial of the mirror therapy in 2015, for half an hour three days a week. The results were surprising: "For the first time I could actually run again without thinking. I wouldn't run a four minute mile but I can go much faster than I could before," she said.

Helen also credits the therapy on Daniel and Monika's device for restoring movement back to her arm. "All of a sudden I was turning on the tap with my right arm and I didn't realise I was doing it. It's the simple things. It's definitely another way of treating people with strokes," she said.

Helen Cassells out walking in Glencar. Pic: Donal Hackett.