Unilateral Strength Training and Mirror Therapy for Enhancing Upper Limb Motor Function Post Stroke

By

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Declaration

I hereby certify that this thesis has been composed solely by myself and that it has not been submitted, in whole or in part, in any previous application for a degree. Except where otherwise stated by reference or acknowledgment, the work presented is entirely my own.

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Unilateral Strength Training and Mirror Therapy for Enhancing Upper Limb Motor Function Post Stroke by Monika Ehrensberger

Abstract

Cross-education of strength appears to be beneficial in the rehabilitation of injuries and illnesses causing bilateral asymmetry. Furthermore, evidence for the effectiveness of mirror therapy to enhance cross-education in the healthy population exists. This thesis firstly aimed to investigate the clinical benefits of cross-education in post-stroke recovery, and secondly aimed to establish if the combination of cross-education and mirror therapy can further enhance positive effects on the upper-limb.

Chapter 2 revealed moderate evidence for the successful application of cross-education in stroke patients. It has a positive impact on muscle strength, which potentially translates into improved functional ability. Additionally, healthcare professionals recognised unilateral strength training as a beneficial adjunct therapy. Chapter 3 established excellent protocol reliability for maximal isometric elbow extension measured with the Biodex System 3 Isokinetic Dynamometer, thus ensuring dependable procedures when assessing the effects of the subsequently applied unilateral strength training programme. Chapter 4 investigated the feasibility and potential efficacy of mirror-aided cross-education training compared to cross-education training only on upper limb motor function post stroke. Compliance was high without adverse effects. Information regarding other important aspects of a randomised controlled trial could also be provided. The additional use of a mirror did not augment the cross-education effect when chronic stroke patients trained isometrically. Nevertheless, the combination of results warrants further investigation of the combination treatment with an altered training protocol.

These findings suggest a positive impact of (mirror-aided) cross-education training on post-stroke recovery. Considering the low risk for adverse effects and the by clinicians identified benefits, the rehabilitation method may have potential as an adjunct therapy to standard rehabilitation. However, to provide conclusive evidence a fully powered trial investigating the beneficial effects of mirror-aided cross-education training has to be conducted.

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ARAT –	Action Research Arm Test
AROM –	Active Range of Motion
AT –	Average Torque over a Single Contraction
CAHAI –	Chedoke Arm and Hand Activity Inventory
CV –	Coefficient of Variation
EMG –	Electromyography
GABA –	Gamma-Amino-Butyric -Acid
ICC –	Intraclass Correlation Coefficient
ICF –	International Classification of Functioning, Disability and Health
IHI –	Interhemispheric Inhibition
iM1 –	Ipsilateral Primary Motor Cortex
iSP –	Ipsilateral Silent Period
LA –	Less-affected
LHS –	London Handicap Scale
M1 –	Primary Motor Cortex
MA –	More-affected
MAS –	Modified Ashworth Scale
MCID –	Minimal Clinically Important Difference
MDC –	Minimal Detectable Change
MMSE –	Mini Mental State Examination
MNS –	Mirror Neuron System
MST –	Mirror and Strength Training Group
MVC –	Maximal Voluntary Contraction
MVIC –	Maximal Voluntary Isometric Contraction
PT –	Peak Torque
RCT –	Randomised Controlled Trial

RI –	Reciprocal Inhibition
RTD –	Rate of Torque Development
SICI –	Short Interval Intracortical Inhibition
SMA –	Supplementary Motor Area
SP –	Silent Period
ST –	Strength Training Only Group
T1 –	Baseline Assessment
T2 –	Post-intervention Assessment
T3 –	Follow-up Assessment
TMS –	Transcranial Magnetic Stimulation

Chapter 1: Introduction and Theoretical Framework

1.1 Introduction

Worldwide fifteen million people suffer a stroke each year, five million are permanently disabled (1, 2) with hemiparesis (3) and spasticity (4, 5) the most commonly experienced physical complications. Six to twelve months after stroke, 56% of patients with initial upper limb hemiparesis will still show symptoms of the one-sided muscle weakness (3, 6) and 20-35% of patients are affected by spasticity (4-6). The reduced arm and hand function has an extensive impact on independent management of Activities of Daily Living and is further associated with high levels of anxiety and poorer perception of health related quality of life (7-9), thus improving upper limb function is deemed a priority in stroke rehabilitation (10).

Presently performed techniques are based on repetitive methods addressing the paretic limb only (10). In many cases the impairment of the more-affected (MA) arm is too great to be engaged in active exercise (11), which denies the possibility of independent home training; therapist or family assistance is needed at all times (10, 12). Thus, therapy sessions mainly take place in acute or outpatient settings and prove to be expensive, labour intensive, and may require quite a lot of travel for patients in rural areas (13, 14). Consequently, there is a need for novel post-stroke rehabilitation methods, which address the less-affected (LA) arm only, ensuring comprehensive, integrated, community-based stroke rehabilitation and long-term management (2).

Cross-education of strength, the performance improvement in the untrained homologous muscle after unilateral training (15, 16), has huge potential to address bilateral limb asymmetry (11) and other aforementioned limitations to stroke rehabilitation by training the LA limb only. Furthermore, recent evidence suggests that cross-education effects may be augmented when combining unilateral strength training with mirror therapy (17-20). To date this area remains largely unexplored and recommendations have been made to investigate the benefits of cross-education interventions and of the combination treatment of cross-education and mirror therapy in the rehabilitation of unilaterally affected stroke patients (11, 20).

In the following section the pathophysiology of physical impairments caused by stroke will be described. Thereafter, cross-education of strength and mirror therapy will be introduced individually, and possible underlying mechanisms discussed. The combination of both rehabilitation methods will also be explored.

1.2. Physical Impairments caused by Stroke

Stroke is an injury to the central nervous system caused by disruption of blood supply and associated oxygen deprivation (21). Neurological deficits can result in physical impairments such as hemiparesis and spasticity, generally associated with the side contralateral to stroke (3, 4, 6, 22). Lesions to the motor cortex disconnect the motivation and concept of a motor plan from its effectors. Thus hemiparesis, the inability or difficulty to voluntarily recruit skeletal motor units, results in compromised force output and movement (23).

No consensus regarding the definition and pathophysiology of spasticity could be reached to date, reflecting its complexity and diversity (24). The core feature of spasticity is the hyperexcitability of the stretch reflex due to abnormal processing in the spinal cord (25), the balance between excitatory and inhibitory signals is disturbed (25, 26). The stretch reflex is controlled by two descending systems: the inhibitory dorsal reticulospinal tract, which is under cortical control, and the faciliatory medial reticulospinal and vestibulospinal tract, which are not under cortical control (25). Spasticity is caused when brain injuries disrupt cortical mechanisms controlling the inhibitory pathways, thus excitatory signals are not counteracted (25, 26). Trompetto et al. (25) illustrates descending pathways schematically (Figure 1.1).

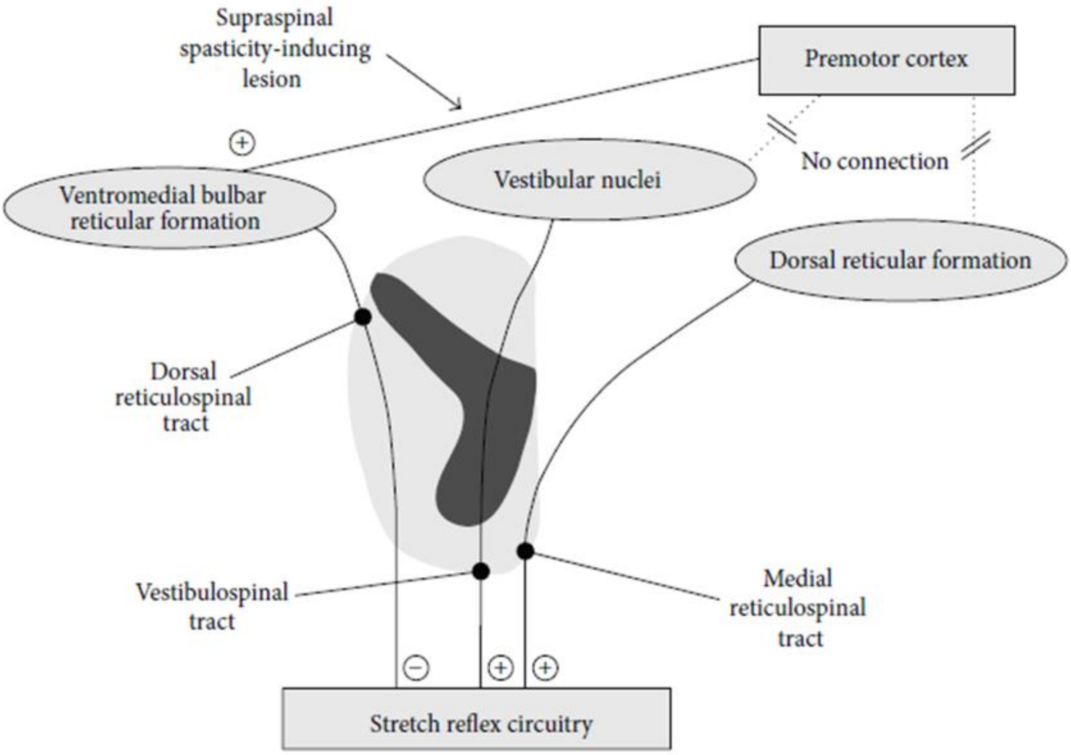

Figure 1.1 (25): Schematic Representation of the Descending Pathways Modulating the Stretch Reflex

The dorsal reticulospinal tract applies its inhibitory control over the stretch reflex through the activation of postsynaptic inhibitory circuits located in the spinal cord (24); their efficiency is generally decreased in patients with spasticity (27-29). Presynaptic inhibition, the reduced release of neurotransmitters in the synaptic cleft, and post-activation depression, which is not mediated by inhibitory spinal circuits, have also been found to be depressed in spastic patients (25, 30-34).

However, according to Gracies (35) spasticity is only one component of spastic paresis and specific manual assessment of abnormal reflex activity proves difficult (36). Thus, soft tissue contracture resulting from disuse, spastic dystonia, which is the inability to rest a muscle, and spastic co-contraction, the simultaneous activity in agonist and antagonist primarily caused by abnormal patterns of supraspinal descending drive, should also be considered (35, 37).

Motor recovery after stroke is attributed to brain plasticity or neural reorganisation. Possible mechanisms include activation of dormant neurons, formation of new synapses and pathways, and increased efficiency of existing networks (38). Furthermore, appropriate sensory feedback from the paretic limb as well as a normalised excitatory-inhibitory balance between the two hemispheres are important factors for motor recovery (17, 37-40).

Cross-education and mirror therapy interventions may have the capacity to influence above-mentioned aspects of post-stroke recovery, thus may be beneficial in rehabilitation.

1.3. Cross-education of Strength

In 1894, Scripture et al. (41) first described a surprising set of observations; improvements in the contralateral upper extremity after a period of unilateral training were noted (41). This phenomenon is broadly referred to as cross-education and is defined as the performance improvement in the untrained homologous muscle after unilateral exercise training (15). Skill as well as strength transfer to the contralateral limb have been observed (42-44). Generally, the terms interlateral, bilateral or interlimb transfer refer to skill related mechanisms, whereas cross-education is used to describe strength transfer (15, 44). This thesis will focus on the latter.

Since its discovery the phenomenon captured the interest of many researchers; numerous studies with very different results have been published (42, 43, 45-53). A recent meta-analysis by Manca et al. (54) found definite evidence supporting the existence of cross-education. For the upper extremity average strength gain in the untrained limb was 9.4% of initial strength ($p < 0.00001$), a significant positive correlation ($r = 0.61$, $p < 0.0005$) between the percentage gain in the trained limb and the untrained limb was also reported (54). However, depending on different aspects of the training protocol, the magnitude of contralateral strength transfer can vary greatly (0% - 100+ %) (48, 49, 55) and strength gains of the untrained limb have previously exceeded strength gains of the trained limb (56, 57).

The contraction type and speed, the chosen intensity, the novelty of the strength task as well as training of the non- dominant or dominant limb play a decisive role in the extent of contralateral strength transfer (15, 42, 45, 46, 55, 58-61).

Eccentric training protocols result in the highest average contralateral strength gain (17.7%, p= 0003), followed by dynamic (15.9%, $p < 0.00001$), concentric (11.3%, $p < 0.00001$) and isometric (8.2%, $p=0.0003$) training regimes (54). Eccentric training appears to modulate corticospinal excitability and inhibition of the untrained hemisphere to a greater extent than other contraction types and provides therefore a more efficient stimulus for cross-education (59, 61). Other training protocol characteristics such as higher contraction speed (45, 58) and higher contraction intensity (> 85% of maximal voluntary contraction) also increase the strength transfer (51). The total number of contractions completed does not seem to have an effect ($r = 0.19$, $p>0.05$) (54).

The novelty of the strength task and training with the dominant compared to the non-dominant limb may be influencing factors (15). The dominant limb is more efficient in learning a novel strength task and obtains a more comprehensive representation of the movement, thus transferring more detailed information leading to greater strength improvements (15, 46). However, a recent study in healthy subjects (42) as well as two studies in clinical populations (62, 63) report positive cross-education effects, irrespective of whether the dominant or non-dominant limb performed the training protocol. Twenty-three right handed, healthy adults were randomly assigned to a right-handed training group (RHT) ($n = 8$), a left-handed training group (LHT) ($n = 8$) or a non-training control group (CG) ($n = 7$). Participants performed a metronome guided unilateral wrist flexion-extension training protocol with the assigned wrist. After 9 sessions, strength in the trained limb improved significantly compared to CG ($p < 0.001$) by 18% and 22% for the RHT and LHT respectively. Strength gains in the untrained limb were not significantly different ($p=0.29$) between the RHT (10%) and LHT (15%), however both groups significantly improved compared to CG ($p < 0.001$). Authors identified the metronome paced training as an influencing factor (42). It has been previously suggested that externally paced unilateral contractions result in corticospinal adaptations replicating responses created by a skill-based task, thus altering cortical activity (64). The different training protocol may have resulted in a different motor learning outcome compared to previous work (42, 46). Overall, it appears that cross-education of strength is less unidirectional than previously thought.

Furthermore, other non-modifiable factors like gender (65) and age (52) do not appear to influence the success of cross-education making unilateral strength training more attractive for rehabilitation. The application of unilateral strength training in post-stroke recovery is a relatively new concept. Chapter 2 discusses novel research findings in detail.

1.3.1. Possible Mechanisms

High intensity unilateral resistance training is suspected to mediate synaptic connectivity within neural circuits allowing for increased and more efficient neural drive to the untrained limb mediating force output (66-68). Two theoretical models, both based on neural plasticity ('Bilateral Access' and 'Cross Activation'), have been proposed to explain the cross-education phenomenon (66, 69). The hypotheses are not mutually exclusive and may not be as diverse as previously believed; their involvement is related to training task characteristics (66, 69). The 'Bilateral Access' theory assumes that a new or improved representation of a movement pattern, resulting from unilateral training, can be accessed by both the trained and the untrained limb (Figure 1.2) (69). It is believed to be predominantly involved during the transfer of novel, skill-based tasks which require sensorimotor integration (69, 70), but can be applied to cross-education of strength as force production involves aspects of motor learning such as the inhibition of antagonists or the co-activation of synergists (15, 66).

The 'Cross Activation' theory suspects that unilateral training causes bilateral cortical activity, which in turn leads to concurrent adaptations in both hemispheres (69). The theory and understanding of cross-education were originally based on the early observations of motor irradiation, a spill over of unintended motor activity to the untrained limb during forceful unilateral strength training (71). Since then research could demonstrate increased excitability of the untrained, ipsilateral primary motor cortex (iM1), and the occurrence of cross-education without motor irradiation (43, 70, 72). Thus, it is now generally accepted that cross-education is mediated by the bilateral cortical activation rather than the resulting motor irradiation (43, 67). Please refer to Figure 1.3 by Ruddy et al. (69) for a schematic representation.

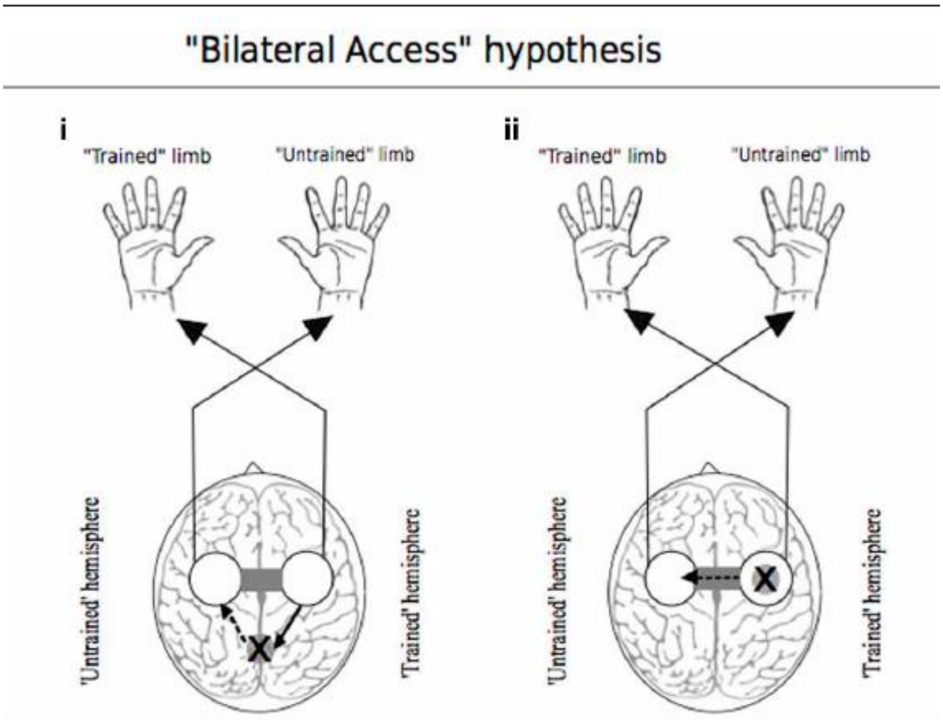

Figure 1.2 (69): Schematic Representation of the Bilateral Access Hypothesis

"X" represents training related adaptations; white circles indicate motor networks. Solid arrows represent processes occurring during unilateral training, dashed arrows represent processes that are specific to subsequent movements of the untrained limb. ***(i)*** *Adaptations generated during unilateral training are established in brain centres accessible to trained and untrained motor networks alike or* ***(ii)*** *are lateralised to motor networks controlling the trained limb and accessible to the untrained limb.*

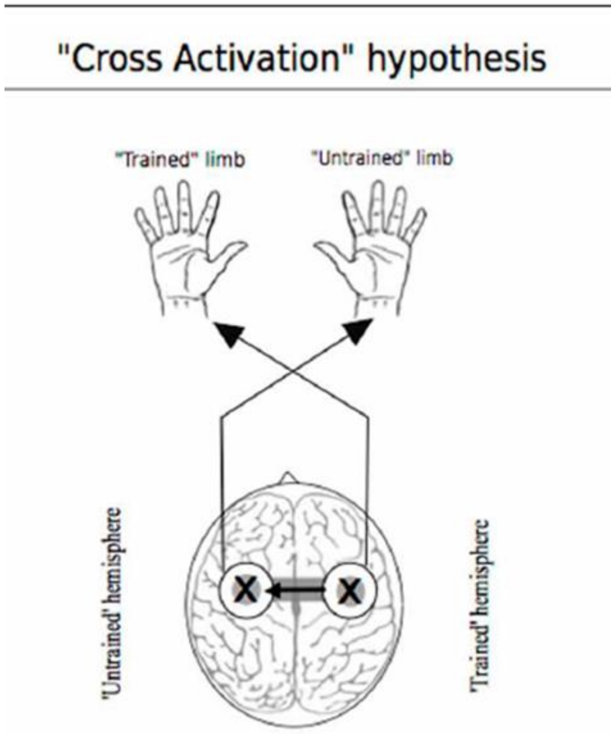

Figure 1.3 (69): Schematic Representation of the Cross Activation Hypothesis

"X" represents training related adaptations, white circles indicate motor networks, the solid arrow represents processes occurring during unilateral training

Hendy et al. (73) provides the most recent evidence supporting the 'Cross Activation' hypothesis, emphasizing the important role iM1 plays in the mediation of cross-education of strength. During a unilateral bicep training programme anodal transcranial direct current stimulation was applied to increase excitability in the iM1. A main effect for group x time was discovered ($F_{2,23}$=10.755, p<0.001), strength gains in the untrained limb of the group receiving anodal transcranial direct current stimulation significantly exceeded those reported for the group receiving sham stimulation (13% vs. 7.6%, p = 0.039) (73).

Most research concentrates on elevated neural activity in the primary motor cortex (M1) during and after unilateral exercise. However, the same applies to other cortical areas

(Table 1.1) (18). Ruddy et al. (74) discovered increased functional connectivity between the right and left supplementary motor area (SMA) after unilateral training ($\beta=0.05$, $T(17) = 1.72$, $d=0.81$); these findings were not predictive of the magnitude of transfer ($r=-0.08-0.18$, $p=0.28-0.79$). However, variations in structural connectivity correlated with training outcomes, a lower degree of SMA – SMA structural connectivity exhibited higher levels of transfer ($r=-0.57$, $p=0.01$) (74). The SMA is believed to play an important role in preventing unwanted mirror movements in the contralateral limb (75). The authors suggest that higher SMA – SMA connectivity represents a more effective non-mirroring network, supressing motor overflow during unilateral training more successfully, thus reducing levels of strength or interlimb transfer (74).

Table 1.1 (18): Brain Activation Resulting from Unilateral Training with the Dominant Right Arm

Brain areas activated in the left hemisphere (trained)	Brain areas activated in the right hemisphere (untrained)
M1*	M1*
Somatosensory cortex	Somatosensory cortex
Middle temporal gyrus	Superior temporal gyrus
Inferior temporal gyrus*	
Occipital gyrus*	Occipital gyrus*
Cerebellum	Cerebellum
Premotor cortex*	
Supplementary motor area*	Supplementary motor area*
Medial frontal gyrus*	
Caudal cingulate cortex	Caudal cingulate cortex
Precentral gyrus*	Precentral gyrus*
Lateral premotor area*	Lateral premotor area*

* activated elements of the Mirror Neuron System during and after unilateral training with the dominant, right arm

Transcranial magnetic stimulation (TMS) studies, focusing on the magnitude and nature of activation in the untrained hemisphere, described a reduction in silent period (SP) duration, a decline in short interval intracortical inhibition (SICI) in the untrained M1, and a decrease in interhemispheric inhibition (IHI) from the trained to the untrained M1 during and after unilateral strength training (42, 43, 61, 76, 77). The duration of the SP is a measure of corticospinal excitation or inhibition, shorter durations indicate increased net corticospinal excitability (42, 78). Kidgell et al. (61) reported a significant reduction in SP of 27% and a 32% decrease in SICI after 4 weeks of unilateral eccentric wrist training compared to a non-training control group (p = 0.008, p = 0.002). Hortobagyi et al. (43) described an IHI reduction of 30.9% over the course of 20 isometric unilateral index finger abduction training sessions (p = 0.008) compared to a control group ($F_{4,72}$ = 8.2, p = 0.010). The decrease in IHI and the transferred strength became progressively and more strongly correlated (r = 0.72, p = 0.008), providing first evidence that cross-education is, at least partially, mediated by changes in IHI (43, 69). Such interhemispheric communication is widely believed to occur via the corpus callosum (55, 71). However, there must be other paths involved, as bilateral activity was noted in patients with complete agenesis of this anatomical structure (71, 79). Discussed inhibitory processes are mediated by the neurotransmitter Gamma-Amino-Butyric-Acid (GABA) (80, 81), and its role in cross-education is currently under review (42, 61, 76, 82). It seems unilateral resistance training reduces the activity of GABA-mediated inhibitory interneurons and GABA receptors in the untrained M1, thus allowing for increased corticospinal excitability of the untrained motor pathway (42, 76, 82-84).

Few studies have investigated spinal mechanisms related to cross-education with conflicting results. In the study by Hortobagyi et al. (48) electrical stimulation training resulted in greater strength transfer (104%) than a voluntary contraction protocol (37%, $p < 0.05$). Furthermore, a decrease in H-reflex excitability in the contralateral limb during unilateral training of the upper limb could be previously noted (77, 85-87). Although the mechanisms mediating the noted depression could not be precisely identified, authors speculated that pre-synaptic inhibition might be responsible (66, 85). Changes in the homologous maximal H-reflex amplitude as a result of chronic unilateral strength training have not been shown so far, however only the lower limb has been investigated (51, 88, 89). A significant decrease of maximal H-reflex amplitude in the antagonistic muscle of the untrained limb ($d=1.05$, $p=0.006$) as well as a non-significant increase with large effect size ($d = 0.91$, $d=0.08$) of the H-reflex amplitude at threshold in the untrained homologous muscle were reported (88). Furthermore, changes in spinal reflex excitability and reciprocal inhibition on the untrained side could be shown after unilateral strength training and cross-education in stroke patients (90). Collectively, these results indicate that spinal circuits may play a small role in cross-education (51, 67, 88-90).

Adaptations in the untrained skeletal muscle seem unlikely to mediate the cross-education effect (57, 66, 91). In healthy individuals, contralateral strength gain is not accompanied by hypertrophy (92-94), modification in contractile protein composition, or adaptations in muscle enzyme concentration or activity (57, 66, 95-98). However, muscle atrophy caused by disuse can be prevented with unilateral strength training (99-101). Thus, suggesting the existence of a mechanism inhibiting protein degradation and/or activating protein synthesis, triggered by unilateral training in a muscle wasting environment (67). Exact underlying mechanism have not yet been investigated and the magnitude of peripheral factors influencing cross-education are probably fairly modest (67).

In summary, adaptations mediating cross-education mostly occur at cortical or supraspinal level, with changes in spinal circuits possibly playing a minor role. Neural alterations lead to more efficient motor command to the untrained muscle, resulting in contralateral strength increase. Contributing adaptations may vary depending on the training protocol and involved muscle groups (42, 91).

1.4. Mirror Therapy

During mirror therapy, a mirror is placed along a person's mid-sagittal plane, reflecting the training limb as if it were the resting limb behind the mirror (Figure 1.4). Thus, movements of a healthy limb can create the visual illusion of normal movement patterns in a compromised limb (102, 103).

Figure 1.4: Example of the Set-Up for Mirror Therapy Training

In the early 90s Ramachandran and colleagues first described positive effects of mirror therapy in arm amputees for phantom limb pain reduction. The visual illusion of a normally functioning limb created by the mirror reflection allowed patients to seemingly 'release' the phantom limb out of painful positions and 'control' movement (40, 102). Mirror therapy has also shown positive effects on post-stroke motor recovery (38, 39, 104, 105). A recent Cochrane review analysing the results of 14 studies with 567 participants concluded that mirror therapy improved motor function of the upper extremity, Activities of Daily Living and pain in participants who had suffered a stroke (105). Furthermore, a case study conducted by the Institute of Technology Sligo Neuroplasticity Research Group, provided first evidence of positive effects of mirror-aided treadmill walking in post-stroke rehabilitation (106). The subject was female, 50 years old and 47 months post stroke. The intervention consisted of 30 minutes of treadmill walking while observing the reflection of the less-affected (LA) (right) limb in a custom-built acrylic mirror apparatus, 3 times a week for 4 weeks. At post-intervention assessment the Modified Ashworth Scale, the Fugl-Meyer Assessment-Lower Extremity and the 10 Metre Walk Test demonstrated clinically meaningful improvements (106).

1.4.1. Possible Mechanisms

Effective motor control and motor learning depends on constant integration of sensory responses, whereby predicted sensory consequences of motor commands are compared with actual sensory feedback (107-109). Conditions such as amputations or stroke can cause incongruence of efferent and afferent signals, possibly leading to learned paralysis and painful spasms (102). Due to the dominance of vision over proprioception (110), mirror therapy may be able to restore the interrupted efference - afference loop and allow for rehabilitation (40, 111, 112). Although it is often claimed that neuroplastic adaptations mediate the positive effects of mirror therapy, exact mechanisms remain speculative. A recent systematic review identified alterations in three functional networks mediating perceptuo-motor control processes, confirming three not mutually exclusive hypotheses (103). The visual illusion of (normal) movement of the limb behind the mirror may cause a shift in attention toward the unseen (paretic) limb (Hypothesis 1) (103, 113). Deconinck et al. (103) reported increased activity in primary and secondary visual and somatosensory areas in the untrained hemisphere associated with conscious awareness of sensory feedback and movement monitoring, information processing and attention (103, 114, 115).

Furthermore, the Mirror Neuron System (MNS) is believed to play a role in mirror therapy (Hypothesis 2) (18, 19, 116): mirror neurons connect sensory neurons with motor neurons, thus movement observation of the mirror image causes subthreshold corticospinal activity imitating the motor command that would regulate the observed action in the limb behind the mirror (116-118). Mirror visual feedback immediately increased activity in the superior temporal gyrus (115) and elevated engagement of the premotor cortex after training (119); both areas have been previously associated with the MNS. Furthermore, a study exploring the electrophysiological manifestation of mirror therapy, reported enhanced measurements associated with both movement execution and observation, also indicating recruitment of the MNS (118).

The third functional network mediated by mirror therapy is the motor network, whereby adaptations may occur in the untrained motor pathway (Hypothesis 3) (103). Numerous studies described increased excitability in the primary and premotor motor cortex associated with the limb behind the mirror (38, 119-122). This is potentially due to neutralisation of IHI from the trained to the untrained hemisphere (103). Furthermore, after 4 days of mirror-aided skill training, intracortical inhibition (ICI) increased in the trained M1 ($p = 0.01$) but decreased in the untrained M1 ($p = 0.04$), indicating decreased excitability of the trained M1, but increased excitability of the untrained M1 (123). Acute stroke patients or stroke patients with poor rehabilitation outcomes show an excitatory-inhibitory imbalance between the two hemispheres, with large excitatory effects in the contralesional hemisphere when moving the paretic limb. As the patient recovers, activation shifts back towards the affected hemisphere (37, 124). As aforementioned, mirror therapy resulted in decreased excitability in the trained and increased excitability in the untrained hemisphere (123), thus mirror therapy may aid normalisation of the activation imbalance. Recent studies carried out in a stroke population indicate a similar trend; increased activation of the affected hemisphere and/or decreased activation of the contralesional hemisphere after mirror therapy were reported(38, 39, 104).

1.5. Cross-education and Mirror Therapy

Inter-limb transfer of skill can be enhanced by mirror therapy (103, 119, 123) and it was previously hypothesised that the same principle applies for cross-education of strength (17, 18). Zult et al. (18) and Howatson et al. (17)suggest that the MNS may not only be involved when implementing mirror therapy, but also during cross-education interventions. Neuroanatomical brain structures representing the MNS are activated during both training methods as illustrated in Table 1.1 and Figure 1.5 by Zult et al. (18).

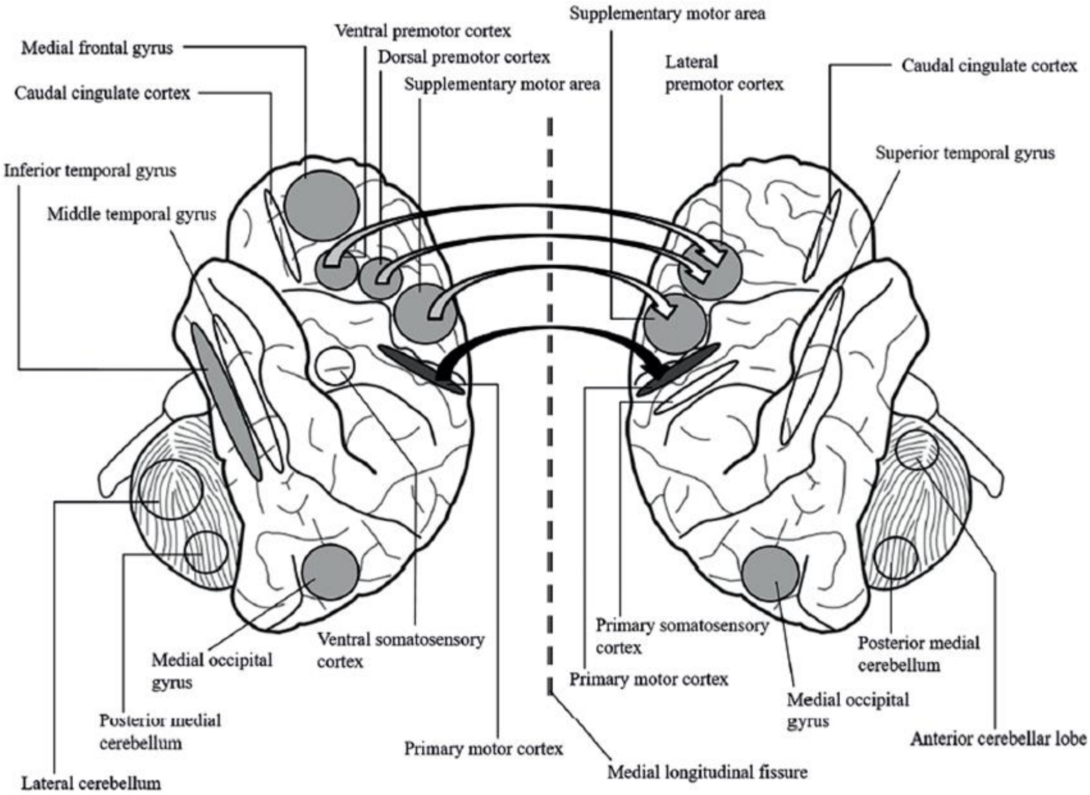

Figure 1.5 (18): Brain Areas involved in Cross-education and Mirror Therapy

The model identifies the brain areas that interconnect the two hemispheres and play a hypothetical (unfilled white arrows) or experimentally verified role (filled black arrows) in cross-education of muscle strength from the trained right to the untrained left limb. Shaded areas indicate regions of the brain involved in the MNS and in mediating cross-education; darker shading means more definitive evidence.

Furthermore, similar excitation and inhibition patterns were noted for both interventions separately (38, 42, 43, 61, 103, 123, 125). A reduction in IHI from the trained to untrained M1 was proven for cross-education (43) and hypothesised for mirror therapy (103). Similarly, a reduction in intracortical inhibition in the untrained M1, and increased excitation of the untrained motor pathway is associated with both training methods (42, 61, 123). Potentiated, repeated activation of cortical areas controlling the untrained limb may be generated and alterations in cortical excitatory or inhibitory processes may be augmented. Thus, activation thresholds of dormant neurons can be altered, and already active neurons can be primed to ultimately increase excitability of cortical areas responsible for motor control of the untrained limb (17, 126). Furthermore, elements of the primary and secondary visual and somatosensory areas, activated by reflection observation in a mirror, may provide additional information to the untrained hemisphere compared to unilateral strength training alone (17, 18, 20, 66, 67, 103). The increased repeated activation of cortical areas controlling the untrained limb along with additional input from visual and somatosensory systems, may result in greater and more efficient neural drive to the untrained limb, leading to greater force production after a combination training of cross-education and mirror therapy (17).

Zult et al. (19) tested the hypothesis with 27 healthy volunteers. The study showed that performing effortful wrist flexions while observing a mirror image of the moving right hand reduced SICI (9%, $p<0.05$) in the untrained M1 compared with no-mirror contraction and resting conditions with and without a mirror ($F_{1,26} = 6.9$; $p = 0.014$; $\eta^2_P = 0.209$). No effect of the mirror on corticospinal excitability of the untrained M1 could be demonstrated. The authors hypothesised that the strong unilateral muscle contractions (60% of maximal voluntary contraction) created a saturation effect, in that the generated level of excitation in the ipsilateral corticospinal pathway could not be further increased by mirror viewing. Mirror induced changes of SICI in the untrained M1 substantiate the idea that mirror-aided cross-education might be more effective than cross-education alone (19). Proof of principle was delivered when Zult el al. (20) conducted a trial including 23 healthy adults randomised into a mirror-training group (MG) and non-mirror training group (NMG). After 15 training sessions, a time main effect for strength changes in the trained wrist flexors was noted ($F_{1,21}$ = 110.5, p < 0.001, η^2_P = 0.840), strength increased by 72% in both groups. In the untrained wrist flexors, a group x time interaction for strength changes was identified ($F_{1,21}$ = 4.5, p = 0.047, η^2_P= 0.176), post intervention maximal voluntary contraction torque was 13% higher in the MG than the NMG (p < 0.05, d = 0.50). Strength gains in the MG (61%) were significantly higher than in the NMG (34%, p = 0.047). Corticospinal excitability increased and SICI decreased in the untrained hemisphere in the mirror as well as in the non-mirror set up, thus mirror-augmented cross-education of strength must be mediated by other mechanisms. The SP measured on the untrained side significantly decreased (16%) ($F_{1, 21}$ = 8.5, p = 0.008, η^2_P = 0.289) and the IHI from the trained to the untrained hemisphere significantly increased (11%) in the MG compared to the NMG ($F_{1, 14}$ = 4.7, p = 0.048, η^2_P = 0.251). The described study provides initial evidence that the use of a mirror can augment cross-education of strength in healthy participants and is, at least in part, mediated by altered inhibition (SP, IHI) (20). The authors strongly recommend investigating the effects of mirror-aided cross-education on motor recovery in clinical populations (17, 18, 20). Considering the low average strength gain in the untrained upper limb (9.4 %) after unilateral training (54), the additional use of a mirror may lead to clinically significant improvements not achievable by cross-education therapy alone.

A case study (under review) conducted by the Institute of Technology Sligo Neuroplasticity Research Group provides first indications of positive effects of mirror-aided unilateral strength training on post-stroke lower limb recovery. After a warm up, the stroke patient (66-year-old male, 6 months post stroke) performed 4 sets of 5 repetitions of maximal isometric ankle dorsiflexor contractions with his LA limb (right) while observing the reflection in a mirror. After 12 sessions carried out over 4 weeks, maximal voluntary contraction strength increased in the trained (LA) and the untrained (MA) limb. The MAS and the 10 Metre Walk Test demonstrated clinically meaningful changes, Timed Up and Go and self-perceived participation measured with the London Handicap Scale (LHS) also showed substantial improvements.

1.6. Knowledge Gaps and Thesis Objectives

Since its first implementation in the early 90s (40, 102), the positive effects of mirror therapy on post stroke recovery have been well established. A recent Cochrane review (105) concluded that mirror therapy improves motor function of the upper extremity, activities of daily living and pain in participants who had suffered a stroke.

Evidence supporting the existence of cross-education in a healthy population was provided by Manca et al. (54) and the application in post-stroke rehabilitation was recommended. However, to date no systematic literature review was conducted to establish possible positive effects in post-stroke recovery.

Furthermore, it was hypothesised that mirror visual feedback can augment the cross-education effect. Zult et al. (20) was the first to explore the theory in healthy participants. Following positive effects, authors suggested to investigate the combination intervention of unilateral strength training and mirror therapy in a stroke population. To date, no research team has followed the recommendation.

Considering the outlined gaps in the literature, this thesis firstly aims to investigate the clinical benefits of cross-education on post stroke motor function recovery. Secondly, it intends to establish the feasibility and potential efficacy of mirror aided unilateral strength training on post-stroke upper limb motor function recovery compared to unilateral strength training alone.

Chapter 2 systematically reviews published literature to gain an understanding of the possible benefits of cross-education in stroke rehabilitation. Considering this is the first literature review in this area of research and due to the discovered shortage of peer-reviewed articles, upper and lower limb studies are considered.

To evaluate the effectiveness of the subsequently applied (mirror-aided) cross-education intervention, strength testing procedures of high reliability are required (127). However, most reliability studies using isokinetic dynamometry concentrate on knee extension and flexion in an isokinetic mode (128-131). Furthermore, concrete guidelines regarding testing procedures such as verbal instructions and the use of analytic software are not available to the research or rehabilitation community. To ensure a reliable strength testing procedure when assessing the effects of the planned upper limb unilateral strength training programme (chapter 4), chapter 3 firstly aims to establish the protocol reliability for maximal isometric elbow extension strength measured with the Biodex System 3 Isokinetic Dynamometer and the Biodex Advantage Software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA). Secondly, unique recommendations addressing different aspects of the assessment process are discussed.

To bridge the gap in knowledge, chapter 4 describes the first pilot study investigating the feasibility and potential efficacy of mirror-aided unilateral strength training compared with unilateral strength training alone on post-stroke upper limb motor recovery. The primary feasibility objectives are (1) to assess the recruitment process, (2) to examine participant compliance, (3) to evaluate adverse effects, and (4) to assess the suitability of efficacy outcome measures. The secondary objective is to investigate the potential efficacy of unilateral strength training combined with mirror therapy on upper limb motor function recovery in chronic stroke patients compared to unilateral strength training alone. Lastly, gained data can be used for sample size calculation for a fully powered trial.

Chapter 5 discusses all findings in relation to the current understanding and identifies future direction for clinical application and research.

Chapter 2: Clinical Application of Cross-education in Stroke Rehabilitation: A Systematic Literature Review

Cross-education of strength has a positive impact on post-stroke rehabilitation: a systematic literature review

Monika Ehrensberger, Daniel Simpson, Patrick Broderick, Dr. Kenneth Monaghan

Topics in Stroke Rehabilitation 2016, 23 (2): 126-35.

Please find the systematic review PRISMA checklist in Appendix A.

The original article was altered to include recent publications for the purpose of this thesis. Please refer to Appendix B for full article.

2.1. Introduction

Cross-education, the performance improvement in the untrained homologous muscle after unilateral exercise training (15, 16), was first described by Scripture et al. (41) in 1894. Since then, the phenomenon captured the interest of many researchers and Manca et al. (54) conducted a meta-analysis investigating the magnitude of cross-education in a healthy population in 2017.

The magnitude of contralateral strength transfer reported in different research papers is ranking between zero (49) and 100+ % of initial strength (48). 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 (15, 46, 55, 58, 59). Manca et al. (54) found definite evidence for the phenomenon of cross-education. The degree of strength gain in the untrained limb is on average 11.9% ($p < 0.00001$) of initial strength, and a significant correlation ($r = 0.61$, $p < 0.0005$) between the percentage of strength gained in the trained limb and the percentage of the contralateral transfer of strength to the untrained limb was established in healthy subjects (54).

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 (55, 91). 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) (68, 85, 91, 132). Hortobagyi (68) 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 (68, 91). 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 (45, 57, 91, 96-98). Accordingly, adaptations on this level are highly unlikely.

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 (91).

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 (11). Cross-education trials imitating one-sided injury in unilaterally immobilised healthy participants, showed positive outcomes regarding strength loss and atrophy (99-101, 133). In a study by Magnus et al. (63) cross-education was proven to have a positive impact on recovery after distal radius fracture. The training group (TG) in this study followed a unilateral strength training intervention combined with standard clinical rehabilitation, the control group (CG) performed standard rehabilitation only. At 12-week post injury, hand grip strength ($F_{3,37} = 4.01$, $p = 0.009$, $n^2_p = 0.098$) as well as range of motion ($F_{2,37} = 8.20$, $p = 0.001$, $n^2_p=0.181$) were significantly improved in the TG versus the CG. The TG and CG showed 62% and 45% of the non-fractured limb strength at week 12 post injury ($p = 0.017$) (63). Unilateral strength training has also been proven beneficial for patients with peroneal nerve injury (56) and multiple sclerosis (134). However, it did not further improve rehabilitation outcomes after anterior cruciate ligament surgery (84).

Hemiparesis, a one-sided muscle weakness, affects 80 – 85% of acute stroke patients (3, 135). 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 (6). Typically, hemiparesis causes asymmetry between the more-affected (MA) and less-affected (LA) side (11) and often the impairment of motor function on the MA side is too great to engage 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 (11). 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 motor function recovery.

2.2. Methods

2.2.1. Search Strategy

Two assessors (ME, DS) carried out the search and completed the suitability screening. In December 2014, the following databases were searched from their date of inception to December 2014 using the key words presented in the search strategy (Table 2.1): CINAHL, CENTRAL, Google scholar, hselibrary, MEDLINE, Open Grey, PEDro, and Web of

Science. 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. For the purpose of this thesis the same literature search was repeated in May 2017.

2.2.2. 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 with stroke, 4) the described intervention had to be applied to the LA limb only, and 5) changes in strength or force generating capacity 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 than 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 assessments or force generating capacity of the MA limb.

2.2.3. Risk of Bias Assessment

Two different bias assessment tools were used. The first one being the PEDro scale, the physiotherapy evidence database assessment tool which is based on the list developed by Verhagen et al. (136) using the Delphi consensus technique. The second tool used was the risk of bias assessment tool from the Cochrane Handbook for Systematic

Reviews of Interventions. 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’ (137).

2.2.4. Data Extraction and Synthesis

Extracted data included (1) study design, (2) sample size, (3) inclusion/exclusion criteria, (4) participant age, (5) participant gender, (6) outcome measures, and (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 was of most interest. Additionally, motor recovery, functional impairment and neurological measures were considered. Pooled analysis of the data was not possible due to heterogeneity between 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 “haemor-rhagic 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. Results

2.3.1. Identification of Studies

The initial electronic database search yielded 4865 results. Using the described inclusion and exclusion criteria, 61 full articles remained eligible for further screening. After screening 3 studies were found to be relevant for this review (Figure 2.1): Kim et al. (138), Dragert and Zehr (90) and Urbin et al. (62).

Furthermore, a study investigating clinicians' perspective on cross-education in stroke rehabilitation was deemed important for this thesis (139), a brief summery is included at the end of the discussion section to allow for a comprehensive insight.

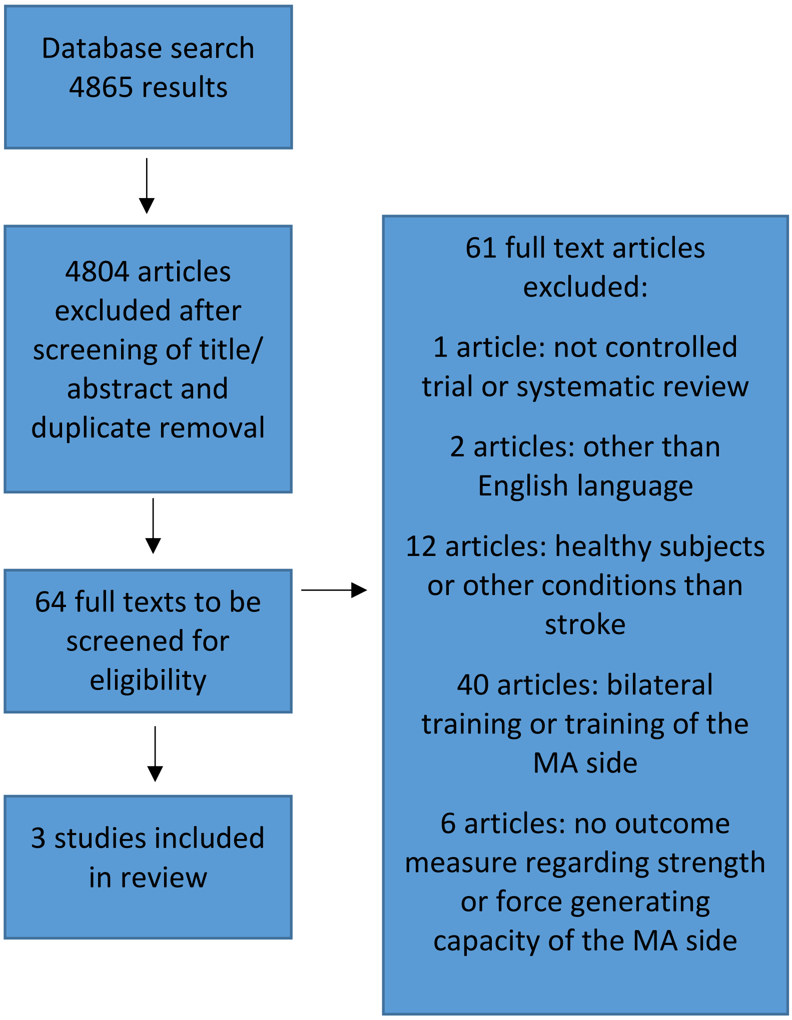

Figure 2.1: Flowchart of Study Selection Process

2.3.2. Description of Studies

The three studies applied physical interventions to the LA side in stroke patients; strength measures or force generating capacity of the MA side were reported. Study characteristics are detailed in Table 2.2. The first study by Kim et al. (138) is a single blinded randomised controlled trial with two experimental (EG1 and EG2) and one control group (CG). Thirty participants took part, 15 male and 15 female with average age in mean years ± SD of CG 61 ± 9, EG1 59 ± 8, and EG2 59 ± 12. 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 orthopaedic impairment, cardiovascular instability, 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, included 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. (138) compared 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 30min 5 times a week. Additionally, all groups received tilt table interventions for 20min 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. (138) include strength outcome measurements, the intervention did not contain strength specific training.

The second study by Dragert and Zehr (90) was a one group non-randomised controlled intervention. Nineteen participants, 15 male and 4 female, age ranging from 26 to 81 years (mean = 58 ± 12) 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 to the intervention and chronic disease comorbidity. Pre- and post-intervention measures included maximal voluntary isometric contraction (MVIC) of the dorsiflexors and plantarflexors bilaterally; electromyography (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); clinical measures (Timed Up and Go, Timed 10m walk, Modified Ashworth Scale, Functional ambulatory category, Berg balance scale, and Fugl-Meyer), and maximal motor waves and reciprocal inhibition (RI) were elicited and recorded. Dragert and Zehr (90) worked with a mixed laboratory and home-based training protocol for the less affected dorsiflexors. The strength training consisted of a 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 (25minutes) per week for 6 consecutive weeks, accumulating to 450 minutes of intervention.

The study by Urbin et al. (62) followed a controlled prospective cohort, repeated measures design. Seven healthy participants (control group), 2 male and 5 female with mean age of 50 ± 12 years and 6 stroke survivors (stroke group), 4 male and 2 female with mean age of 55 ± 14 years took part in the study. Both groups acted as their own control with 2 pre-intervention assessments 4 weeks apart. Inclusion criteria for stroke participants consisted of: (1) clinical diagnosis of ischemic or haemorrhagic stroke as determined by a stroke neurologist, (2) $\geq$ 3 months post stroke, and (3) Medical Research Council Scale for Strength score of 0 (no movement) to 2 (movement with influence of gravity removed) in the paretic wrist extensors. Exclusion criteria for control and stroke participants were: (1) (other) neurological conditions, (2) presence of musculoskeletal conditions affecting the bones and/or soft tissues of the upper extremity, (3) history of resistance training involving the wrist extensors, (4) presence of aphasia, and (5) contraindications to transcranial magnetic stimulation (TMS). Pre- and post-intervention strength of the trained and untrained side of the control group and the trained (LA) side of the stroke group was assessed with a single-column pulley. The force-generating capacity of the untrained (MA) side of the stroke group was measured using AROM against gravity. The Action Research Arm Test (ARAT), and TMS to determine corticospinal excitability and inhibition were applied also. The wrist extensor strength training consisted of a warm up, followed by 6 sets of 6-8 repetitions at 80% of one-repetition-maximum with 90 seconds rest between sets. Each participant completed 4 sessions a week for 4 weeks, accumulating to 16 sessions. In all studies post-test measurements were compared to pre-test results to identify changes.

2.3.3. Description of Results

Results of each study for strength assessments and motor recovery outcome measures are displayed in Table 2.2. Kim et al. (138) found no significant differences between pre-test and post-test strength measures in the LA limb of all 3 groups ($p > 0.05$). 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 one leg standing training group strength gains range from 13.7% to 53.2% (mean = 22.6%) (t = -11.42 – -4.23, p = 0.04 – 0.00) the dorsiflexor strength increased by 23% (t = -8.12, p = 0.00). For the task-oriented training group improvements from 28.5% to 48% were noted (mean = 39.5%) (t = -19.54 – -5.05, p = 0.02 – 0.00) with a dorsiflexor strength gain of 45.5% (t = 19.54, p = 0.00). The CG showed no significant strength increase in the MA side ($p > 0.05$). Furthermore, the strength gains in knee flexors, knee extensors, ankle dorsiflexors and ankle plantarflexors were significantly greater in EG2 than EG1 (F = 104.14 – 10.01, p = 0.04-0.00). In all gait characteristics significant improvements could be shown for EG2 against CG (F = 30.05-7.45, p=0.03-0.00). Also stride length, gait symmetry ratio and double support period significantly improved in EG2 compared to EG1 (F = 14.23-7.45, p=0.03-0.00). All characteristics, except stride length, showed a significant improvement in EG1 against CG (F = 30.05-7.45, p=0.03-0.00). There were no significant changes noted in the CG ($p > 0.05$). In the trial by Dragert and Zehr (90) dorsiflexor MVIC significantly increased by 33.5% (d=0.5, p=0.02) in the trained limb and by 31.4% (d=0.6, p = 0.009) in the untrained, MA limb. After intervention Timed Up and Go was significantly reduced from 18.61s to 17.41s (d=0.6, p=0.05). There were no other significant changes observed in functional impairment or clinical measures. Range of motion of the LA ankle increased significantly (p=0.04), this improvement did not translate into the MA side. After the training period, EMGmax increased significantly in the tibialis anterior muscle in both limbs (LA: d=0.7, $p = 0.02$, MA: d=0.6, $p = 0.03$). When walking, an increase in muscle activation was recorded in the tibialis anterior of the more-affected side ($p = 0.03$) and in the soleus muscle of the less-affected and more-affected side ($p = 0.005$, $p = 0.04$). During training sessions co-activation within the untrained limb was noted. Measurements of RI showed significant changes in the MA tibialis anterior after intervention ($p < 0.05$). Urbin et al. (62) reported no time x group interaction for strength gains in the trained wrist extensors ($F_{2,22} = 1.23$, $p = 0.31$, $\eta^2 = 0.10$). Strength increased in both groups (control 38.0 ± 13.4%, stroke 29.0 ± 11.0%, $p < 0.05$) with no between group difference ($p = 0.2$). In the control group, untrained wrist extensor strength increased significantly by 18% ($p < 0.01$) ($F_{2,5} = 28.02$, $p < 0.01$, $\eta^2 = 0.92$). In the stroke group, AROM and the ARAT improved significantly by 25° (~100%, $p < 0.01$) ($F_{2,4} = 15.63$, $p < 0.01$, $\eta^2 = 0.89$) and 2.4points (4%) ($t_{(5)} = -2.72$, $p = 0.04$) respectively. Strength and functional improvements in the MA side in stroke patients were accompanied by increased net excitation of the corticospinal pathway, inclusive of all inhibitory and excitatory inputs (n = 2).

Table 2.2. Description and Results of Each Study

Study	Kim et al. (2014)			Dragert & Zehr (2013)	Urbin et al. (2015)
Description					
Study Design	Single blinded randomized controlled trial			One-group nonrandomized controlled intervention	Controlled prospective cohort, repeated measures design
Sample Size	30			19	13 (7 healthy/ 6 stroke)
Gender	15F/ 15M			4F/ 15M	7F/ 6M
Mean age ± SD	CG: 61±9, EG1: 59±8, EG2: 59±12			58±12	Healthy: 50±12 Stroke: 55±14
Paretic side left/right	CG: 7/3, EG1: 4/6, EG2: 5/5			12/7	NR
Stroke type ischemic/ haemorrhagic	CG: 5/5, EG1: 4/6, EG2: 7/3			NR	5/1
Intervention	• 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			• Dorsiflexion isometric strength training on less-affected side 5sets of 5 maximal isometric contractions held for 5seconds • 3 sessions per week for 6 weeks	• Dynamic wrist extension training 6 sets of 6-8 repetitions at 80% (1 RM) • 4 sessions per week for 4 weeks
Outcome measures	• muscle strength hand held dynamometer • Gait parameters: velocity, cadence, stride length, gait symmetry, double support percentage			• MVIC measured with load cell • EMG • M-wave • RI • Gait kinematics • Clinical measures	• wrist extensor muscle strength with a single-column pulley • MA wrist extensors with AROM • ARAT • TMS
Results					
Strength/ force generating capacity %-changes of the MA side (p-value)					
	CG	EG1	EG2		
Hip Flexion	-14.2 (0.02)	53.2† (<0.01)	48† (<0.01)		
Hip Extension	-0.6 (0.07)	16.6† (0.03)	28.5† (0.02)		
Knee Flexion	-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)		
Dorsiflexion	-1.4 (0.37)	23† (<0.01)	45.5†‡ (<0.01)	31.4 (0.009)	
Plantarflexion	0.6 (0.6)	14.8† (0.03)	35.4†‡ (<0.01)	-4.5 (0.77)	
Wrist Extension					100 (<0.01) (AROM)
%-change in gait parameters (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	0.8 (0.45)	0.7 (0.661)	8.3†‡ (<0.01)		
Gait Symmetry Ratio	-5 (0.07)	-50.6† (0.04)	-64.1†‡ (0.01)		
Double support period	-1.4 (0.11)	-14.7† (0.04)	-28.0†‡ (<0.01)		
Significant %-change in clinical measures (p-value)					
Time Up and GO				-6.4 (0.05)	
ARAT					4 (0.04)

F female, M male, CG control group, EG experimental group, NR not reported, SFT standard function training, MVIC maximal voluntary isometric contraction, EMG electromyography, RI reciprocal inhibition, 1RM one repetition maximum, AROM active range of motion, ARAT action research arm test, TMS transcranial magnetic stimulation, MA more-affected, † significantly different compared to CG, ‡ significantly different compared to EG1

2.3.4. Bias

The study by Kim et al. (138) is a single blinded randomised controlled trial (RCT) allowing for comparisons between intervention and control groups. Eight out of 11 items on the PEDro scale (136) were satisfactory and the study was considered to have a low risk of bias according to the Cochrane risk of bias assessment tool (137). However, allocation concealment, blinding of participants and therapists were 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 and Zehr (90) is a one group non-randomised controlled intervention. The assessment of bias using the PEDro scale and the Cochrane risk of bias assessment tool 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 of which 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, undertraining or incorrect technique remains. Participant profile showed a wide range of heterogeneity regarding age, time after stroke, lower extremity functional capacity etc. Participant drop-out resulted in a small sample size (n = 19), however Dragert and

Zehr (35) stated that the Cohen's d effect size calculations suggest robust results. Overall, the study scored 4 out of 11 on the PEDro scale; the risk of bias using the Cochrane risk of bias assessment tool was considered unclear.

Again Urbin et al. (62) does not follow a randomised controlled design, making the risk of bias assessment difficult. For the PEDro scale 9 out of the 11 items were appropriate, 5 of which were reported to the assessor's satisfaction. Blinding of therapists, participants and outcome assessor was not reported. Strength in the trained side was significantly different between control group (healthy participants) and stroke group at baseline ($p < 0.05$). Furthermore, changes in strength in the untrained, MA side was assessed using the AROM against gravity assessment tool, thus strength changes cannot be quantified and between group comparison is difficult. The small sample size was also identified as limiting factor in this study. Overall the study scored 5 out of 11 on 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 2.3 and 2.4.

Table 2.3: PEDro Risk of Bias Assessment for All Three Studies

Item		Kim et al. (2014)	Dragert & Zehr (2013)	Urbin et al. (2015)
1	Eligibility criteria were specified	Yes	Yes	Yes
2	Subjects were randomly allocated to groups	Yes	N/A	N/A
3	Allocation was concealed	Not reported	N/A	N/A
4	The groups were similar at baseline regarding most important prognostic indicators	Yes	N/A	No
5	There was blinding of all subjects	Not reported	Not reported	Not reported
6	There was blinding of all therapists who administered therapy	Not reported	Not reported	Not reported
7	There was blinding of all assessors who measured at least one key outcome	Yes	Not reported	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	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 analysed by "intention to treat"	Yes	Yes	Yes
10	The results of between-group statistical comparison are reported for at least one key outcome	Yes	N/A	Yes
11	The study provides both point measures and measures of variability for at least one key outcome	Yes	Yes	Yes
Total		**8/11**	**4/11**	**5/11**

Table 2.4: Cochrane Risk of Bias Assessment for All Three Studies

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 à 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"
Urbin et al. (2015)	N/A	N/A	Unclear risk, not reported	Unclear risk, not reported	Low risk	Low risk	Small sample size Between group difference at baseline for strength of the tained limb

2.3.5. Confounders

Kim et al. (138) recruited all participants from a single inpatient setting which represents a limited sample population. Dragert and Zehr (90) recruited participants via community stroke support groups, posters in medical offices/hospitals, and newspaper articles. Urbin et al. (62) recruited stroke patients from a Brain Recovery Registry, control participants answered online advertisements. This suggests participants of all three trials were recruited on a voluntary basis which may result in participants with a high level of motivation and efficacy. The level of motivation and efficacy in participants was not measured or reported pre-test or post-test in any of the three trials; this could present a possible confounder of results.

2.3.6. Strength of Results

In general, the standard of evidence in randomised controlled trials (RCT) is regarded higher than in non-randomised controlled studies. RCTs 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 (140). The only RCT included in this review did not specifically use unilateral strength training (138). Different outcome measures for strength changes in the untrained side of healthy participants (control) and stroke patients were used by Urbin et al. (62), compromising comparability of results. Furthermore, definite strength changes in the untrained, MA limb of participating stroke patients could not be quantified with AROM assessments. The only study applying specific strength training to the LA side and measuring strength changes in the MA side was a one group non-randomised controlled trial (90).

Based on best evidence synthesis guidelines (141) 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, none of the studies report long-term follow-up measurements, the sustainability of improvements is therefore unclear.

2.4. 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 motor function recovery. A first systematic literature search (2014) yielded 2 studies complying with the inclusion criteria, a third study was added during an update (2017). The first study included, Kim et al. (138), is 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 by Dragert and Zehr (90) was a non-randomised one group-controlled trial. Again, the within group results give a strong indication that cross-education of strength exists in the post-stroke hemiplegic patient, supporting the findings of Kim et al. (138). The strength gain achieved in the untrained, more-affected limb was 31.4% greater when 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. The third study by Urbin et al. (62) did not entirely comply with inclusion criteria. Changes in the untrained, MA wrist extensors were measured with the AROM against gravity assessment tool, denying exact quantification of strength changes and comparison with the healthy subject control group. However, it was the first trial investigating cross-education of the upper limb in a stroke population and was therefore considered important for this thesis. The untrained, MA side significantly improved by 100% $p < 0.01$ (25°) which also translated to a small but significant improvement in the ARAT (2.4 points, 4%, $p = 0.04$).

Dragert and Zehr (90) and Urbin et al. (62) provide first indications of possible corticospinal adaptations occurring after unilateral strength training in a stroke population. Motor irradiation during training could be shown and EMG activity significantly increased bilaterally as a result of the strength training programme (90). After assessing absolute stimulator output and ipsilateral silent period, Urbin et al. (62) concluded that net excitation of the corticospinal pathway, including all inhibitory and excitatory inputs, is increased resulting in improved communication between corticomotor and spinal motor neurons. Furthermore, reported changes in RI in the untrained limb may indicate involvement of spinal circuits in the cross-education process (90). Combined results suggest neurological adaptations underlying cross-education are still possible after stroke (62, 90), thus alleviating previously expressed uncertainty (84).

Comparison of the two lower limb studies indicates that task-oriented strength training (138) resulted in a higher overall (mean = 39.5%) and dorsiflexor strength gain (45.5%) than a specific dorsiflexor isometric contraction programme (31.4%) (90). The smaller strength increase might be due to the different training protocols used in the two trials. Dragert and Zehr (90)worked with a mixed laboratory and home training programme which might negatively impact on adherence of the intended exercise protocol. The participants of the other trial (138) were consistently supervised throughout all training sessions. Furthermore, the latter were training 5 days a week compared to 3 days a week in the dorsiflexor trial. Total intervention times given by the authors indicates longer training periods in the trial by Dragert and Zehr (90) accumulating to 450min compared to 300min in the study by Kim et al. (138). 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 require approximately 5 minutes of training time per session, accumulating to 90 minutes of total intervention time (90). Even though there is no breakdown of the actual training time in the study by Kim et al. (138), 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 pre-intervention of the more-affected leg was 3.4Nm in the trial by Kim et al. (138) compared to 9.18Nm for Dragert and Zehr (90, 142). This difference in baseline strength combined with the fact that a more novel task-oriented training programme was used by Kim et al. (138) could also be an influencing factor in the high variation of strength gains between the studies. It has been shown that lower strength levels at the beginning of a strengthening programme allows for higher and more rapid improvements (142). Likewise, the more novel or less familiar a training task is, the greater the potential strength transfer (58). Further Dragert and Zehr (90) had no inclusion/exclusion criteria regarding the Modified Ashworth Scale. Six out of the 19 participants were graded 2 and higher; this is very much in contrast to the tilt table trial (138), 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. Another factor contributing to higher training effects in the trial by Kim et al. (138) 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 (143, 144). Direct comparison with the trial by Urbin et al. (62) regarding strength gains of the untrained, MA side is impossible due to differing assessment tools. However, the noted improvement of 100% in the AROM assessment tool seems substantial and the translation into functional improvements very promising.

Characteristics of participants in the trial by Dragert and Zehr (90) were very much heterogeneous e.g. months post stroke ranged from 6 – 284, whereas participants in Kim et al. (138) and Urbin et al. (62) show more homogeneity. Such heterogeneity could be a possible influence on study results and make specific interpretations more challenging.

In a meta-analysis by Manca et al. (54) it is clearly stated that strength increase in the untrained limb corresponds to increases seen in the trained limb. Surprisingly, Kim et al. (138) reported no significant strength increase in the less-affected, trained lower limb and there is no attempt to explain this finding.

During the original literature search 2 studies which trained the MA side and reported strength outcome measures of the LA, untrained side were discovered. This did not comply with the inclusion criteria 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 mention. Clark and Patten (145) 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. (146) 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 was reported. For this review only results of the DMTE intervention were of interest, the unilateral exercises performed were weight-bearing with the more-affected arm (elbow fixed) and opening the hand with finger extension. After completion, a significant isometric strength increases for the MA upper limb was reported, however this did not carry over to the LA, untrained side. There were no significant isokinetic strength gains noted. It appears that cross-education of strength from the MA limb to the LA limb is possible, providing sufficient intensity and overload. Even though these studies do not comply with inclusion criteria, they support the theory that cross-education of strength is achievable after stroke.

Russell et al. (139) investigated clinicians' perspectives on cross-education in stroke rehabilitation. Focus groups consisting of occupational therapists ($n = 23$) and physical therapists ($n = 2$) at four different sites participated in a semi-structured interview. Participants' experience ranged from newly graduated to 30 years. The primary outcomes were captured within three descriptive categories: 1) Cross-education is contradictory to general therapist knowledge. Current rehabilitation concentrates on a forced-use paradigm with treatment focusing on the MA limb. However, therapists recognised that this paradigm did not meet the needs of all patients. 2) There is a gap in current practice, with limited treatment options for patients with severe impairment. 3) In general cross-education was considered a promising addition to routine therapy. It was deemed a safe and easy way to increase volume of rehabilitation and an opportunity to strengthen the LA side, protecting it from compensation injuries. Overall, clinicians found cross-education to be paradoxical to current rehabilitation methods yet promising as an adjunct therapy (139).

2.4.1. Limitations

Articles included in this systematic literature review had to be accessible in the English language. For two studies, the abstract could be retrieved in the English language, however a translated version of the full paper was not available. Considering the thesis title which clearly refers to motor function recovery of the upper limb in stroke patients, the inclusion of trials applying interventions to upper and lower extremities can be identified as a limitation. However, a shortage of peer-reviewed articles in the field as well as the fact that this is the first systematic review carried out in this area of research, justify a broader approach. When implementing the search in preparation for the pilot trial (chapter 4) in December 2014 only studies addressing the lower limb could be identified. The first study applying cross-education to the upper limb was Urbin et al. (62), which was included when repeating the search in May 2017.

2.5. Conclusion and Contribution to Knowledge

This is the first systematic literature review investigating possible benefits of cross-education in post-stroke motor function recovery addressing the first objective of this thesis. In summary, there is moderate evidence (141) that the phenomenon of cross-education from the LA side to the MA side can be applied in stroke patients and that it 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. Clinicians identified a gap in current rehabilitation methods which can be addressed by cross-education interventions. However, due to the small number of studies with restricted numbers of participants and the trials' limitations, more high-quality randomised control trials are needed to achieve a more satisfying conclusion regarding 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 the findings and to further support the use of cross-education in stroke rehabilitation.

Chapter 3: Protocol Reliability for Maximal Isometric Elbow Extension Measured with the Biodex System 3 Isokinetic Dynamometer

Peak torque, rate of torque development and average torque of isometric ankle and elbow contractions show excellent test–retest reliability

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3.1. Introduction

First introduced as a device for muscle strength measurement in 1967 by Thistle et al. (147), isokinetic dynamometry is the gold standard for assessing muscular functionality among athletic populations as well as populations engaging in rehabilitation programmes (148). The application of isokinetic dynamometry for assessing muscular strength in research, sport or clinical practice requires testing procedures of high reliability, which refers to consistent reproduction of results when tests are performed multiple times under similar conditions (127). When assessing the effectiveness of strength training programmes, testing protocols with high reliability provide certainty that achieved changes are predominantly due to the intervention with low influence of measurement error (149).

Drouin et al. (150) 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 for isokinetic dynamometry with excellent results (ICC > 0.75), primarily assessing in an isokinetic mode and focusing on knee extension or flexion (128-131). Other joint actions in an isometric mode, which is regarded as safer and more appropriate for maximal strength testing in populations who have restricted range of motion or are unable to comply with isokinetic procedures, are currently underexplored (151).

Furthermore, Peak Torque, representing maximum torque produced at a single point of contraction (152, 153), is the most widely used strength parameter in reliability studies and when assessing the effects of training or rehabilitation programmes (154). However, from a functional perspective, the ability to generate torque quickly, assessed by the strength parameter Rate of Torque Development, and to maintain torque, measured by the strength parameter Work or Average Torque over a single contraction, may be more important. 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 (155). Average Torque over a single isometric contraction can replace the commonly used isokinetic parameter Work (156). Work represents the capability to generate muscle torque throughout the full range of movement (153, 157); 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 (156), which is an important factor when performing activities of daily living. Daily tasks generally do not require maximal strength output, but the maintenance 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. 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, with Peak Torque often returning to normal before Average Torque or Work (158). Considering the importance of this strength parameter 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 investigated. A comprehensive muscle function assessment should include Peak Torque, Rate of Torque Development and Work or Average Torque over a single contraction (155, 158).

In the subsequent chapter of this thesis, an isometric elbow extension strength training programme is applied in a chronic stroke population. To reliably evaluate its effectiveness regarding comprehensive muscle function recovery, strength testing procedures of high reliability are required. However, the only study evaluating the reliability of the named joint action was carried out in a highly specific population of elite swimmers and included Peak Torque only (ICC = 0.92) (159). To the author's knowledge, there is currently no study investigating the protocol reliability for maximal isometric elbow extension strength including all three outlined important strength parameters.

To address this gap in knowledge and to ensure dependable testing procedures when assessing the effectiveness of the subsequently applied strength training protocol in a stroke population (chapter 4), this reliability study is carried out.

Specific objectives are: 1) to establish the protocol reliability for maximal isometric elbow extension strength and 2) to develop novel recommendations that ensures excellent reliability when assessing isometric Peak Torque, Rate of Torque Development and Average Torque over a single contraction using the Biodex System 3 Isokinetic Dynamometer with the Biodex Advantage Software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA)

3.2. Methods

3.2.1. Design

This study followed a repeated measures design for test re-test reliability. 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.

3.2.2. Participants

Potential participants answered to posters displayed in the Institute of Technology Sligo. Following eligibility assessment, twelve participants (Table 3.1), 6 males and 6 females (mean age 40 ± 16 years, height 1.68 ± 0.09m, weight 74.1 ± 11.1Kg) took part in this study. Both genders were recruited as previous studies using the Biodex System 3 for isometric strength uses the same protocol for both males and females (160, 161). 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 C). All participants received an information sheet (Appendix D) prior to providing written informed consent (Appendix E) 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

3.2.3. 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 shoulder/elbow unit attachment with limb support was used for elbow extension strength assessment (Figure 3.1). Before testing each subject, the system was calibrated according to the procedure in the Biodex System 3 manual (162).

Figure 3.1: Participant Positioning for Elbow Extension Strength Assessment

3.2.4. Participant Positioning

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) (163), where 0° refers to full elbow extension, the shoulder joint was positioned at 45° shoulder flexion (164). 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. Please refer to Appendix F for a detailed description of participant positioning for elbow extension assessment according to the Biodex System 3 manual (162).

All joint angles were measured with a hand-held goniometer; range of motion measurement followed the Biodex procedure. Participant positioning i.e. chair height, dynamometer height, attachment length etc. was recorded during familiarisation to ensure consistent set-up for all testing sessions.

3.2.5. Test-Protocol

All testing was performed on the Biodex System 3 Isokinetic Dynamometer in the Health Science & Physiology Laboratory at the Institute of Technology Sligo. The protocol was performed at three time points: **Familiarisation** (Pre-Test), **Test 1** (> 48 hours post familiarisation) and **Test 2** (at least 7 days after test 1). For all participants, laboratory conditions were consistent, and all testing was conducted on the right side only to facilitate data collection (165).

The warm-up consisted of 3 minutes of arm cycling performed at a level of perceived exertion of 10-12 on the Borg scale (166) 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 (167). Following the warm-up, maximal isometric elbow extension strength was assessed using 4 maximal isometric contractions held for 5 seconds, separated by 45 seconds of rest (168).

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 push their fist towards the ground as 'hard and as fast as possible'. Each participant was asked to give maximal effort 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’.

3.2.6. Data Analysis

From each set of four 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 (Appendix G). The time of contraction onset was identified manually (gold standard) (169, 170), 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 (171).

3.2.7. Statistical Analysis

Data was 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 (172). 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 (127).

Typical Error is expressed in the measurement unit it refers to and calculated as:

Typical Error = $SD_1/\sqrt{2}$, where SD_1 is the standard deviation of the differences between the two measurements (127, 152).

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 (173).

3.3. Results

Twenty-one out of 96 (21.8%) maximal elbow extension contractions 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 (p>0.05).

3.3.1. Reliability Analysis

Relative reliability (ICC) was excellent (Peak Torque 0.98, Rate of Torque Development 0.92, and Average Torque 0.98).

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.

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

	Elbow Extension					
	PT (Nm)		RTD (Nm/s)		AT (Nm)	
Subject ID	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2
1	23.7	24.1	47.5	21.5	20.3	19.1
2	81.6	94.8	194.0	249.0	66.1	81.0
3	67.7	80.7	234.5	169.5	61.0	61.1
4	29.7	28.6	105.5	94.0	25.6	23.5
5	45.0	41.5	147.0	81.5	36.4	34.6
6	35.9	33.0	148.0	126.0	33.4	29.1
7	31.9	33.4	80.5	97.5	29.1	28.4
8	24.4	25.6	70.5	76.5	21.8	23.9
9	70.2	58.7	193.0	218.5	61.2	52.2
10	65.8	61.4	223.5	214.0	57.7	57.1
11	68.7	72.5	123.5	156.5	60.2	57.7
12	37.0	33.9	74.0	55.5	34.6	30.1

PT = Peak Torque, RTD = Rate of Torque Development, AT = Average Torque, Nm = Newton Meter, Nm/s = Newton Meter 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 ($Nm \cdot s^{-1}$)**	**Average Torque (Nm)**
Elbow Extension			
Test 1 (n=12)	48.5 ± 20.8	136.8 ± 63.5	42.3 ± 17.5
Test 2 (n=12)	49.0 ± 23.8	130.0 ± 71.5	41.5 ± 19.5
T1-T2 Difference p-value	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 calculate means, standard deviations and for the reliability analyses. ICC = Intraclass correlation coefficient, CI = Confidence Interval, CV = Coefficient of variation.

3.4. Discussion

According to Fleiss (174), 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 over a single contraction for maximal isometric 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 (127). The combination of all three strength parameters offers a comprehensive analysis of muscle function or recovery (158).

Relative and absolute reliability established in this study are higher than previously reported values (159, 164). Former reliability studies for ankle dorsiflexion and elbow extension have reported Peak Torque ICC values ranging from 0.80 to 0.98 (159, 164).

Contraction mode may be an influencing factor; joint movement during isokinetic testing appears to result in lower reliability values (164). Furthermore, it is important to record participant positioning to ensure exact replication of protocol (159). 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 (164).

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 (175). However, Rate of Torque Development ICC values in this study are higher than in previous studies implementing maximal isometric strength testing (0.84 – 0.86) (176). 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) (162). 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 (176, 177). Considering that Rate of Torque Development is an indicator of initial contraction torque (178, 179), 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.

To the authors' knowledge, 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 elbow extension (ICC 0.98). Considering its importance in the assessment of muscle function recovery (158), it is recommended to include this parameter in future isometric strength testing studies. To assess a participant's torque generating capacity in all aspects, it is important to include Peak Torque, Rate of Torque Development and Average Torque over a single contraction, 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 (better) than previously reported (167, 176). The lack of familiarisation with the testing equipment and procedure in other studies may be responsible (176). Scores of the second testing session may differ from scores of the first testing session due to learning effects (176). Dynamic modes also appear to result in lower absolute reliability (167) i.e. higher typical error and CV values.

Early contractions and counter movements occurred frequently during testing. During elbow extension, strength assessment the upper arm cannot be firmly strapped to the elbow support due to contraction restriction, potentially resulting in a high level of 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 and highly variable sample (n = 12). 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 (180, 181). 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 as follows (182):

$$k = \frac{8z_{\frac{\alpha}{2}}^{2}(1-p)^{2}(1+(n-1)p)^{2}}{w^{2}\,n(n-1)}$$

k = number of subjects rated, n = number of tests, p = ICC value, w = width of 95% confidence interval.

Recommendations for Achieving Excellent Reliability

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 effort 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 was 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.

3.4.1. Limitations

The aim of this study was to establish the protocol reliability of maximal isometric elbow extension strength testing to ensure dependable procedures when assessing the effectiveness of a subsequently applied strength training protocol in a stroke population (chapter 4). However, participants in this study were healthy adults, stroke survivors were not included. During participant recruitment for a case study involving stroke survivors, the barrier of transportation to attend the Institute of Technology Sligo was identified (106). Due to this complication, the research team decided to carry out the reliability study on healthy adults only. To resemble some of the characteristic of the highly heterogenic stroke population, male and female participants with a wide age range were included. Furthermore, the relatively small sample size is sufficient for reliability testing, however it does not allow for subgroup analysis, i.e. age categories, sex, dominant vs. non-dominant side. Although assessors in the ICC model chosen are considered to be representatives of a larger population of assessors with similar characteristics (172), interrater reliability was not specifically assessed.

3.5. Conclusion & Contribution to Knowledge

This is the first study investigating the test-retest reliability of maximal isometric elbow extension Peak Torque, Rate of Torque Development and Average Torque over a single contraction using the Biodex System 3 Isokinetic Dynamometer. Excellent reliability was established for all three strength measures important for comprehensive muscle function assessment with specific focus on the never before reported parameter Average Torque over a single isometric contraction. When the recommended procedures are closely followed, this testing protocol can be confidently applied.

Chapter 4: Unilateral Strength Training and Mirror Therapy for Enhancing Upper Limb Motor Function Post Stroke: A Pilot Randomised Controlled Trial

Unilateral Elbow Extension Strength Training and Mirror Therapy for Post-Stroke Motor Recovery: A Pilot Randomised Controlled Trial.

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4.1. Introduction

Worldwide fifteen million people suffer a stroke each year, five million are permanently disabled (1, 2), with hemiparesis (3) and spasticity (4, 5, 22) the most commonly experienced physical complications. Due to the associated impact on activities of daily living (7), high levels of anxiety and reduced self-perceived quality of life (8, 9); upper limb function is deemed a priority in post-stroke rehabilitation (10).

Current rehabilitation techniques are mainly based on repetitive methods addressing the paretic limb (10). However, the more-affected (MA) limb is not always strong enough to engage in active exercise (11), thus requiring therapist or family assistance (10, 12), which in the acute or outpatient settings can prove expensive and labour intensive (12, 14).

Cross-education of strength, the performance improvement in the untrained homologous muscle after unilateral training (15, 16), may offer a solution. Cross-education can address strength deficits in both the trained less-affected (LA) limb and the untrained MA limb (183). Adaptations, contributing to cross-education, are most likely to occur on cortical and subcortical level, with potential alterations in spinal circuits (43, 55, 91). Unilateral contractions appear to increase activity and excitability in the ipsilateral primary motor cortex (iM1) (68) and the corticospinal path (184-186) controlling the untrained limb. Since contralateral strength gains are mediated through neural pathways damaged by stroke (69), cross-education is considered highly relevant in rehabilitation (11). Ehrensberger et al. (187) suggested that cross-education post stroke has positive effects on lower limb motor function recovery, while Urbin et al. (62) provide initial evidence for post-stroke upper limb benefits.

Mirror therapy, where the Mirror Neuron System (MNS) becomes active while observing the training LA limb, improves upper limb motor function, activities of daily living and pain post stroke (105). Recent reviews suggest that mirror therapy may augment the cross-education effect. Mirror neurons are present in a number of cortical areas also associated with cross-education (17, 18). Observing the reflection of the LA limb in the mirror while exercising may further enhance ipsilateral corticospinal excitability and corticomotor activity than unilateral strength training alone, thus increasing strength transfer (110, 120). Zult et al. (20) was the first to explore the theory in wrist flexors. Strength increase in the untrained wrist flexor was significantly ($p = 0.047$) higher in the cross-education and mirror therapy group (61%) compared to the cross-education only group (34%) ($F_{(1,21)} = 4.5$, $p = 0.047$, $\eta 2P= 0.176$), coinciding with a reduction in the contralateral silent period (cSP) ($F_{(1,21)} = 8.5$, $p = 0.008$, $\eta 2P = 0.289$) and an increase in interhemispheric inhibition (IHI) ($F_{(1,14)} = 4.7$, $p = 0.048$, $\eta 2P = 0.251$). This suggests that a mirror can augment the cross-education effect, and it is recommended to explore possible benefits of the combined intervention post stroke (84). Considering the relatively low average strength transfer (9.4%) (54) to the untrained upper limb following unilateral strength training, a functionally meaningful level of mirror augmenting effects is unclear (84).

The aim of this pilot study was to investigate the feasibility and potential benefit of unilateral strength training combined with mirror therapy on post-stroke upper limb motor recovery. The primary feasibility objectives were (1) to assess the recruitment process, (2) to examine participant compliance, (3) to evaluate adverse effects, and (4) to assess the suitability of efficacy outcome measures. The secondary objective was to investigate the potential efficacy of unilateral strength training combined with mirror therapy on upper limb motor function recovery in chronic stroke patients compared to unilateral strength training alone. The authors hypothesised that the combination intervention would lead to significant improvements in upper limb motor function recovery compared to unilateral strength training alone. Lastly, the authors intended to provide data to inform a power analysis to determine sample size for a future trial.

4.2. Methods

A pilot randomized controlled parallel group study with blinding of the independent assessor and allocation concealment was carried out. The Research Ethics Committee at Sligo University Hospital granted ethical approval (Appendix H).

4.2.1. Participants

Rehabilitation professionals in Sligo and South Donegal referred 36 potential participants (Figure 4.1). All participants lived in Sligo or South Donegal. Inclusion criteria were: (1) >18 years of age, 2) >6 months post stroke; (2) discharged from formal rehabilitation; (3) no diagnosis of addition neurological, musculoskeletal or cardiovascular illness that would prevent maximal isometric strength training. Exclusion criteria were: (1) impaired cognition that would affect the ability to make informed consent (MMSE < 21) (Appendix I); and (2) visual impairments that would interfere with the ability to participate safely in isometric training and observe mirror images. All participants were instructed not to change their typical care or physical activity regime for the trial duration. After baseline assessment, computer generated block random numbers (blocks of four) were used to randomly assign the participants to either the experimental group, which performed mirror-aided strength training (MST) (n=18) or the control group, which performed strength training only (ST) (n=17). Allocation concealment was implemented using numbered and sealed, opaque envelopes with aluminium foil inside. A third-party independent researcher conducted the entire balanced randomization (1:1) process.

4.2.2. Procedure

Rehabilitation professionals identified potential participants in their care. With patient's consent (Appendix J), contact information was given to the researcher and a study information sheet was sent out (Appendix K). Subjects who were interested in partaking, were then invited to the Institute of Technology Sligo for an eligibility screening (MMSE, inclusion and exclusion criteria). All participants provided written informed consent according to the Declaration of Helsinki (Appendix L). The same chartered physiotherapist, who was blinded to the treatment assignment, performed all assessments in the Institute of Technology Sligo Health Science & Physiology Laboratory. Baseline measurements (T1) were obtained within 7 days of intervention beginning, post-intervention assessment (T2) took place at least 48 hours, but no longer than 7 days, after the last training session, and follow-up measurements (T3) were obtained 3 months after T2. Laboratory conditions were consistent for all participants for all assessments.

4.2.3. Outcome Measures

Feasibility Outcome Measures

4 primary objectives to assess the feasibility of conducting the mirror-aided unilateral strength training protocol were investigated:

(1) To assess the recruitment process, steps taken to initiate or enhance recruitment as well as monthly recruitment rate were recorded.

(2) To examine participant compliance, training session and assessment attendance was recorded.

(3) To evaluate adverse effects, participants were asked ‘if they were aware of any changes’ before and after each training session.

(4) To assess the suitability of efficacy outcome measures the percentage of participants unable to complete each one was calculated.

Efficacy Outcome Measures

Outcome measures covered the three levels of the International Classification of Functioning, Disability and Health (ICF) (188). Each outcome measure is briefly described in the following section, more detailed information is provided in Appendix M. Values for Minimal Clinically Important Difference (MCID) and/ or Minimal Detectable Change (MDC) are included when available (189).

The level of function or impairment refers to any temporary or permanent loss or abnormality of a body structure or function (188, 190).

Following equipment familiarisation, **maximal voluntary isometric elbow extension strength** was assessed using the Biodex System 3 Pro Isokinetic Dynamometer with the Biodex Advantage Software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA). General set-up, testing protocol and data analysis followed the procedures outlined in Chapter 3. After a warm-up of 1 minute of dynamic elbow extensions without resistance, and 5 isometric elbow extensions performed at perceived 50% of maximal voluntary contraction, strength was assessed at 85° elbow flexion and 45° shoulder flexion (163, 164). Four maximal isometric contractions held for 5 seconds, separated by 45 seconds of rest were first measured for the LA side, followed by the MA side. Peak

Torque (PT), Rate of Torque Development (RTD), and Average Torque (AT) over a single contraction were analysed. If participants could not initiate the Biodex System 3 Isokinetic Dynamometer (threshold 3Nm), PT was defined as 2.99Nm. Thus, detection of positive change between assessments was possible without the likelihood of overestimation. However, assessment of RTD and AT was not possible for such participants. Excellent reliability for the applied protocol was established in Chapter 3. Values for MCID or MDC are not available for isometric elbow extension strength in stroke patients. However, a 19.5% improvement in hand grip strength has been reported as clinically significant after distal radius fracture (191).

Spasticity was measured with the gold standard Modified Ashworth Scale (MAS), which shows good to very good reliability (192, 193). Scores range from 0 – 4 with 6 choices, a higher score representing a more rigid limb (194). A change of one point reflects the MDC (195). MAS scores will be presented as a mean score of the muscles creating movement around the shoulder (flexion, extension, adduction, abduction), the elbow (flexion, extension) and the wrist (flexion, extension, ulnar deviation, radial deviation) joint.

The ICF **activity level** is subdivided into actual and self-perceived performance and refers to the ability to execute a task or action (190, 196).

The Chedoke Arm and Hand Activity Inventory – 8 Version (CAHAI - 8) was used to assess upper limb task execution capacity. This test was developed to address the need for a valid, clinically relevant, responsive functional assessment of the recovering paretic upper limb; it is in consistence with the ICF activity domain and World Health Organisation guidelines (197, 198). Eight items, defined according to literature and stroke patients' experience, are scored on a 7-point scale, 1 point standing for total assistance, 7 points standing for complete independence. Reliability was reported to be excellent, and MDC of 7% or 4 points was established (197, 199, 200).

The **ABILHAND** questionnaire measures a patient's self-reported ability to perform complex hand activities for 23 daily situations (201). The given answers (easy, difficult, or impossible) can be transformed into a percentage score, the higher the score, the higher the self-perceived task execution capacity. Reliability is again excellent, neither MCID nor MDC are reported for this outcome measure. However, the Standard Error of Measurement (SEM) is established at 15.2% and the Smallest Real Difference (SRD) at 42% (202, 203).

The **participation level** refers to the involvement in normal life situations and was assessed with **the London Handicap Scale (LHS)**. The questionnaire measuring self-perceived impact of stroke over 6 domains of a patient's life (mobility, physical independence, occupation, social integration, orientation, and economic self – sufficiency) showed favourable psychometric results (204, 205). No values for MCID or MDC are established.

4.2.4. Intervention

The intervention took place between November 2015 and May 2017. It comprised of a home-based training programme performed 3 times a week for 4 weeks (12 sessions) under constant supervision of two exercise therapists. Each training session latest approximately 20 min. For consistency, all participants were asked to remove jewellery, watches and other adornments to avoid visual or kinaesthetic distractions or inconsistencies between limbs. During the intervention, all participants sat comfortably in a chair in front of their own kitchen table. Participants in both groups performed the same unilateral maximal isometric strength-training programme, designed in line with a recent successful cross-education study in a stroke population (90) and maximal strength training guidelines (206, 207). Furthermore, isometric contractions are considered to be the safest form of strength training (151) and allow for a high level of comparability as range of movement is eliminated as an influencing factor.

To perform contractions, the participant's less-affected upper limb was strapped into an arm brace consistently holding the elbow joint at an 85° angle (163), the more-affected arm was resting on the table.

The warm-up consisted of 1 minute of dynamic elbow extensions without resistance, followed by 1 set of 5 repetitions of unilateral (less-affected side) isometric elbow extensions performed at perceived 50% of maximal voluntary contractions. The main part consisted of 4 sets of 5 maximal effort unilateral (less-affected side) isometric elbow extensions held for 5 seconds with 5 seconds rest between repetitions and 3 minutes rest between sets. Participants in the mirror-aided strength training group (MST) viewed a reflection of their less-affected limb in a Perspex mirror positioned in their mid-sagittal plane while strengthening (Image 1). The strength training only group (ST) exercised without a mirror entirely. Prompts to focus on the mirror reflection were given to the MST group only; other verbal cues were identical for all participants of both groups.

Figure 4.1: Participant Set-Up during each Training Session (MST group)

4.2.5. Statistical Analysis

Data were analysed using the Statistical Package for Social Sciences (SPSS) for Windows (Version X, Chicago, IL, USA). All variables were tested for conformity to normal distribution using a combination of the visual method (histograms) and the Shapiro-Wilk test (208). Possible differences between groups at baseline were analysed using the independent-t-test or Chi-square test. RTD, the CAHAI and the ABILHAND were log transformed to correct for nonnormally distributed data. The main analysis, used for examining the between group difference for each outcome measure was a group (MST, ST) x time (T1, T2, T3) two-way mixed ANOVA. Where appropriate, interaction effects were subjected to a Tukey HSD post hoc pairwise comparison. With-in group differences were analysed with the one-way repeated measures ANOVA. Where appropriate, paired-sample t-tests were used for post-hoc multiple comparisons. Partial eta squared (partial η^2) was calculated as measure of effect size. Cut-offs for partial η^2 are ≥ 0.01 (small), ≥ 0.06 (medium), and ≥ 0.14 (large) (209). Demographic characteristics and outcome variables of the groups are described as mean ± SD. For this pilot study p-values < 0.05 were considered to be statistically significant.

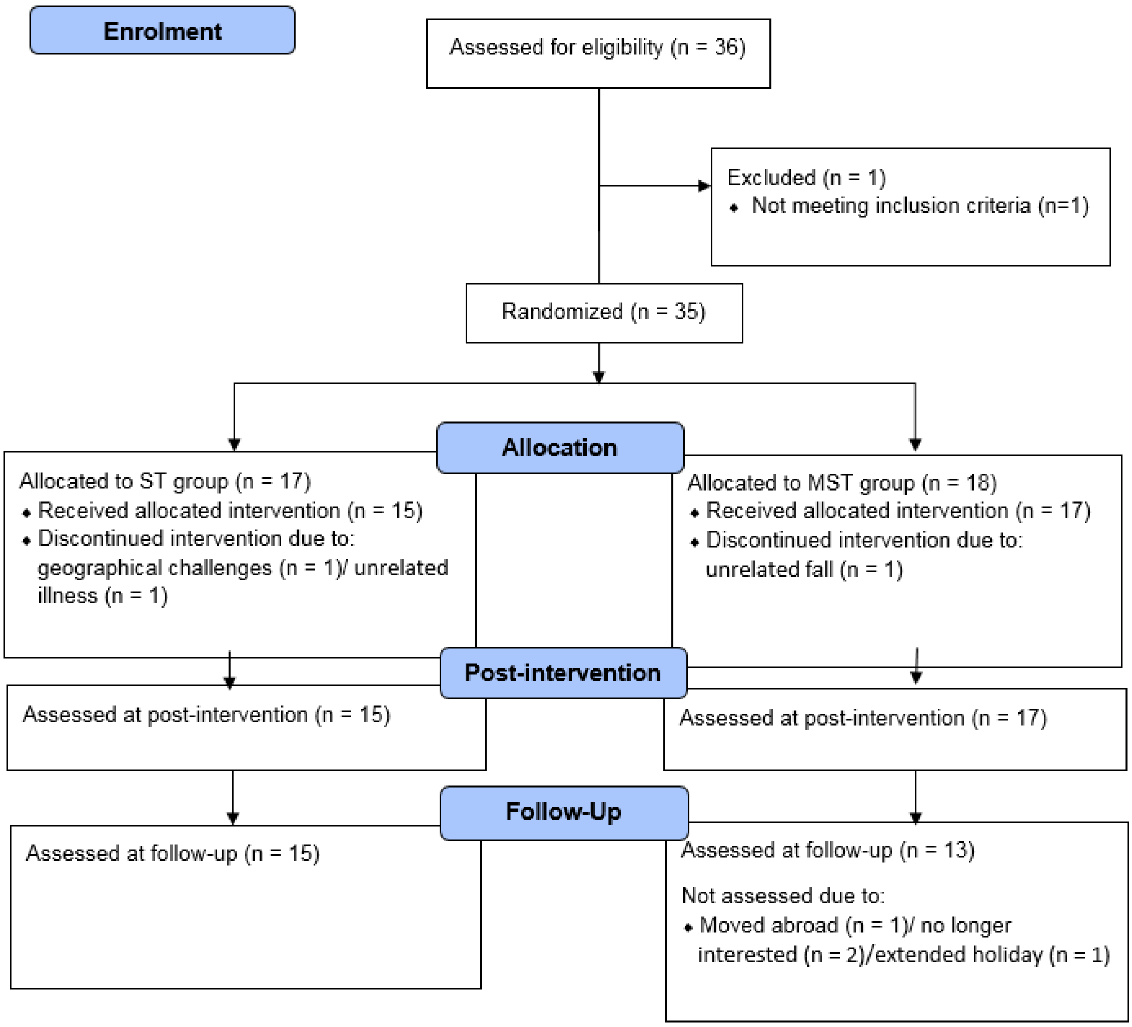

Figure 4.2: Flow Diagram of Study Process

4.3. Results

Out of the 36 referred participants, 35 were randomised into either the MST group (n=18) or the ST group (n=17). Thirty-two participants (mean age 62 ± 14 years, mean time after stroke of 82 ± 78months) completed the intervention, 28 participants attended follow-up assessments (Image 4.2). At baseline, there were no statistically significant differences between groups for all demographical characteristics (Table 4.1).

Table 4.1: Demographic Characteristics of Participants at Baseline Mean ± SD (Range)

Characteristic	ST Group T1	MST Group T1	ST vs MST differences p-value
Sex, male : female	11 : 4	10 : 7	0.62
Age in years	64 ± 12 (36 - 80)	61 ± 15 (32 - 90)	0.62
Type of stroke, Ischemic : haemorrhagic	9 : 6	12 : 5	0.80
Time since stroke in months	90 ± 83 (16 - 276)	75 ± 75 (6 - 207)	0.59
MA side, Right : Left	8 : 7	7 : 10	0.74
Trained side, dominant : non-dominant	7 : 8	9 : 8	1.00

ST = Strength Training Only group, MST = Mirror and Strength Training group, T1 = baseline assessment

4.3.1. Feasibility Outcome Measures

(1) Recruitment process:

Steps taken to initiate/ enhance recruitment: (a) An information letter with the request to refer patients was sent to rehabilitation professionals in Sligo and South Donegal in September 2015, (b) a presentation outlining the pilot study and provisional results was given in Sligo University Hospital Physiotherapy Department and St. John's Community Hospital in March 2016, (c) an article describing the study was published in the Sligo Champion local newspaper in January 2017. Please refer to table 4.2 for recruitment rate per month.

Table 4.2: Recruitment rate per month

	2015			2016					
Month	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun
Number of participants	3 8%	2 6%	1 3%	0 0%	1 3%	8 22%	5 14%	3 8%	1 3%

	2016						2017		
Month	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar
Number of participants	0 0%	1 3%	0 0%	0 0%	1 3%	0 0%	0 0%	8 22%	2 6%

(2) Participant compliance: Out of the 32 participants who completed the intervention and whose data was included in the results analysis, 23 participants (72%) attended all 12 training sessions, eight participants (25%) attended 11 sessions, while one participant (3%) attended 10 sessions. Non-attendance for participants was due to ill health unrelated to the intervention.

3 out of the 35 randomised participants (9%) dropped out from pre- to post-intervention. Again, unrelated to the intervention, one participant suffered a fall, another participant reported an illness. The third participant lived 55km away, with bad weather conditions the travelling exercise therapists decided to cease treatment. A further 4 participants dropped out from post-assessment to follow-up assessment, raising the overall dropout rate to 20%. Two participants expressed to have lost interest, 1 participant moved abroad, and one participant was on an extended holiday.

(3) Adverse effects: No adverse event occurred.

(4) Suitability of efficacy outcome measures: 5 out of the 35 randomised participants (14%) were unable to complete the maximal isometric strength assessment. Reasons for non-completion were (a) anxiety using the Biodex Dynamometer (n=2), (b) inability to initiate the Biodex Dynamometer (n=1), (c) inability to analyse data due to early contractions (n=1), (d) fall prior to post assessment (n=1). One participant (3%) refused to complete the CAHAI and the ABILHAND questionnaire, the participant felt uncomfortable to carry out both outcome measures. All participants completed the MAS and the LHS.

4.3.2. Efficacy Outcome Measures

All results as well as the number of participants included for analysis for each outcome measure are displayed in table 4.3. Data for certain outcome measures was unavailable due to the reasons stated in 4.3.1. Furthermore, when analysing results with the ANOVA design, only data of participants completing all three assessment is included for analysis.

Trained Side: Peak Torque (PT)

The two groups did not differ in PT at baseline ($t_{(28)}$ = -0.296, p = 0.769). There was no statistically significant interaction between intervention and time on PT of the trained limb ($F_{(1.4, 33.7)}$ = 2.257, p =0.134, partial η^2 = 0.086). The main effect of time showed no statistically significant difference in mean PT of the trained side at the different time points, ($F_{(1.4, 33.7)}$ = 0.098, p = 0.838, partial η^2 = 0.004). The main effect of group showed no statistically significant difference in mean PT of the trained side between intervention groups ($F_{(1, 24)}$ = 0.722, p = 0.404, partial η^2 = 0.029).

The mirror-aided unilateral strength training intervention did not elicit statistically significant changes in PT in the trained limb over time ($F_{(1.3, 13.9)} = 0.869$, $p = 0.393$, partial $\eta^2 = 0.073$).

The unilateral strength training intervention did not lead to statistically significant changes in PT in the trained limb over time ($F_{(2, 26)} = 1.557$, $p = 0.230$, partial $\eta^2 = 0.107$).

Trained Side: Rate of Torque Development (RTD)

The two groups did not differ in RTD at baseline ($t_{(27)} = -0.842$, $p = 0.407$). There was no statistically significant interaction between the intervention and time on RTD of the trained limb ($F_{(2, 46)} = 1.222$, $p = 0.304$, partial $\eta^2 = 0.050$). The main effect of time showed no statistically significant difference in mean RTD of the trained side at the different time points ($F_{(2, 46)} = 0.519$, $p = 0.599$, partial $\eta^2 = 0.022$). The main effect of group showed no statistically significant difference in mean RTD of the trained side between intervention groups ($F_{(1, 23)} = 1.597$, $p = 0.219$, partial $\eta^2 = 0.065$).

The mirror-aided unilateral strength training intervention did not elicit statistically significant changes in RTD in the trained limb over time ($F_{(2, 22)} = 0.228$, $p = 0.798$, partial $\eta^2 = 0.02$).

The unilateral strength training intervention did not lead to statistically significant changes in RTD in the trained limb over time ($F_{(2, 24)} = 1.415$, $p = 0.263$, partial $\eta^2 = 0.105$).

Trained Side: Average Torque (AT)

The two groups did not differ in AT at baseline ($t_{(27)} = -0.565$, $p = 0.577$). There was no statistically significant interaction between the intervention and time on AT of the untrained limb ($F_{(1.5, 33.8)} = 2.078$, $p = 0.152$, partial $\eta^2 = 0.083$). The main effect of time did not show statistically significant difference in mean AT of the trained side at the different time points ($F_{(1.5, 33.8)}$ = 0.846, p = 0.406, partial η^2 = 0.035). The main effect of group showed no statistically significant difference in mean AT of the trained side between intervention groups ($F_{(1, 23)}$ = 1.044, p = 0.317, partial η^2 = 0.043).

The mirror-aided unilateral strength training intervention did not elicit statistically significant changes in AT in the trained limb over time ($F_{(1.3, 14.6)}$ = 0.473, p = 0.555, partial η^2 = 0.041).

The unilateral strength training intervention did not lead to statistically significant changes in AT in the trained limb over time ($F_{(2, 24)}$ = 2.838, p = 0.078, partial η^2 = 0.191).

Untrained Side: Peak Torque (PT)

The two groups did not differ in PT at baseline ($t_{(28)}$ = -0.098, p = 0.922). There was no statistically significant interaction between the intervention and time on PT of the untrained limb ($F_{(2, 50)}$ = 2.83, p =0.068, partial η^2 = 0.102). The main effect of time showed no statistically significant difference in mean PT of the untrained side at the different time points ($F_{(2, 50)}$ = 2.550, p = 0.088, partial η^2 = 0.093). The main effect of group showed no statistically significant difference in mean PT of the untrained side between intervention groups ($F_{(1, 25)}$ = 0.073, p = 0.790, partial η^2 = 0.003).

The mirror-aided unilateral strength training intervention elicited statistically significant changes in PT in the untrained limb over time ($F_{(2, 24)}$ = 3.613, p = 0.042, partial η^2 = 0.231). Post hoc analysis revealed that PT was significantly increased from baseline to post-intervention assessment by 16.2% (3.9 (95% CI, 0.5 to 7.4) Nm, p = 0.03)

The unilateral strength training intervention did not lead to statistically significant changes in PT in the untrained limb over time ($F_{(2, 26)} = 1.09$, $p = 0.350$, partial $\eta^2 = 0.08$).

Untrained Side: Rate of Torque Development (RTD)

The two groups did not differ in RTD at baseline ($t_{(27)} = -1.252$, $p = 0.221$). There was no statistically significant interaction between the intervention and time on RTD of the untrained limb ($F_{(2, 48)} = 0.565$, $p = 0.572$, partial $\eta^2 = 0.023$). The main effect of time showed no statistically significant difference in mean RTD of the untrained side at the different time points ($F_{(2, 48)} = 0.251$, $p = 0.779$, partial $\eta^2 = 0.010$). The main effect of group showed no statistically significant difference in mean RTD of the untrained side between intervention groups ($F_{(1, 24)} = 0.724$, $p = 0.403$, partial $\eta^2 = 0.029$).

The mirror-aided unilateral strength training intervention did not elicit statistically significant changes in RTD in the untrained limb over time ($F_{(1.3, 15.3)} = 0.835$, $p = 0.403$, partial $\eta^2 = 0.065$).

The unilateral strength training intervention did not lead to statistically significant changes in RTD in the untrained limb over time ($F_{(2, 24)} = 0.038$, $p = 0.963$, partial $\eta^2 = 0.003$).

Untrained Side: Average Torque (AT)

The two groups did not differ in AT at baseline ($t_{(27)} = -0.147$, $p = 0.885$). There was no statistically significant interaction between the intervention and time on AT of the untrained limb ($F_{(2, 48)} = 2.903$, $p = 0.065$, partial $\eta^2 = 0.108$). The main effect of time showed statistically significant difference in mean AT of the untrained side at the different time points ($F_{(2, 48)} = 3.403$, $p = 0.041$, partial $\eta^2 = 0.124$). AT of the untrained side increased across groups by 9.6% from T1 to T2 (2 (95% CI, 0.1 to 3.9) Nm, $p = 0.039$)

from T1 to T3 (2.1 (95% CI, 0.3 to 3.9) Nm, $p = 0.028$). The main effect of group showed no statistically significant difference in mean AT of the untrained side between intervention groups ($F_{(1, 24)} = 0.002$, $p = 0.961$, partial $\eta^2 = 0.000$).

The mirror-aided unilateral strength training intervention elicited statistically significant changes in AT in the untrained limb over time ($F_{(2, 24)} = 4.030$, $p = 0.031$, partial $\eta^2 = 0.252$). Post hoc analysis revealed that AT was significantly increased from baseline to post-intervention assessment by 18.7% (3.9 (95% CI, 0.7 to 7.0) Nm, $p = 0.020$).

The unilateral strength training intervention did not lead to statistically significant changes in AT in the untrained limb over time ($F_{(2, 24)} = 1.937$, $p = 0.166$, partial $\eta^2 = 0.139$).

Modified Ashworth Scale (MAS)

The two groups did not differ in MAS score for the muscles surrounding the shoulder joint (sMAS) at baseline ($t_{(30)} = -0.605$, $p = 0.550$). There was no statistically significant interaction between the intervention and time on sMAS ($F_{(2, 52)} = 0.106$, $p = 0.900$, partial $\eta^2 = 0.004$). The main effect of time showed statistically significant difference in mean sMAS at the different time points ($F_{(2, 52)} = 24.127$, $p < 0.001$, partial $\eta^2 = 0.481$). sMAS reduced across groups from T1 to T2 by 0.6 MAS points (95% CI, 0.5 to 0.8, $p < 0.001$) and from T1 to T3 by 0.5 MAS points (95% CI, 0.3 to 0.7, $p < 0.001$). The main effect of group showed no statistically significant difference in mean sMAS between intervention groups ($F_{(1, 26)} = 0.350$, $p = 0.559$, partial $\eta^2 = 0.013$).

The mirror-aided unilateral strength training intervention elicited statistically significant changes in sMAS over time ($F_{(2, 24)} = 12.017$, $p < 0.001$, partial $\eta^2 = 0.500$). Post hoc analysis revealed that sMAS was significantly decreased by 0.6 MAS points (95% CI, 0.3

to 0.9, p = 0.001) from baseline to post-intervention assessment and by 0.5 MAS points (95% CI, 0.3 to 0.8, p = 0.001) from baseline to follow-up assessment.

The unilateral strength training intervention also lead to statistically significant changes in sMAS over time ($F_{(2, 28)} = 12.600$, $p < 0.001$, partial $\eta^2 = 0.474$). Post hoc analysis revealed that sMAS was significantly decreased by 0.7 MAS points (95% CI, 0.5 to 0.9, p < 0.001) from baseline to post-intervention assessment and by 0.5 MAS points (95% CI, 0.2 to 0.9, p = 0.006) from baseline to follow-up assessment.

The two groups did not differ in MAS score for the muscles surrounding the elbow joint (eMAS) at baseline ($t_{(30)} = -0.786$, $p = 0.438$). There was no statistically significant interaction between the intervention and time on eMAS ($F_{(2, 52)} = 0.363$, $p = 0.697$, partial $\eta^2 = 0.014$). The main effect of time showed statistically significant difference in mean eMAS at the different time points ($F_{(2, 52)} = 31.714$, $p < 0.001$, partial $\eta^2 = 0.550$). eMAS reduced across groups from T1 to T2 by 0.8 MAS points (95% CI, 0.6 to 0.9, $p < 0.001$) and from T1 to T3 by 0.6 MAS points (95% CI, 0.4 to 0.8, $p < 0.001$). The main effect of group showed no statistically significant difference in mean wMAS between intervention groups ($F_{(1, 26)} = 0.747$, $p = 0.395$, partial $\eta^2 = 0.028$).

The mirror-aided unilateral strength training intervention elicited statistically significant changes in eMAS over time ($F_{(2, 24)} = 21.698$, $p < 0.001$, partial $\eta^2 = 0.644$). Post hoc analysis revealed that eMAS was significantly decreased by 0.8 MAS points (95% CI, 0.5 to 1.0, p < 0.001) from baseline to post-intervention assessment and by 0.5 MAS points (95% CI, 0.3 to 0.8, p<0.001) from baseline to follow-up assessment.

The unilateral strength training intervention also lead to statistically significant changes in eMAS over time ($F_{(2, 28)} = 14.246$, $p < 0.001$, partial $\eta^2 = 0.504$). Post hoc analysis revealed that wMAS was significantly decreased by 0.8 MAS points (95% CI, 0.5 to 1.0, $p < 0.001$) from baseline to post-intervention assessment and by 0.7 MAS points (95% CI, 0.3 to 1.1, $p = 0.002$) from baseline to follow-up assessment.

The two groups did not differ in MAS score for the muscles surrounding the wrist joint (wMAS) at baseline ($t_{(30)} = -0.384$, $p = 0.704$). There was no statistically significant interaction between the intervention and time on wMAS ($F_{(2, 52)} = 0.158$, $p = 0.855$, partial $\eta^2 = 0.006$). The main effect of time showed statistically significant difference in mean wMAS at the different time points ($F_{(2, 52)} = 43.215$, $p < 0.001$, partial $\eta^2 = 0.624$). wMAS reduced across groups from T1 to T2 by 0.8 MAS points (95% CI, 0.6 to 0.9, $p < 0.001$) and from T1 to T3 by 0.6 MAS points (95% CI, 0.4 to 0.8, $p < 0.001$). The main effect of group showed no statistically significant difference in mean wMAS between intervention groups ($F_{(1, 26)} = 0.096$, $p = 0.759$, partial $\eta^2 = 0.004$).

The mirror-aided unilateral strength training intervention elicited statistically significant changes in wMAS over time ($F_{(2, 24)} = 22.776$, $p < 0.001$, partial $\eta^2 = 0.655$). Post hoc analysis revealed that wMAS was significantly decreased by 0.7 MAS points (95% CI, 0.4 to 1.0, $p < 0.001$) from baseline to post-intervention assessment and by 0.6 MAS points (95% CI, 0.3 to 0.9, $p<0.001$) from baseline to follow-up assessment.

The unilateral strength training intervention also lead to statistically significant changes in wMAS over time ($F_{(2, 28)} = 22.039$, $p < 0.001$, partial $\eta^2 = 0.612$). Post hoc analysis revealed that wMAS was significantly decreased by 0.8 MAS points (95% CI, 0.6 to 1.0, $p < 0.001$) from baseline to post-intervention assessment and by 0.7 MAS points (95% CI, 0.3 to 1.0, $p = 0.001$) from baseline to follow-up assessment.

Chedoke Arm and Hand Activity Inventory (CAHAI)

The two groups did not differ in CAHAI score at baseline ($t_{(29)} = 0.033$, $p = 0.974$). There was no statistically significant interaction between the intervention and time on the CAHAI score ($F_{(1.3,\ 31.7)} = 0.263$, $p = 0.667$, partial $\eta^2 = 0.010$). The main effect of time showed statistically significant difference in mean CAHAI score at the different time points ($F_{(1.3,\ 31.7)} = 4.371$, $p = 0.036$, partial $\eta^2 = 0.149$). CAHAI score increased across groups from T1 to T2 by 7% (2.4 (95% CI, 1.2 to 3.7) points, $p = 0.001$). The main effect of group showed no statistically significant difference in mean CAHAI score between intervention groups ($F_{(1,\ 25)} = 0.001$, $p = 0.981$, partial $\eta^2 = 0.000$).

The mirror-aided unilateral strength training intervention did not elicit statistically significant changes in CAHAI scores over time ($F_{(2,\ 24)} = 1.388$, $p = 0.269$, partial $\eta^2 = 0.104$).

The unilateral strength training intervention did not lead to statistically significant changes in CAHAI scores over time ($F_{(2,\ 26)} = 2.589$, $p = 0.094$, partial $\eta^2 = 0.166$).

ABILHAND Questionnaire

The two groups did not differ in ABILHAND score at baseline ($t_{(29)} = 0.300$, $p = 0.766$). There was no statistically significant interaction between the intervention and time on the ABILHAND score ($F_{(1.6,\ 39.9)} = 0.302$, $p = 0.691$, partial $\eta^2 = 0.012$). The main effect of time showed no statistically significant difference in mean ABILHAND score at the different time points ($F_{(1.6,\ 39.9)} = 0.531$, $p = 0.552$, partial $\eta^2 = 0.021$). The main effect of group showed no statistically significant difference in mean ABILHAND score between intervention groups ($F_{(1,\ 25)} = 0.290$, $p = 0.595$, partial $\eta^2 = 0.011$).

The mirror-aided unilateral strength training intervention did not elicit statistically significant changes in ABILHAND scores over time ($F_{(2, 24)} = 0.160$, $p = 0.853$, partial $\eta^2 = 0.013$).

The unilateral strength training intervention did not lead to statistically significant changes in ABILHAND scores over time ($F_{(2, 26)} = 0.337$, $p = 0.717$, partial $\eta^2 = 0.025$).

London Handicap Scale (LHS)

The two groups did not differ in LHS score at baseline ($t_{(30)} = -1.141$, $p = 0.263$). There was no statistically significant interaction between the intervention and time on the LHS score ($F_{(2, 52)} = 0.319$, $p = 0.728$, partial $\eta^2 = 0.012$). The main effect of time showed no statistically significant difference in mean LHS score at the different time points, ($F_{(2, 52)} = 0.975$, $p = 0.384$, partial $\eta^2 = 0.036$). The main effect of group showed no statistically significant difference in mean LHS score between intervention groups ($F_{(1, 26)} = 0.226$, $p = 0.639$, partial $\eta^2 = 0.009$).

The mirror-aided unilateral strength training intervention did not elicit statistically significant changes in LHS scores over time ($F_{(2, 24)} = 2.093$, $p = 0.154$, partial $\eta^2 = 0.149$).

The unilateral strength training intervention did not lead to statistically significant changes in LHS scores over time ($F_{(2, 28)} = 0.085$, $p = 0.918$, partial $\eta^2 = 0.006$).

According to Sakpal (210) the following sample size calculation was performed with a 30% allowance for participant drop-out:

n = $[(Z_{\alpha/2} + Z_{\beta})^2 \times \{2(ó^2)\}] / (\mu 1 - \mu 2)^2$, where

n = sample size required in each group

$\mu 1$ = mean change in AT of the untrained side from baseline to post-intervention for mirror-aided cross-education 3.5 ± 5.0 Nm (n=16) (treatment A)

$\mu 2$ = mean change in AT of the untrained side from baseline to post-intervention for cross-education only 0.1 ± 4.0 Nm (n=13) (treatment B)

$\mu 1$-$\mu 2$ = clinically significant difference

ó = standard deviation treatment A

$Z_{\alpha/2}$: This depends on level of significance, for α = 5% this is 1.96

Z_{β}: This depends on power, for 80% this is 0.84

n = 34 participants per treatment arm

n adjusted for 30% drop-out rate = **45 participants in each treatment arm**.

Table 4.3: Results for each Outcome Measure in Mean ± SD

Outcome Measure	Treatment Group	Number of Participants included in Analysis	T1	T2	T3
Trained side PT in Nm	MST	12	38.4 ± 17.3	36.4 ± 16.6	35.5 ± 13.8
	ST	14	39.9 ± 12.3	43.0 ± 18.0	42.7 ± 16.2
Trained side RTD in Nm/s	MST	12	52.3 ± 41.6	54.1 ± 36.3	47.9 ± 29.3
	ST	13	62.8 ± 41.4	73.0 ± 58.4	80.5 ± 57.7
Trained side AT in Nm	MST	12	31.6 ± 13.3	31.4 ± 14.5	30.0 ± 11.5
	ST	13	34.1 ± 11.4	37.3 ± 14.6	37.2 ± 13.4
Untrained side PT in Nm	MST	13	24.1 ± 17.9	28.0 ± 19.9*	26.2 ± 19.6
	ST	14	24.0 ± 13.9	23.8 ± 14.4	25.4 ± 16.0
Untrained side RTD in Nm/s	MST	13	33.1 ± 38.8	39.5 ± 41.9	31.8 ± 31.6
	ST	13	46.4 ± 30.3	45.6 ± 40.2	47.5 ± 42.0
Untrained side AT in Nm	MST	13	20.3 ± 15.2	24.1 ± 17.0*	22.4 ± 17.1
	ST	13	21.3 ± 11.3	21.4 ± 12.0 ǂ	23.3 ± 14.0 ǂ
MAS shoulder	MST	13	1.8 ± 0.9	1.2 ± 0.9*	1.3 ± 0.8*
	ST	15	2.0 ± 0.5	1.3 ± 0.6 ǂ *	1.4 ± 0.6 ǂ *
MAS elbow	MST	13	1.4 ± 0.6	0.7 ± 0.6*	0.9 ± 0.8*
	ST	15	1.7 ± 0.6	0.9 ± 0.8 ǂ *	1.0 ± 0.6 ǂ *
MAS wrist	MST	13	1.4 ± 0.8	0.7 ± 0.7*	0.8 ± 0.7*
	ST	15	1.5 ± 0.4	0.7 ± 0.6 ǂ *	0.8 ± 0.6 ǂ *
CAHAI	MST	13	34.8 ± 21.8	37.5 ± 23.0	35.2 ± 22.2
	ST	14	34.6 ± 21.9	36.7 ± 21.5	35.6 ± 21.3
ABILHAND	MST	13	62.0 ± 15.5	62.8 ± 12.2	62.0 ± 14.6
	ST	14	57.2 ± 13.8	59.8 ± 19.6	59.9 ± 22.2
LHS	MST	13	0.5 ± 0.2	0.5 ± 0.2	0.5 ± 0,2
	ST	15	0.5 ± 0.2	0.5 ± 0.3	0.5 ± 0.3

T1 baseline assessment, T2 post-intervention assessment, T3 follow-up assessment, PT peak torque, RTD rate of torque development, AT average torque, MAS modified ashworth scale, CAHAI chedoke arm and hand activity inventory, LHS london handicap scale, MST mirror and strength training group, ST strength training only group, ǂ significantly ($p<0.05$) different to T1 across groups, * significantly ($p<0.05$) different to T1 within group

4.4. Discussion

This is the first study investigating the feasibility and potential efficacy of unilateral strength training combined with mirror therapy compared to unilateral strength training only on upper-limb motor recovery in a chronic stroke population. According to the definition of pilot trials (211), insightful information regarding important componence of a definite RCT could be provided. Furthermore, authors established that mirror therapy did not augment the cross-education effect in chronic stroke patients when training isometrically. However, considering the small sample size, the borderline between group significant difference for AT ($p = 0.065$) combined with the large effect size (partial $\eta^2 = 0.124$) may still indicate potential benefits of the combination therapy (212), warranting further investigation.

4.4.1. Feasibility results

The participant recruitment rate consistently increased after active communication with rehabilitation professionals or the general public indicating that repeated interactions with involved parties must be scheduled to ensure sufficient participant referrals. According to Crosbie et al. (213), non-compliance is defined as receipt of less than 66.6% of planned training sessions. With all participants completing 83 – 100% of training sessions, this pilot trial can be classed as feasible regarding compliance. Furthermore the drop-out rate of 9% from baseline to post-intervention assessment was below the stipulated 15% for low risk of bias (136). However, at follow-up assessment the dropout rate was above this threshold (20%). This should be considered when calculating the sample size for a fully powered trial. Both interventions proved safe in this sample of chronic stroke patients. Alt Murphy et al. (203) states that there are no clear recommendations regarding the most suitable upper extremity outcome measures after stroke to date. All outcome measures in this trial were carefully chosen according to topical and current literature (148, 198, 203, 204). Isokinetic dynamometry is the gold standard for assessing muscular functionality among athletic populations as well as populations engaging in rehabilitation programmes (148). The mechanical reliability of the Biodex System 3 (Biodex Medical Systems, Inc., Shirley, New York, USA) (150) as well as the protocol reliability (Chapter 3) and reliability of dynamic elbow strength measurements in patients after stroke are excellent (164). Furthermore, the Biodex Advantage Software version 3.45 allows for comprehensive analysis of several strength parameters. However, use and set-up of the Biodex System 3 for moderate to severely disabled participants proved challenging. Most participants needed manual assistance when transferring into the Biodex seat. The lowest setting for chair height is still too high for impaired users, denying easy access. To initiate the Biodex System 3, limb weight plus a threshold of 3 Nm has to be overcome. Due to the clinical population, it was decided not to weigh the limb during set-up, thus less strength is needed to initiate measurements. Five out of the 35 participants were unable to complete the maximal isometric strength assessment. A less intimidating portable dynamometer with lower initiation threshold could be an alternative. However, the assessment of RTD and AT, which are important parameters when evaluating the rehabilitation process (155, 158), would not be possible. Thus, the use of isokinetic dynamometry for detailed evaluation of muscle performance is advisable. The ability and willingness to use the Biodex System 3 for bilateral strength assessment may therefore be a valuable extension to inclusion criteria for the fully powered trial. Minimal detectable change (MDC) and/or minimal clinically important difference (MCID) should also be estimated in future research to allow for a higher degree of interpretation of results.

The Modified Ashworth Scale (MAS) is widely used as current clinical standard (198) and it was chosen for this study to allow for comparability with other research (90, 214). However, it has been questioned if the MAS is a valid measure of spasticity (198) and if it can distinguish between stretch reflex hyperexcitability and spastic paresis (215). The MAS may be a combined measure of stiffness rather than spasticity alone (36). All participants in this pilot trial completed the MAS assessment.

According to a recent literature review (203) four activity task execution capacity outcome measures demonstrate high levels of measurement quality and clinical utility and are therefore recommended for the evaluation of upper extremity function post stroke: Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Box and Block Test (BBT), and the Chedoke Arm and Hand Activity Inventory (CAHAI). The ARAT was not chosen due to existing significant floor and ceiling effects, it is not sensitive enough for patients with severe impairments or near normal function. Furthermore, an extensive collection of items and a specialized table are required, which has to be built or purchased (198, 216). The WMFT can take up to 45min to administer, most information regarding reliability and validity has been based on ratings of videotaped testing sessions rather than direct observation (198, 217). The BBT is a performance-based measure of gross manual dexterity only, it does not provide assessment of a range of different tasks (198). Items of the CAHAI have been specifically selected to be meaningful and relevant to the stroke population and comply with World Health Organization (WHO) guidelines. This test covers a wide range of functions including normative upper limb movements of manipulation, reach and grasp, non-gender-specific tasks, and bilateral tasks (197). Only easily obtained cheap equipment is needed and the 8-task long version applied in this study was completed within 10-15 minutes (197-200). There may be a floor effect and sensitivity issue when testing highly impaired participants, however this has never been statistically investigated. Ten of the 32 participants scored the lowest possible score of 8 points at baseline assessment and only 4 out of the 10 showed a change thereafter. The CAHAI may not allow assessment of highly impaired patients' actual level of ability and minimal improvements. However, this test could be completed by all but one participant, was specifically designed for stroke patients, equipment consists of everyday items, it is short in duration and proved easy to follow, and thus it is advisable to continue to use the CAHAI in the fully powered trial.

The ABILHAND questionnaire (201) was deemed the only assessment tool for perceived task execution capacity demonstrating high levels of psychometrics and clinical utility (203). Rating the 23 upper limb tasks took from 3 to 15 minutes and could be completed by all but one participant.

The Stroke Impact Scale (SIS) was reported to be the most used post stroke participation assessment tool, followed by the London Handicap Scale (LHS) (204). However, the SIS only met 1 out of 4 psychometric criteria (internal consistency, test-retest reliability, content validity, and construct validity), the LHS complied with 3 and was therefore chosen for this feasibility trial (204). The questionnaire could be completed by all participants.

In summary, a fully powered randomised controlled trial is considered feasible regarding all tested aspects. Repeated, planned interactions with referring rehabilitation professionals is advised and inclusion criteria might need to be adjusted to ensure the appropriate use of the Biodex System 3 Isokinetic Dynamometer to assess muscle performance. Alternatively, the use of a handheld dynamometer may be considered. Future research should also identify MDCs and MCIDs for all included outcome measures to allow for comprehensive interpretation of results.

4.4.2. Efficacy results

As previously stated no significant between group results were found when the sample of chronic stroke patients trained isometrically. Although within group results do not represent a high standard of evidence (140) and can reflect placebo effects (218), considering this is the first trial comparing mirror-aided cross-education with cross-education only in a stroke population, they may add valuable information and contribute to a comprehensive understanding.

High intensity unilateral strength training leads to increased activation in the untrained primary motor cortex (M1) (43, 67, 73), as well as increased excitability in the untrained motor pathway (20, 42, 76, 83), ultimately resulting in enhanced and potentially more efficient motor drive to the untrained side (66-68). Similarly, training limb observation in a mirror modifies corticospinal activity of the untrained side via three perceptuo-motor networks (17, 38, 103, 119, 120, 123). Elements of primary and secondary visual and somatosensory cortical areas associated with attention are involved; parts of the MNS and the untrained motor network are activated. Furthermore, mirror observation allows for congruence between visual feedback and motor command, enhancing motor control and recovery (40, 108).

When combining both therapies, corticospinal net excitation in the untrained corticospinal pathway may be potentiated and additional cortical areas may be activated, resulting in increased neural input to the untrained hemisphere compared to unilateral strength training alone (17, 18, 20). The reoccurring activation may contribute to neural reorganisation in stroke patients (37), thus mirror therapy could augment strength transfer and functional recovery in the untrained limb (17, 18, 20, 66).

Pre- to post-intervention strength improvements in the untrained arm of the MST group equated to 16.2% (p=0.03) for PT and 18.7% (p=0.02) for AT. The only other study, comparing cross-education with and without a mirror in a healthy population, found a significant between group difference for strength gain (PT) in the untrained limb in favour of their MST group (20). After 3 weeks (15 sessions) of unilateral, dynamic wrist flexor training (80% MVC) with mirror visual feedback, the magnitude of strength gain (PT) in the untrained limb was 4 times greater (61%) than the improvement achieved in this pilot trial. The strength training intervention in this study comprised of isometric contractions, which previously proved effective and safe in stroke populations (90, 219); however dynamic strength training may have been more effective. Zult et al. (19) established that short interval intracortical inhibition (SICI) in the ipsilateral M1 reduced only when a slowly contracting hand was viewed in a mirror; no change was observed under non-mirror condition. In line with these findings, Reissig et al. (220) showed that mirror viewing of isometric index finger abductions did not change ipsilateral SICI compared with the no vision condition. Thus, it seems only reflections of moving limbs modulate SICI and may therefore augment cross-education effects. Furthermore, effective motor control and motor learning depend on constant integration of sensory responses, whereby predicted sensory consequences of motor commands are compared with actual sensory feedback (107-109). Conditions such as stroke can cause incongruence of efferent and afferent signals, possibly leading to learned paralysis (40). Due to the dominance of vision over proprioception (110) mirror therapy may be able to restore the interrupted efference - afference loop and allow for rehabilitation (40, 111, 112). However, visual feedback from a static contraction may not be as effective as dynamic movement observation. The position of the untrained limb behind the mirror should also be considered. Fourkas et al. (221) showed larger facilitation of Motor Evoked Potentials when the real-life position of the hand was identical with the movement participants were instructed to imagine. To avoid discomfort, positioning of the untrained arm in this study did not exactly match the position of the training limb which may have compromised benefits of the mirror visual feedback (17).

Contrary to similar studies implementing maximal isometric unilateral strength training without a mirror in a stroke population did find (90, 219), this pilot trial did not result in significant pre- to post- intervention strength improvements in the trained arm of either group, or in the untrained arm of the ST group. Dragert and Zehr (90) found strength improvements (PT) of 34% ($p=0.02$) and 31% ($p=0.009$) in the trained and untrained ankle dorsiflexor after a 6-week (18 sessions) training programme. Likewise, Sun et al. (219) reported a 42% ($F_{(1,23)} = 5.603$, $p = 0.027$) and 35% ($F_{(1,23)} = 4.510$, $p = 0.045$) strength gain in the trained and untrained wrist flexor after a 5-week (15 sessions) training programme. The difference in the number of training sessions seems to be one obvious reason for lower strength gains in this pilot trial. However, a recent meta-analysis investigating cross-education in a healthy population established no significant correlation between the total number of contractions and strength gains in the trained (r=0.19) and untrained (r=0.11) limb (54). In contrast, patients with multiple sclerosis did not show significant strength transfer after the first 3 weeks of unilateral dorsiflexion training, but an improvement of 37.9% of initial untrained limb strength was elicited ($p<0.05$) after 6 weeks (134). The chronicity of participants may also influence results. However, time post stroke in this pilot trial was comparable with the study by Dragert and Zehr (90) who saw much larger strength gains with a similar training protocol. Authors (90) concluded that the findings indicate the ability to induce improvements well beyond typical post-stroke rehabilitation timelines. Chosen training stimuli such as intensity has been shown to affect the trained and untrained muscle in a highly specific manner (51, 222). Although participants were instructed to contract maximally in this pilot trial, contrary to Sun et al. (219) training intensity was not measured. It is possible that participants performed contractions well below the requested maximum effort. Thus, if participants in this study did not train close to maximal intensity, post-intervention strength of the trained limb cannot be expected to be significantly altered. Similarly, Fimland et al. (51) concludes that training intensities of > 85% MVC result in greater cross-education effects. Importantly, despite the possible lower training intensity a significant strength improvement in the untrained side of the MST group could be noted. Mirror visual feedback may reduce the threshold for cross-education; hence, strength transfer may be facilitated at a lower training intensity, which may be helpful in post-stroke rehabilitation to avoid unnecessary fatigue.

A high intensity, dynamic strength-training programme of longer duration and congruent positioning of both limbs may have significantly augmented strength outcomes.

As described in Chapter 3, the three most important strength parameters (PT, RTD, AT) were included in this pilot study to ensure comprehensive muscle function assessment. PT, representing maximum strength produced at a single point of contraction (223) and RTD, explosive muscle strength defined as the rate of rise in contractile torque at the onset of a muscle contraction (178, 179), are frequently used during strength assessment in athletes or clinical populations (159, 224-226). To the authors' knowledge, this is the first study to include AT over a single contraction, measuring the ability to maintain torque throughout the contraction time interval (153, 156, 157). Work or the equivalent isometric strength parameter AT is considered the most precise indicator of functional muscle rehabilitation (158). AT of the untrained side increased significantly across groups by 9.6% from T1 to T2 (p=0.039) and remained at that level of improvement at T3 (p=0.028). The within-group analysis of the MST group revealed a significant improvement in AT of the untrained limb by 18.7% (p=0.02) from T1 to T2.

The hyperexcitability of the stretch reflex is the main cause of spasticity, whereby the balance between excitatory and inhibitory signals is disturbed (25). Brain injuries such as stroke, lead to a disruption in cortical mechanisms controlling inhibitory pathways; excitatory signals are not counteracted (25, 26). The efficiency of presynaptic and postsynaptic inhibition as well as post-activation depression were found to be decreased in patients with spasticity (24, 27-29). Please refer to Chapter 1 and Figure 1.1 for detailed explanations.

Previous cross-education studies could show a decrease in H-reflex (stretch reflex) excitability in the contralateral limb during unilateral training of the upper limb (71, 77, 85-87). Although the mechanisms mediating the noted depression could not be precisely identified, authors speculated that pre- and post-synaptic inhibition might be responsible (66, 85). Presynaptic inhibition only lasts for hundreds of milliseconds and can therefore not be the single mechanism involved in the > 30 second depression. Postsynaptic inhibition may contribute to the prolonged depression time after contraction. Cervicomedullory MEPs (CMEPs), which activate motoneurons through the corticospinal tract, were unchanged during contractions but reduced after (85). Dragert and Zehr (90) also found decreased spinal reflex excitability in the untrained side and conclude that repeated bouts of high-intensity unilateral dorsiflexion training could lead to increased contralateral sensitivity of inhibitory interneurons and larger suppression of alpha-motoneuron excitability in stroke patients (90, 227). Mechanisms underlying mirror therapy occur on cortical level only (103), and do not appear to influence spinal excitability, thus mirror therapy may not stimulate spasticity improvements. However, according to Gracies (35) spasticity is only one component of spastic paresis caused by stroke. Soft tissue contracture, spastic dystonia, and spastic co-contraction should also be considered (35). Similarly, the Modified Ashworth Scale (MAS), although frequently used in research and clinical assessment, may measure stiffness caused by spastic paresis, rather than abnormal reflex activity alone (36). More efficient motor output to the untrained limb (66, 90) initiated by (mirror-aided) cross-education interventions may lead to improved spastic dystonia and spastic co-contraction, possibly translating to reduced MAS scores.

In this pilot trial, mean MAS scores for the muscles surrounding all upper limb joints (shoulder, elbow, wrist) reduced significantly across groups with large effect size (partial n^2 = 0.481-0.624, p<0.001) suggesting no augmentation with mirror therapy. Improvements were noted for both groups from T1 to T2 and from T1 to T3. However, the decrease in MAS scores (≤ 0.8 points) did not reach the previously reported MDC of 1 point (195). No previous study measures the cross-education effect on upper limb spasticity in stroke patients. Urbin et al. (62) demonstrated a significant improvement of 25° (p < 0.01) in wrist extension Active Range of Motion (AROM) in the MA side following strength training of the LA side. AROM is not a direct measure of spasticity, however these findings suggest an influence of cross-education on spastic paresis and stiffness (35). Dragert and Zehr (90)(reported no significant changes in lower limb spasticity after cross-education training of the LA dorsiflexor in stroke patients. This is especially surprising considering that adaptations in spinal reflex excitability were noted. Mean values for pre-intervention MAS measurements do not appear to differ meaningfully between this pilot study and the study by Dragert and Zehr (90). However, 5 out of the 19 participants (26%) taking part in the unilateral dorsiflexor strength training (90) scored a '0' for dorsiflexion spasticity at baseline assessment. In this pilot trial pre-intervention spasticity was noted for all participant. If no spasticity improvement was possible for 26% of participants, it was less likely to register a significant improvement overall. Furthermore, it was suggested previously that mechanisms underlying cross-education may vary among individuals and muscle groups (91), training effects regarding spasticity may therefore differ between the upper and lower limb.

It is beyond the scope of this study to specifically determine neurophysiological mechanisms leading to the significant decrease in MAS scores. Based on the current understanding of adaptations initiated by cross-education (66, 67, 71, 77, 85, 86) (mirror therapy did not augment improvements in spasticity) and the pathophysiology of spasticity (25, 35), alterations in spinal reflex excitability or improvements in cortical motor output seem possible. If the latter applies, adaptations in neural drive in the ST group were sufficient to facilitate improvements in spasticity but not in maximal isometric strength. Generally, unilateral training is considered to only cause minor adaptations on spinal level (67), therefore changes on cortical level may be a more likely explanation for the significant reduction in MAS scores noted in this study.

The mean CAHAI score showed a main effect of time ($F_{(2, 50)} = 3.668$, $p = 0.033$, partial $\eta^2 = 0.128$) with an improvement of 2.8% ($p=0.003$) across groups. However, the 2.8% improvement did not reach previously reported values for MDC of 7% (197, 199), but the results are in agreement with Urbin et al. (62) who reported a small (4%), but significant ($p = 0.04$) improvement in the Action Research Arm Test (ARAT) after unilateral strength training of LA wrist flexors.

No significant changes could be established for the ABIILHAND questionnaire or the LHS.

4.4.3. Intervention and Equipment

The barrier of transport and attendance at the Institute of Technology Sligo was first identified during early recruitment for a case studies conducted by the research team (106). To accommodate patient's needs and ensure acceptable sample size, the research team felt a home-based exercise programme would be most beneficial. The initial ethical approval was based on an intervention located in the Institute of Technology

Sligo, thus an amendment regarding the site of intervention was submitted and granted in July 2015 (Appendix H).

To facilitate home training, a training device, strong enough to withhold maximal contractions and transparent to allow for reflection observation, had to be designed. The research team initially worked with Mr Padraig Kelly (University Hospital Sligo Plaster Technician) who created a Plaster of Paris of the upper limb at the 85° elbow extension training angle (163). Thereafter contact was made with a Mould Room Clinical Specialist in Cork University Hospital (Adrian J. Cubbin) who offered to turn the Plaster of Paris mould into a Perspex shell, usually used in radiation therapy. Unfortunately, the Plaster of Paris mould had to be delivered to Cork University Hospital within hours of production which was impractical, thus the research team had to investigate other possible ways of creating a brace. Eventually, collaborations with Institute of Technology Sligo Department of Creative Design (Dr David Roberts) resulted in the production of an innovative, cost effective upper limb training device made from clear plastic (Figure 4.1). The safe, user friendly and comfortable isometric strength brace combined all characteristics needed to successfully apply the combination therapy. The research team (Ehrensberger M., Simpson D., Monaghan K. and Roberts D.) decided to investigate the possible commercialisation of a Mirror Strengthening Brace. Collaboration with Institute of Technology Sligo Innovation Centre (Dr. Niall McEvoy) lead to the submission of an Invention Declaration. The device was declared patentable in early 2016. In further collaboration with Enterprise Ireland Commercialisation Specialist Paul Butler, the research group was advised to first apply for the Enterprise Ireland Commercial Case Feasibility Grant (€15000) and pending promising results, to apply for the Enterprise Ireland Commercialisation Fund worth up to €350.000. To date the research team was awarded €15000 to investigate the scope of the commercial case of the Mirror Strengthening Brace. The resulting, very promising market research report will support the application for the Enterprise Ireland Commercialisation Fund.

Elbow extension was chosen due to its representation in everyday upper limb functional movements such as reaching (164) and to counteract the frequent pattern of arm spasticity with flexion at the elbow affecting 79% of patients (4, 228). The contraction type (isometric) was selected to reduce injury risk (151), and to increase comparability of results as differences in range of motion between patients and between MA and LA sides was eliminated as influencing factor. Also, maximal isometric contractions allow for training at highest intensity without complex equipment, which is associated with greatest cross-education of strength effects (51). The 85° training angle represents the position in which the triceps brachii can produce most force (163). Most strength gain in untrained individuals was identified when training was performed 3 times a week and individual muscle groups were exercised for 4 sets (229). Furthermore, the number of sets and repetitions, and the duration of rest periods were chosen according to maximal strength training guidelines (206, 207). Collaboration with healthcare professionals lead to the protocol timeframe of 4 weeks. Stroke patients indicated that they were not willing to commit to a longer training period. Furthermore, cross-education interventions of 3 and 4 weeks proved previously successful in healthy participants (42, 94, 101). This was the first study comparing mirror-aided cross-education training with cross-education training only. Efficacy results did not show a mirror augmenting effect when training isometrically. However, evidence exists that an alternative training protocol may elicit motor function improvements (17, 19, 20, 54). A dynamic strength training protocol with a higher number of contractions, measurement of training intensity and congruent positioning of the trained and untrained limb may be more beneficial (17, 54, 134). Specific protocol characteristics such as ideal number of sets, repetitions and duration of rest have to be established.

4.4.4. Limitations

Guided by the Cochrane (137) and PEDro (136) risk of bias assessment tools, efforts were made to keep limitations and risk of bias as low as possible. However, some limitations remain. Due to the nature of the exercise intervention, blinding of therapists was impossible. Furthermore, according to ethical approval, the information letter sent to potential participants had to include descriptions of cross-education and mirror therapy, thus blinding of participants was also impossible. To reduce the risk of differential behaviour, all participants were treated according to a strict protocol following Cochrane guidelines (137). The study did not control for possible mirror placebo effects. This could be addressed by including an experimental group, training with a mirror angled in such a way that participants cannot see the reflection of the training limb. Due to the high heterogeneity of the cohort, it is impossible to specify patient groups the intervention is most beneficial for. As previously mentioned, the training intensity was not measured during home-based strength training sessions. It is possible that the training intensity was not high enough for cross-education to occur. The level of motivation and efficacy in participants was not measured, this could present a possible confounder. Mechanisms underlying cross-education, mirror therapy or the combination of both is mostly based on trials including healthy participants. Discussed possible adaptations when applying named rehabilitation methods in stroke patients are therefore hypotheses only and must be treated as such.

4.4.5. Summery and Recommendations for Future Research

As a first objective, this study established the feasibility of a fully powered randomised controlled trial comparing the effects of mirror-aided unilateral strength training with unilateral strength training only on motor function recovery post stroke. Secondly, it identified that the use of a mirror did not augment the cross-education effect when a population of chronic stroke patients trained isometrically. However, the combination of large effect sizes with borderline significance in a small sample of participants warrants further investigation of the combination therapy.

A future randomised controlled trial should implement all outlined changes to the training protocol. A dynamic strength training programme with a higher number of contractions, measurement of training intensity and congruent positioning of the trained and untrained limb should be applied. It would be beneficial to establish MDCs and MCIDs for all outcome measures to allow for categorisation of achieved change. Specific protocol characteristics such as ideal sessions per week, number of sets and repetitions, duration of rest periods and contraction intensity have to be investigated.

Furthermore, the combination treatment of cross-education and mirror therapy should be applied to other stroke subgroups (e.g. acute or sub-acute) to identify most beneficial time points for the rehabilitation method. It is also advisable to investigate other predicting factors for most successful application such as level of disability.

In a next step, the novel rehabilitation method should be investigated as an adjunct therapy to standard rehabilitation. Furthermore, its benefits should be compared to other promising treatment approaches. Thus, in time knowledge about best general and individual rehabilitation practices can be gained.

Unilateral strength training combined with mirror therapy may also be beneficial for other illnesses or injuries causing bilateral asymmetry (e.g. multiple sclerosis, fractures, and joint replacements). The effectiveness of such treatment amongst other patient groups should be investigated.

To allow the possible incorporation of (mirror-aided) cross-education training, the further development of the mirror strengthening brace should be a priority also.

4.5. Conclusion & Contribution to Knowledge

Following recommendations in previous literature, this pilot study was first to investigate the feasibility and potential efficacy of mirror-aided unilateral strength training compared to unilateral strength training alone on upper-limb motor function recovery in a chronic stroke population. The feasibility of a fully powered trial was established and insightful information regarding different study components could be provided. Furthermore, authors established that mirror therapy did not augment the cross-education effect in chronic stroke patients when training isometrically. However, considering the small sample size, the borderline between group significant difference combined with the large effect size still warrants further investigation. An altered training programme with adjusted protocol characteristics may results in improved functional outcomes.

Chapter 5: General Discussion and Conclusion

5.1. Main Results & Contribution of Knowledge

The positive effect of mirror therapy in post stroke rehabilitation was established by a recent Cochrane review (230). Although the application of cross-education in rehabilitation after stroke was previously recommended (11), no high quality literature review investigating its effects was conducted to date. Chapter two addressed this gap in knowledge and concluded that there is a moderate level of evidence (141) supporting the successful application of cross-education for motor function recovery after stroke. Two out of the three included studies showed significant strength transfer to the untrained, more-affected limb (31.4 % and 45.5%) (90, 138). All three trials resulted in significant improvements in task execution capacity (62, 90, 138).

To evaluate the efficacy of the subsequently applied (mirror-aided) unilateral strength training programme, strength testing procedures of high reliability were required. However, the protocol reliability and exact testing procedures for maximal isometric elbow extension measured with the Biodex System 3 isokinetic dynamometer was never before established. Furthermore, the strength parameter Average Torque over a single isometric contraction, which is regarded as highly relevant when interpreting the rehabilitation progress (158), had not been reported to date. Chapter 3 addressed these gaps in knowledge. The established reliability scores for the three most important strength parameters for comprehensive muscle function assessment (Peak Torque, Rate of Torque Development, Average Torque over a single contraction) were in the excellent range (ICC = 0.92-0.98). A detailed description of recommendations addressing different aspects of the testing protocol such as instructions for participants and data analysis were provided, allowing assessors to achieve excellent reliability when measuring maximal isometric elbow extension strength with the Biodex System 3 isokinetic dynamometer with the Biodex Advantage Software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA).

It was previously hypothesised that mirror visual feedback can augment the cross-education effect (17, 18). Zult et al. (20) verified the theory with healthy participants and recommended to explore the effects of the combination therapy in a stroke population. Chapter 4 describes the first study investigating the feasibility and potential efficacy of mirror-aided unilateral strength training in post-stroke upper limb motor recovery compared to unilateral strength training alone. The study established the feasibility of a fully powered trial and insightful information regarding different study components. Repeated, planned interactions with referring rehabilitation professionals is advised to ensure consistent and sufficient participant referrals. The study proved feasible regarding participant compliance (213) with all patients completing 83-100% of training sessions. The 20% drop-out rate from baseline to follow-up assessment exceeded the 15% threshold stipulated for low risk of bias (136). However, this was addressed when calculating the sample size (n = 90) required for a fully powered trial (210). Both interventions proved safe in this sample of chronic stroke patients without any noted adverse events. Five participants (14%) were unable to complete the maximal strength assessment carried out with the Biodex System 3 Isokinetic Dynamometer. To ensure the successful measurement of maximal isometric muscle performance, the ability and willingness to use the Biodex System 3 may be a valuable extension to inclusion criteria. Alternatively, the use of a handheld dynamometer may be considered. All other outcome measurements used in this pilot trial proved suitable.

The efficacy results showed no mirror augmenting effect on cross-education training when chronic stroke patients performed isometric contractions. However, considering the small sample size, the borderline between group significant difference for AT ($p = 0.065$) combined with the large effect size (partial $\eta^2 = 0.124$) may still indicate potential benefits of the combination therapy (212). When interpreting the results in light of the current evidence base, it immerged that an altered training protocol may augment effects. Knowledge gained has the potential to guide future research. Firstly, to achieve a mirror augmenting effects, dynamic contractions may have to be performed. Recent publications (19, 220) indicate that cortical excitability is only increased when moving reflections are observed. Furthermore, visual feedback from an isometric contraction may not be sufficient to balance efferent and afferent signals. Thus, motor learning and rehabilitation may not be efficiently supported (40). The position of the untrained limb behind the mirror may also influence mirror augmenting effects. To avoid kinaesthetic distractions, it should be congruent to the training limb (17) . Fourkas et al. (221) showed larger facilitation of Motor Evoked Potentials when the real-life position of the hand was identical with the movement participants were instructed to imagine. Compared to previously published cross-education studies in stroke populations (90, 219), this pilot trial resulted in lower strength gains in the trained and untrained limb. The difference in the number of training sessions seems to be one obvious reason. Patients with multiple sclerosis did not show significant strength transfer after the first 9 training session of unilateral dorsiflexion training, but improvements were noted after 18 (134). In contrast, Manca et al. (54) reported no significant correlation between the total number of contractions and strength gains in either limb in a healthy population. Training intensity has been shown to affect the trained and untrained muscle in a highly specific manner (51, 222). Although participants were instructed to contract maximally in this pilot trial, exact training intensity was not measured. If participants did not train close to maximal intensity, post-intervention strength of the trained and untrained limb cannot be expected to be significantly altered. Importantly, despite the possible lower training intensity a significant strength improvement in the untrained side of the MST group could be noted. Thus, mirror visual feedback may reduce the threshold for cross-education; hence, strength transfer may be facilitated at a lower training intensity. In conclusion, a high intensity, dynamic strength-training programme of longer duration and congruent positioning of both limbs may significantly augment strength outcomes and should be implemented in future studies.

5.2. Future Directions and Recommendations

By training the less-affected upper limb only, (mirror-aided) cross-education has the capacity to address current limitations in stroke rehabilitation. Clinicians identified (mirror-aided) cross-education as a promising treatment option to increase therapy time and allow for independent training in highly impaired patients (139). Furthermore, no adverse effects were noted during the literature review or the pilot study. Considering the favourable risk-benefit ratio, rehabilitation professionals may include (mirror-aided) cross-education as an adjunct therapy in individual cases.

However, to provide conclusive evidence for the application of mirror-aided unilateral strength training in stroke rehabilitation, further research must be carried out.

Guided by information and results gained from the pilot trial, a fully powered randomised controlled trial investigating the efficacy of mirror-aided unilateral strength training compared to unilateral strength training only on post-stroke upper limb rehabilitation should be conducted. To establish the benefits of including (mirror-aided) cross-education to typical rehabilitation procedures, a study comparing standard rehabilitation and standard rehabilitation + (mirror-aided) cross-education should be carried out. Furthermore, to ensure the evolvement of best practice rehabilitation methods, the combination treatment of cross-education and mirror therapy has to be compared with other novel treatment approaches such as virtual reality training.

Considering that the novel therapy approach may allow the patient to train independently, effects of a supervised, therapist guided programme should be compared with an independent home intervention. To support mentioned trials and the future implementation of mirror-aided cross-education in standard rehabilitation, the mirror strengthening brace designed in the Institute of Technology Sligo has to be further developed and tested. It would also be beneficial to investigate predicting factors for most successful application (e.g. time after stroke, level of disability) and ideal training protocol characteristics (e.g. sessions per week, number of sets and repetitions, training intensity).

The effects of (mirror-aided) unilateral strength training on the recovery of other conditions causing bilateral imbalance such as multiple sclerosis or orthopaedic injuries should be explored. Corticospinal adaptations, underlying mechanisms in healthy or specific clinical populations also have to be investigated.

5.3. Conclusion

Results presented in this thesis indicate beneficial effects of (mirror-aided) cross-education on post-stroke upper limb motor recovery. The use of a mirror did not augment the cross-education effect when chronic stroke patients trained isometrically. Nevertheless, the combination of results warrants further investigation and the feasibility of a fully powered trial comparing the combination treatment of cross-education and mirror therapy to cross-education only was established. Novel recommendations regarding a potentially more effective training protocol should be followed.

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Appendices

Appendix A: Systematic Review PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	28
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	N/A in thesis
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	29-31
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	31-32
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No registration exists
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	32
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	32
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	34
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	32
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	32-33
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	33
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	33
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A no meta-analysis

			possible
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A no meta-analysis possible

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not applied
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	34-35
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	36-38
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	42-43
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	39-40
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Not applied
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	47
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	52-53
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	53
FUNDING			

Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A in thesis

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix B: Cross-education of Strength has a Positive Impact on Post-Stroke Rehabilitation: A Systematic Literature Review

REVIEW

Cross-education of strength has a positive impact on post-stroke rehabilitation: a systematic literature review

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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 randomized controlled trials are conducted to further support the findings.

Keywords: Stroke, Rehabilitation, Cross-education, Unilateral strength training, Strength transfer

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 and a systematic literature review was conducted by Carroll et al. in 2006[4].

The magnitude of contralateral strength transfer reported in different research papers is ranking between 3[5] to 104% of initial strength[6]. 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.[1,7–11] Carroll et al.[4] found definite evidence for the phenomenon of cross-education and the degree of strength transfer is on average 8% of the initial strength, or 52% of the strength increase observed in the trained limb.

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.[4,7] 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).[4,12–14] Hortobágyi[14] 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.[1,4,14] 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.[4,15–19] Accordingly adaptations on this level are seen as highly unlikely; however the authors of a review on cross-education warn that muscular processes

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should not be discarded completely, as measuring methods might lack sensitivity.[4] In summery 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.[20] In a study by Magnus *et al.*[21] 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 45% of the non-fractured limb strength at week 12 post injury.[21]

Hemiparesis, a one sided muscle weakness, affects 80 – 85% of acute stroke patients.[22,23] 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[24]. Typically hemiparesis causes asymmetry between the more-affected (MA) and less-affected (LA) side[20] and often the impairment of motor function on the MA side is too great to be engaged in a strength training program. 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.[20]

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.

Methodology

Search strategy

During December 2014 the following databases were searched: CINAHL, CENTRAL, Google scholar, hselibrary, 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 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 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

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.

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.[25] 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".[25] 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.[26] using the Delphi consensus technique.

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.

Results

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 Fig. 1

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. The first study[27] included is a single blinded randomized controlled trial with two experimental (EG1 & EG2) and one control group (CG). 30 participants took part, 15male 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.[27] 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 30min 5 times a week. Additionally all groups received tilt table intervention for 20min 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.[27] include strength outcome measurements, the intervention did not contain strength specific training. The second study[28] was a one group non-randomized controlled intervention. 19 participants, 15 male and 4 female, age ranging from 26 to 81 years (mean = 58.3 ± 12.2) took part. Inclusion criteria consisted of: >6months 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 <3months 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

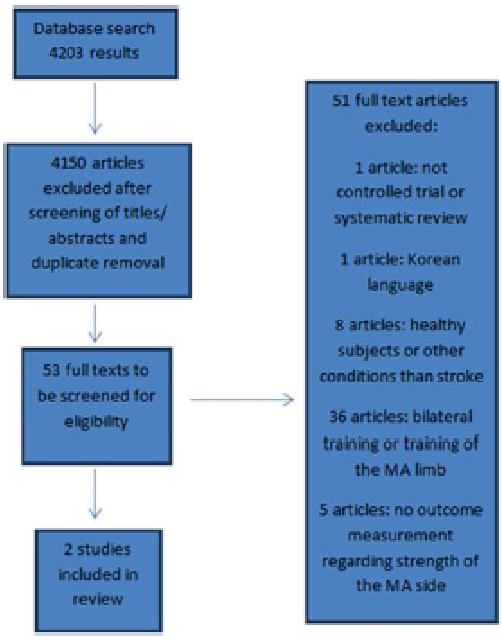

Figure 1. Flowchart of study selection process.

Table 2 Description of each study

Study	Study design	Sample Size	Gender	Mean age ± SD	Paretic side left/ right	Stroke type ischemic/ hemorrhagic	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, nonrandomized 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 kinemati s 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.

scale, and Fugl-Meyer). Dragert & Zehr[28] work with a mixed lab and home based training protocol for the less affected 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 450minutes of intervention. In both studies post-test measurements were compared to pre-test results to identify changes.

Description of results

Kim et al.[27] found no significant differences between pre-test and post-test strength measures in the less – affected limb of all 3 groups. However the more-affected side showed a significant strength improvement for all measured muscle groups in EG1 (one leg standing training) and EG2 (task oriented training). For the one leg standing training group strength gain ranges from 13.7% to 53.2% (mean = 22.6%) the 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% ($p < 0.01$). 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 3. In the trial by Dragert & Zehr[28] 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, more-affected 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 more affected side ($p = 0.03$) and in the soleus muscle of the less affected and more affected side ($p = 0.005$, $p = 0.04$) was recorded. Further the range of motion of the less affected ankle increased significantly ($p = 0.04$), this improvement did not translate into the more affected side.

Bias

The study by Kim et al.[27] is a single blinded randomized controlled trial (RCT) allowing for comparisons between

Table 3 Results of each study

		Kim et al. 2014			Dragert and 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† (<0.01)	45.5†‡ (<0.01)	31.4 (0.009)
	Ankle plantarflexors	0.6 (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 (0.07)	-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 and go				-6.4 (0.05)

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

intervention and control groups. 8 out of 11 items in the PEDro scale[26] were satisfactory and the study was considered to have a low risk of bias according to the Cochrane risk of bias assessment tool[25]. However, allocation concealment, 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[28] is a one group non randomized 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. Further 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, undertraining or incorrect technique etc. 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[28] 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 table 4 and 5.

Confounders

Dragert & Zehr[28] 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.[27] 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 this could present a possible confounder of the results.

Table 4 Cochrane risk of bias assessment tool

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 numberLow risk: power analysis determined sample sizeSubjects choose angle of tilt table individually a 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 5 PEDro risk of bias assessment tool

Item		Kim et a. 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 key 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 analysed 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**	

Strength of results

In general the standard of evidence in a RCT is regarded higher than in a one group non-randomized controlled study. Randomized 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[29]. The only overlapping outcome measure between the two studies is strength increase of the untrained limb. Based on best evidence synthesis guidelines[30] 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.

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.[27]) is 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 by Dragert & Zehr[28] was a non-randomized one group controlled trial. Again the results give a strong indication that cross-education of strength exists in the post-stroke hemiplegic patient, supporting the findings of Kim et al.[27]. The strength gain achieved in the untrained, more affected 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[27] resulted in a higher overall (mean=39.5%) and dorsiflexor strength gain (45.5%) than a specific dorsiflexor isometric contraction program (31.4%). The smaller strength increase might be due to the different training protocols used in the two trials. Dragert & Zehr[28] work with a mixed laboratory and home training program 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 and bad technique etc. which may negatively affect the magnitude of strength gain. The participants of the other trial (Kim et al.[27]) were consistently supervised throughout all training sessions. In a comparison of a supervised clinical exercise program with a home based exercise program to treat osteoarthritis in the knee, Deyle et al.[31] found that subjects in the clinic treatment group achieved about twice as much improvement than subjects who performed similar unsupervised exercises at home. Further the latter were training 5 days a week compared to 3 days a week in the dorsiflexor trial. Total intervention times given by the authors, indicates longer training periods in the trial by Dragert & Zehr[28] accumulating to 450min compared to 300min[27]. 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[28] require approximately 5minutes of training time per session, accumulating to 90min of total intervention time. Even though there is no breakdown of the actual training time in the study by Kim et al.[27], 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 pre-intervention of the more-affected leg was 3.4Nm in the trial by Kim et al.[27] compared to 9.18Nm for Dragert & Zehr[28]. This difference in baseline strength combined with the fact that a more novel task-oriented training program was used by Kim et al.[27] 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 program allows for higher and more rapid improvements[32]. Likewise the more novel or less familiar a training task is, the greater the potential strength transfer[10]. Further Dragert & Zehr[28] 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[27], 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.[33] 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.[27] 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[34, 35]. Characteristics of participants in the trial by Dragert and Zehr[28] were very much heterogeneous e.g. months post stroke ranged from 6 – 284, whereas participants in Kim et al.[27] 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.[27] reported no significant strength increase in the less-affected, 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 less-affected, 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 and Patten[36] conducted a high intensity resistance training intervention for the MA lower extremity. After completion a significant increase in power in the less-affected, untrained limb was reported. Results showed increased power in the eccentric strength training group ($P < .0001$) following resistance training, with the eccentric phase increase (+14%) being marginally larger than the concentric phase increase (+12%, $P = .05$). Whitall et al.[37] 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 was reported. For this review only results of the DMTE intervention were of interest, the unilateral exercises performed were weight bearing with the more-affected arm (elbow fixed), and opening the hand with finger extension. After completion there was significant isometric strength increases for the more-affected upper limb reported, however this did not carry over to the less-affected, untrained side. There were no significant isokinetic strength gains noted for the more-affected, trained limb nor for the less-affected, 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.

Conclusion

Overall there is moderate to strong evidence[30] that the phenomenon of cross-education from the LA affected side to the MA side can be applied in stroke patients and has an impact on the recovery of muscle strength. Further 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 effects of cross-education of strength on motor recovery after stroke. It is recommended that additional high quality randomized 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.

Conflict of Interest

All contributors to this review are independent authors, there are no conflicts of interest regarding this article.

Financial Support

Monika Ehrensberger: IT Sligo President's Bursary Fund. Daniel Simpson & Patrick Broderick: Institutes of Technology Ireland Postgraduate Research Scholarship. Dr. Kenneth Monaghan: Lecturer at IT Sligo.

Ethics approval

The protocol of this systematic review did not include research procedures which require ethical approval. No ethical issues arose during this systematic review. Included studies were independently ethically approved.

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Appendix C: Ethical Approval for the Study Titled ‘Protocol Reliability for Maximal Isometric Ankle Dorsiflexion and Elbow Extension Measured with the Biodex System 3 Isokinetic Dynamometer’

An Institiúid Teicneolaíochta, Sligeach

Monika Ehrensberger
School of Science
IT Sligo
Ash Lane
Sligo

March 20th 2016

Re. Research Ethics Application

Dear Ms Ehrensberger,

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 D: Subject Information Sheet for the Study Titled ‘Protocol Reliability for Maximal Isometric Ankle Dorsiflexion and Elbow Extension Measured with the Biodex System 3 Isokinetic Dynamometer’

Subject information sheet

Re: Reliability of isometric ankle dorsiflexion and elbow extension measured with 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 triceps and right dorsiflexor. Isometric means you will contract muscles without initiating movement like clenching a tight fist. The triceps muscle is activated when you straighten your arm; the dorsiflexor enables you to pull your toes towards your shin. 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 (Monika & Daniel) will be present during each assessment and will explain the protocol thoroughly.

The protocol consists of:

- Warm – up: 3min 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

Ms Monika Ehrensberger & Mr Daniel Simpson

Contact details

Ms. Monika Ehrensberger / Mr. Daniel Simpson

Job Title: Principal researcher

Phone number: 0868416498 / 0870531507

Email: monika.ehrensberger@mail.itsligo.ie / daniel.simpson@mail.itsligo.ie

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

Appendix E: Participation Consent Form for the Study Titled ‘Protocol Reliability for Maximal Isometric Ankle Dorsiflexion and Elbow Extension Measured with the Biodex System 3 Isokinetic Dynamometer’

Participation Consent Form

Reliability of isometric ankle dorsiflexion and elbow extension measured with Biodex System 3 Isokinetic Dynamometer

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.

________________________ ______________________________

Name of patient Date Signature

Appendix F: Participant Positioning for Elbow Extension Strength Assessment according to the Biodex System 3 Manual

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

Clinical Applications of Biodex Operating Modes

Isokinetic Mode

1. The isokinetic mode may be used to work the elbow bi-directionally. In this way job specific tasks, functional tasks, or sports activities may be simulated.

Passive Mode

1. The passive mode may be used to treat inflammatory conditions of the elbow. Many times when rest is recommended it does not mean total immobilization but the elimination of activities that cause pain. The passive mode may be used for the effects of continuous passive motion.

2. The passive mode may be used to perform non-reciprocal contractions, e.g., working the extensors at the end range of motion both concentrically and eccentrically, as it is not uncommon for elbow extension to be compromised after injury or fracture.

Isometric Mode

1. Isometrics may be used when pain or inflammation is a concern. Multi-angle isometrics are recommended.

Isotonic Mode

1. To simulate a functional activity, set the isotonic force accordingly to a patient task.
2. Perform eccentric/concentric movements to do biceps-only exercise.

Reactive Eccentric Mode

1. The eccentric mode may be used to simulate job specific tasks, e.g., the eccentric mode may be used to work the elbow flexors, eccentrically as if the worker were lowering a heavy box.

Additional Comments

1. It has been recommended by some clinicians that the dominant arm should be 5% stronger than the non-dominant arm in recreational athletes and 10% stronger in competitive athletes.

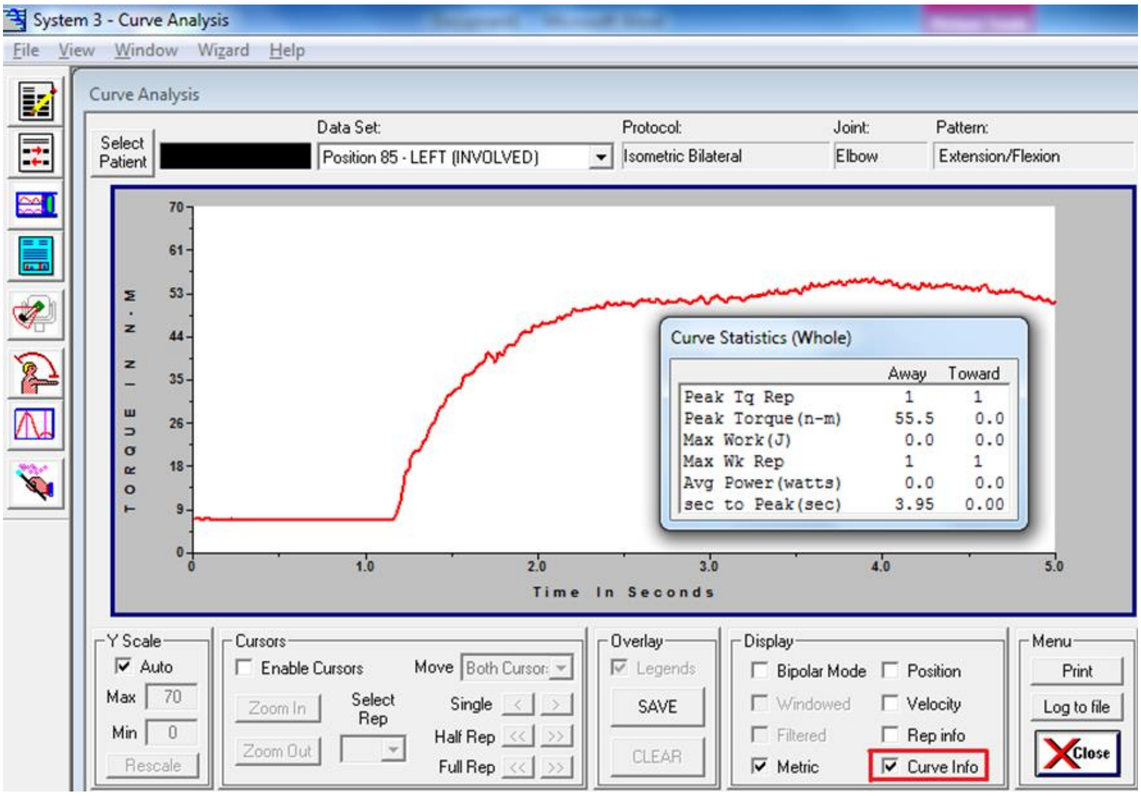
2. Ice may be applied to the site of the lesion while the patient is in the passive mode for approximately fifteen minutes.

3. For cases of capsular tightness. Place the patient in the passive mode. Red range of motion limit set buttons may be set to encompass a slightly greater range of motion than the patient currently is capable of moving. The percent range dials should be turned down to 55% and the patient should be placed on the unit. Slowly and with caution, the percent ROM dials should be turned up. *NEVER EXCEED A COMFORTABLE OR PHYSIOLOGICAL RANGE OF MOTION. ALWAYS HAVE THE COMFORT STOP AVAILABLE*. The pause may also be used for a passive stretch at end range.

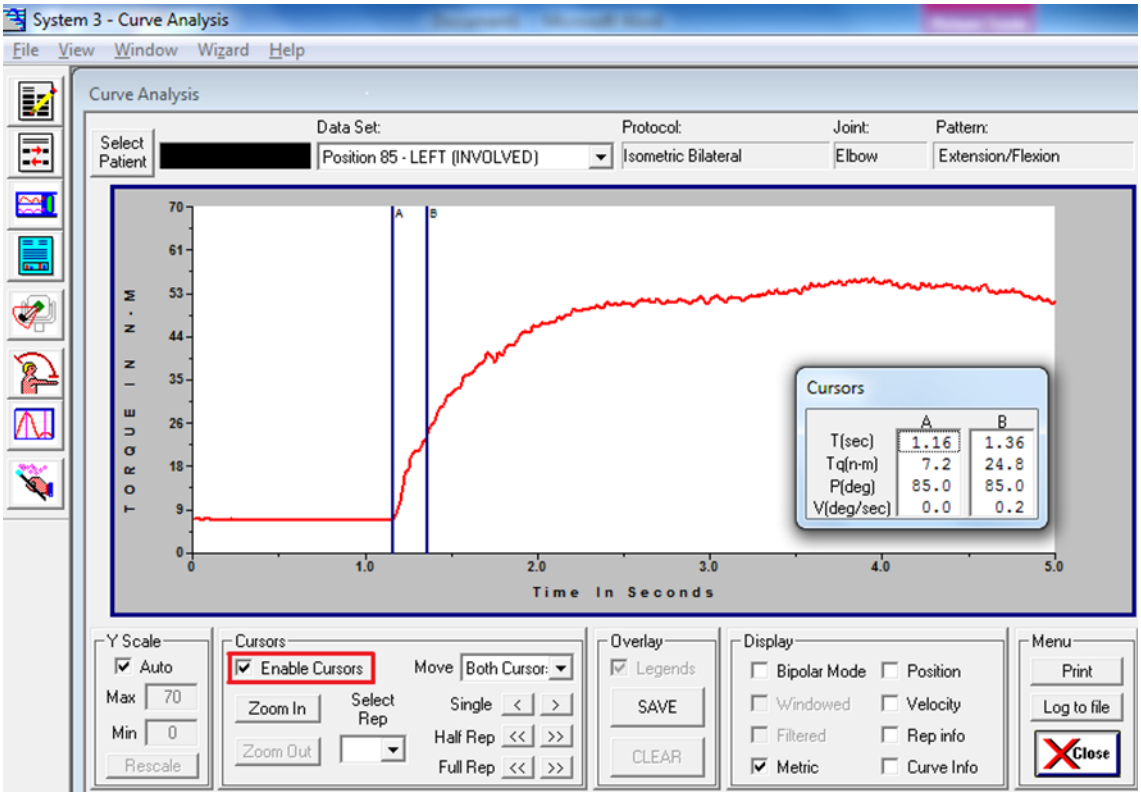
4. The elbow is frequently injured by the repeated application of stresses. Throwing injuries commonly occur secondary to throwing too frequently and throwing repeatedly at maximum force. These injuries may be treated by working either passively, isokinetically, or eccentrically at submaximal levels.

5. Position the handgrip to concentrate on specific muscle groups. If desired, keep the handgrip loose to obtain active supination or pronation.

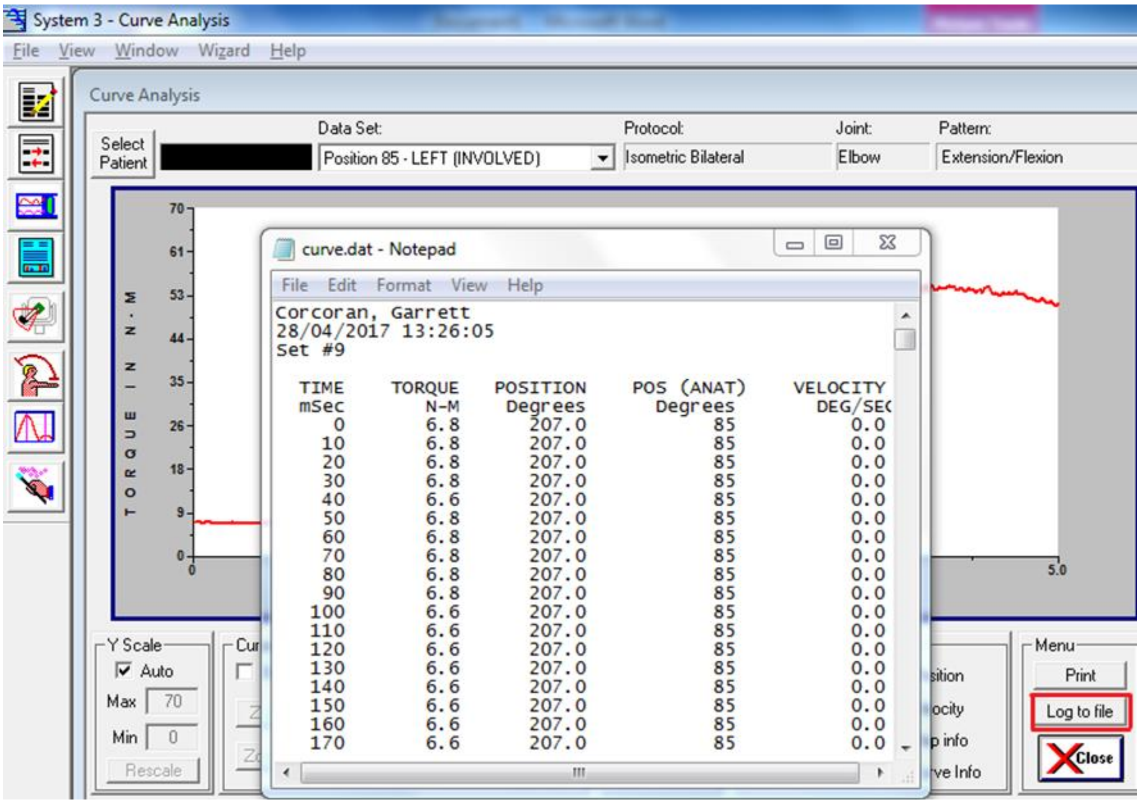
Appendix G: Analysis of Peak Torque, Rate of Torque Development and Average Torque over a single contraction using the Biodex Advantage Software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA)



The highest Peak Torque was obtained using the 'Curve Info' application in the Biodex Software curve analysis



For Rate of Torque Development measurements, curser A was placed at contraction onset; curser B was placed at 0.20sec from contraction onset



Average Torque was obtained using the 'log to file' application and saving the data as a text document

Appendix H: Ethical Approval for the Study Titled ‘Unilateral Strength Training and Mirror Therapy for Enhancing Upper Limb Motor Function Post Stroke: A Pilot Randomised Pilot Study’

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

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

Monika Ehrensberger
IT Sligo
Ash Lane
Sligo

March 18 2015

Re. Research Ethics Application

Dear Ms Ehrensberger,

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 of the upper limb after stroke: 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. Section A6: Should 'unaffected' be replaced by 'affected'?
b. Please outline how patient safety will be protected during the intervention.
c. Replace 'first' with 'fist' in information sheet
d. In the letter to health professionals add a statement to say that consent will be sought from patients at the initial assessment.
e. 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?

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

Monika Ehrensberger
IT Sligo
Ash Lane
Sligo

April 20th 2015

Re. Research Ethics Application

Dear Ms Ehrensberger,

The Research Ethics Committee (REC) at Sligo General Hospital has received your revised submission of the study "*Mirror therapy and unilateral strength training for enhancing motor function of the upper limb after stroke: A pilot randomised controlled trial* ". 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 2016.

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

Monika Ehrensberger
IT Sligo
Ash Lane
Sligo

July 10th
~~April 20th~~ 2015

Re. Research Ethics Application

Dear Ms Ehrensberger,

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 of the upper limb after stroke: A pilot randomised controlled trial* ". The REC Chairman has granted a favourable opinion on the amendment.

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,

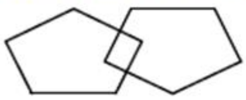
Dr John Williams
Chairman

Appendix I: Mini Mental State Examination

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 J: Consent to Contact form for the Study Titled 'Unilateral Strength Training and Mirror Therapy for Enhancing Upper Limb Motor Function Post Stroke: A Pilot Randomised Pilot Study'

Consent to Contact Form

Unilateral strength training and mirror therapy for enhancing upper limb motor function post stroke: A randomised pilot study

1. I confirm that I have been contacted by my health professional concerning the above study.

2. I have given my permission for my health professional to give my personal contact details to the study research team.

3. I understand that a member of the study research team will contact me personally concerning my possible participation in the research study of the above name.

4. I understand that the provision of my personal details is voluntary and that I can decide to withdraw these details at any time and opt not to be contacted.

5. I have had time to consider whether to provide my contact details.

__________________________ ___________________________________

Name of patient Date Signature

Appendix K: Subject Information Sheet for the Study Titled 'Unilateral Strength Training and Mirror Therapy for Enhancing Upper Limb Motor Function Post Stroke: A Randomised Pilot Study'

Subject information sheet

Unilateral strength training and mirror therapy for enhancing upper limb motor function post stroke: A randomised pilot study

Introduction

Hello, first of all 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 combining 'Unilateral Strength Training' with 'Mirror Therapy'. 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), however the principal researcher/ research student Monika Ehrensberger will travel to your home at arranged dates to guide you through the training sessions.

Unilateral Strength Training

Unilateral strength training means that only one of the two limbs is trained. In the case of this study you will only train your unaffected arm. Evidence shows that strength improvements in the trained limb can be transferred into the untrained limb this is known as cross-education.

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.

The combination of unilateral strength training and mirror therapy means that you will train your unaffected limb while watching its reflection in a mirror.

Study

This study is being conducted as part of a research masters and PhD qualification by post graduate student Monika Ehrensberger. Monika has attained an honors bachelor degree in Exercise Therapy & Sport Science and has been working in the rehabilitation sector with different patient groups over the past 4 years. Monika's supervisor is Dr. Kenneth Monaghan, who lectures in IT Sligo. Kenneth is a chartered Physiotherapist who specializes in stroke rehabilitation and has attained a PhD in this area from Trinity College Dublin.

Monika will call to your home for 30 minutes, 3times a week for 4 weeks to guide you through the training sessions. At each session, you will be required to perform an isometric strength program with your unaffected arm. Isometric means you will contract muscles without initiating a movement like clenching a tight fist. Your arm will be placed into an arm brace, made out of well-padded fiberglass cast material and Velcro straps to hold it in place. The brace will insure that the elbow joint is held at 80° (fully extended is 0°) when the isometric elbow extensions are performed. During the therapy sessions you will be seated comfortable in a chair with back support with your arms resting on a table. The lead researcher (Ms. Monika Ehrensberger) will be present at all times during your session. 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 unilateral strength training and mirror therapy, the second will receive unilateral strength training. It is necessary to have two groups within this study to clearly see the effects of mirror therapy on unilateral strength training. However, no matter what group you are assigned to, you will receive the proven benefits of strength training for a 4-week period.

Location

All rehabilitation sessions will take place at your own home with the principal researcher (Monika Ehrensberger) present. Formal assessments will be taken 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.

Study Description

If you choose to take part in the study, the principal researcher (Monika Ehrensberger) will call to your home 3 days a week for 4 weeks to guide you through the strength training program. All visits will approximately take 30 min and will be prearranged with you to take your other commitments into account. The rehabilitation activity requires you to perform an isometric strength training program with your unaffected arm. This is an individual activity and the researcher will be present at all times during the training sessions so as to monitor progress.

Assessments

All assessments will be carried out by two chartered physiotherapists. 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 three-month gap.

Confidentiality

All personal information and results from the study are treated as highly confidential. All final results are anonymized; this means that names or any other information that could identify you as a participant are removed after the initial testing period with researchers. All personal information collected is legally protected under both the Data

Protection Act and the Institute of Technology 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 anonymized 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 upper limb functioning.

Personal benefit

Previous studies from around the world involving unilateral strength training/ mirror therapy 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 upper limb functioning will improve following the 4 weeks of unilateral strength training and mirror therapy 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

Ms. Monika Ehrensberger

Job Title: Principal researcher

Phone number: 0868416498

Email: s00083283@mail.itsligo.ie

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

Appendix L: Participation Consent Form for the Study Titled 'Unilateral Strength Training and Mirror Therapy for Enhancing Upper Limb Motor Function Post Stroke: A Randomised Pilot Study'

Participation Consent Form

Unilateral strength training and mirror therapy for enhancing upper limb motor function post stroke: A randomised pilot study

6. 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.

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

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

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

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

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

_________________________ ________________________________

Name of patient Date Signature

Appendix M: Outcome Measure Protocols and Recording Sheets

BIODEX SYSTEM 3 ISOKINETIC DYNAMOMETER – PARTICIPANT SETTINGS

ID: **DOB:**

Height: **Weight:**

Dominant side: **More affected side:**

Time of stroke:

Settings	Upper Limb		Lower Limb	
	Left	Right	Left	Right
Chair Front				
Chair Height				
Chair Rotation				
Dynamometer Left/Right				
Dynamometer Height				
Dynamometer Tilt				
Dynamometer Rotation				
Attachment Length				
Seat back fore/aft				
Seat Tilt				

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.

The Chedoke Arm and Hand Activity Inventory

Administration Guidelines version 2

CAHAI LICENSE

IMPORTANT - PLEASE READ CAREFULLY: This license is a legally binding agreement between you and Susan Barreca for the Chedoke Arm and Hand Activity Inventory ("CAHAI").

BY USING THE CAHAI, YOU AGREE TO BE BOUND BY THE TERMS OF THIS LICENSE. IF YOU DO NOT AGREE, PLEASE DO NOT USE THE CAHAI.

TERMS OF USE

1. **RIGHTS GIVEN BY THE LICENSE**

   Provided you comply with all the terms and conditions of this license, Ms. Barreca grants you a royalty-free license to use the CAHAI for clinical, academic or research purposes.

2. **COMMERCIAL DEALING PROHIBITED**

   You must not sell, license or distribute copies of the CAHAI unless you have written permission from Ms. Barreca.

3. **DISCLAIMER OF WARRANTIES**

   Ms. BARRECA IS PROVIDING YOU WITH THE CAHAI "AS IS" WITH ALL FAULTS AND WITHOUT WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTIES THAT THE CAHAI IS MERCHANTIBLE, ACCURATE OR FIT FOR A PARTICULAR PURPOSE.

4. **ASSUMPTION OF RISK**

   YOU ASSUME ALL RISK AND RESPONSIBILITY FOR THE SELECTION, USE, QUALITY, PERFORMANCE, AND RESULTS OBTAINED FROM THE CAHAI.

5. **DISCLAIMER OF LIABILITIES**

   IN NO EVENT SHALL MS. BARRECA BE LIABLE TO YOU FOR ANY DAMAGES OF ANY KIND WHATSOEVER IN ANY WAY ARISING OUT OF OR IN CONNECTION WITH THE CAHAI, ITS USE OR PERFORMANCE, OR THIS LICENSE.

   BY AGREEING TO THESE TERMS AND CONDITIONS, YOU SHALL INDEMNIFY MS. BARRECA FOR ANY THIRD PARTY CLAIMS IN RELATION TO THE CAHAI.

6. **OWNERSHIP**

   Ms. Barreca owns the title, copyright and all other intellectual property rights in the CAHAI. The CAHAI is licensed to you, not sold.

7. **TERM AND TERMINATION**

   This License shall commence on the date the CAHAI is electronically or physically delivered to you. This License shall terminate immediately without notice if you fail to comply with any of the terms and conditions of this License.

8. **COMPLETE AGREEMENT**

   You acknowledge that this License is the complete and exclusive statement between you and Ms. Barreca, relating to the CAHAI, and supersedes any proposal or prior agreement, oral or written, and any other communication between us with respect to the CAHAI.

General Instructions for Administering the CAHAI

The purpose of this measure is **to evaluate the functional ability of the hemiplegic arm and hand to perform tasks** that have been identified as important by stroke survivors. It is NOT designed to measure the client's ability to complete the task using only their unaffected hand, but rather to encourage bilateral function.

Explain to your clients that some tasks are difficult and they should not get frustrated if unable to complete all the tasks. Encourage them to give their best effort using BOTH arms and hands. *The client may attempt each task twice.*

When attempting each task, always consider safety, especially for Stage I upper limb.

Standard starting position

Posture: seated in chair without armrests or in wheelchair with armrests removed, encourage erect posture, feet flat on the floor
Height of table: at the level of the last costal rib
Distance from table: client's elbow comes to the table edge
Hands: resting on the table

Variations from the standard starting position will be indicated at the top of the task page.

To ensure the client's understanding:

Every effort should be made to ensure the client understands the task.

- each task should be demonstrated once, twice if needed
- the client may be cued to use both hands twice
- the client may be reminded not to rest elbows on the table twice

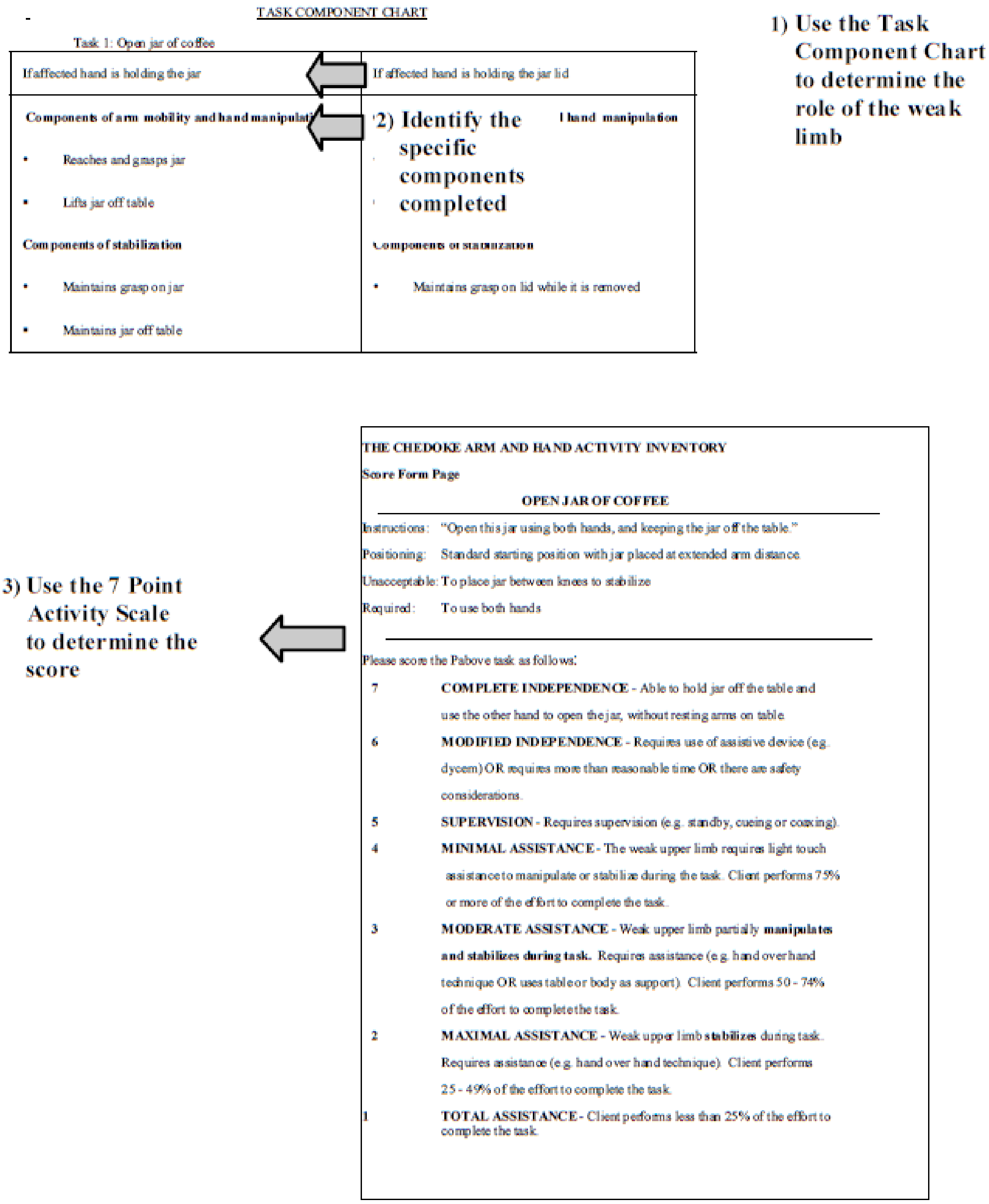
Scoring

Score the performance of the affected upper limb using the 7 point Activity scale (*fig. 1.0*). Observe the performance of the affected upper limb and:

1) Use the Task Component Chart to determine what part of the task the affected limb performed. e.g. affected hand turning the lid or affected hand stabilizing the jar
2) Identify the specific components of manipulation and stabilization the affected limb completed
3) Use the 7 point Activity Scale to determine the score.

If different performances are observed then assign the lower score. Record which part of the task the affected hand performed in order for retesting to be consistent.

Figure 1.0



TASK COMPONENT CHART

Task 1: Open jar of coffee

If affected hand is holding the jar	If affected hand is holding the jar lid
Components of arm mobility and hand manipulati	**l hand manipulation**
• Reaches and grasps jar	
• Lifts jar off table	
Components of stabilization	**Components of stabilization**
• Maintains grasp on jar	• Maintains grasp on lid while it is removed
• Maintains jar off table	

THE CHEDOKE ARM AND HAND ACTIVITY INVENTORY

Score Form Page

OPEN JAR OF COFFEE

Instructions: "Open this jar using both hands, and keeping the jar off the table."

Positioning: Standard starting position with jar placed at extended arm distance

Unacceptable: To place jar between knees to stabilize

Required: To use both hands

Please score the Pabove task as follows:

7 **COMPLETE INDEPENDENCE** - Able to hold jar off the table and use the other hand to open the jar, without resting arms on table

6 **MODIFIED INDEPENDENCE** - Requires use of assistive device (e.g. dycem) OR requires more than reasonable time OR there are safety considerations.

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing).

4 **MINIMAL ASSISTANCE** - The weak upper limb requires light touch assistance to manipulate or stabilize during the task. Client performs 75% or more of the effort to complete the task.

3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance (e.g. hand over hand technique OR uses table or body as support). Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task. Requires assistance (e.g. hand over hand technique). Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client performs less than 25% of the effort to complete the task.

THE CHEDOKE ARM AND HAND ACTIVITY INVENTORY

The Chedoke Arm and Hand Activity Inventory is designed to compliment the Chedoke-McMaster Stroke Assessment. The scoring key is similar to that used in the Functional Independence Measure (Adult FIM^{SM}).
SCORE EACH ITEM IN THE BOXES PROVIDED; THEN SUM THE SCORES AT THE END OF THE COLUMN.

DESCRIPTION OF THE LEVELS OF FUNCTION FOR THE ACTIVITY SCALE

7 **COMPLETE INDEPENDENCE** - All of the tasks are performed safely, without modification, assistive devices or aids, and within reasonable time.

6 **MODIFIED INDEPENDENCE** - Activity requires any one or more of the following: an assistive device, more than reasonable time, or there are safety (risk) considerations.

5 **SUPERVISION** - The client requires no more help than standby, cueing or coaxing, without physical contact. A helper sets up needed items or applies orthoses.

4 **MINIMAL ASSISTANCE** - With physical contact the client requires no more than touching, and client expends 75% or more of the effort.

3 **MODERATE ASSISTANCE** - Weak limb **manipulates and stabilizes** during the task. The client requires more help than touching, or expends

2 **MAXIMAL ASSISTANCE** - Weak limb stabilizes during task. The client expends less than 50% of the effort, but at least 25%.

1 **TOTAL ASSISTANCE** - The client expends less than 25% of the effort.

Score 6 if more than reasonable time is required. (e.g. more than 3 times the normal time is required)

Score 6 if assistive devices (e.g. built up handles, dycem, cock-up/ dynamic splints) are used

Score 6 if there are safety concerns in doing upper limb tasks (e.g. impulsivity, balance, poor motor control)

Score 5 if you need to cue throughout the clients' second attempt of the task

Score 4 if client touches table very briefly

Score 3 if client continually uses table for support

Score 1 if client uses only one arm/hand

Score 1 if two people are required to assist in completing task

Score 1 if you feel it is unsafe to try the task.

Administration time (approximately 30 minutes)

Questions: Please contact Susan Barreca at sbarreca@cogeco.ca or Lisa Masters at mastersl@hhsc.ca

Equipment required:

CAHAI-7 Version (Items 1-7) requires all items in Equipment List A

<u>Equipment List A</u>

- height adjustable table
- chair/wheelchair without armrests
- dycem
- 200g jar of coffee
- push-button telephone
- 12”/30cm ruler
- 8.5” x 11” paper
- pencil
- 2.3L plastic pitcher with lid
- 250 ml plastic cup
- wash cloth
- wash basin (24.5 cm. in diameter, height 8 cm.)
- Pull-on vest with 5 buttons (one side male & one side female)
- bath towel (65cm X 100cm)

CAHAI-8 Version (Items 1-8) requires all items in Equipment List A and B

<u>Equipment List B</u>

- 75ml toothpaste with screw lid, >50% full
- toothbrush

CAHAI-9 Version (Items 1-9) requires all items in Equipment List A, B, and C

<u>Equipment List C</u>

- dinner plate (Melamine or heavy plastic, 25 cm. in diameter)
- medium resistance putty
- knife and fork
- built up handles the length of the utensil handle

CAHAI-13 Version (Items 1-13) requires all items in Equipment List A, B, C, and D

<u>Equipment List D</u>

- 27”/67cm metal zipper in polar fleece poncho
- eyeglasses
- handkerchief
- Rubbermaid 38L container (50 x 37 x 27cm)
- 4 standard size steps with rail
- plastic grocery bag holding 4lb/2kg weight

Chedoke Arm and Hand Activity Inventory: Score Form

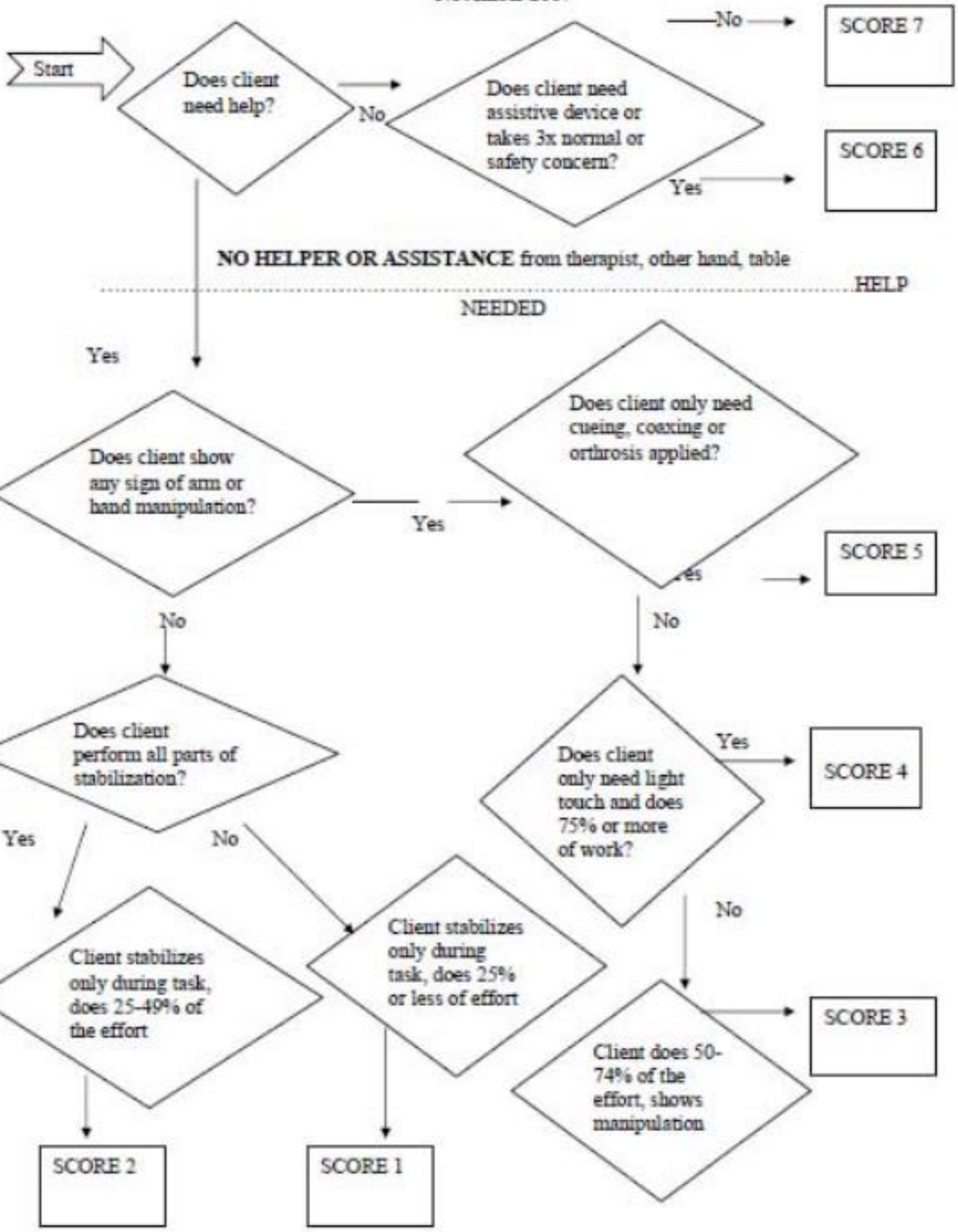
CAHAI-8 Version

Name: **Date:**

Activity Scale			
1. total assist (weak U/L < 25%) 2. maximal assist (weak U/L = 25-49%) 3. moderate assist (weak U/L = 50-74%) 4. minimal assist (weak U/L > 75%)	5. supervision 6. modified independence (device) 7. complete independence (timely, safely)		
	Affected Limb:		Score
1. Open jar of coffee	☐ holds jar	☐ holds lid	☐
2. Call 911	☐ holds receiver	☐ dials phone	☐
3. Draw a line with a ruler	☐ holds ruler	☐ holds pen	☐
4. Pour a glass of water	☐ holds glass	☐ holds pitcher	☐
5. Wring out washcloth			☐
6. Do up five buttons			☐
7. Dry back with towel	☐ reachs for towel	☐ grasps towel end	☐
8. Put toothpaste on toothbrush	☐ holds toothpaste	☐ holds brush	☐
Total Score			☐ /56
Comments			

Funded by The Ontario Ministry of Health and Long Term Care

Algorithm for application of the Chedoke Arm and Hand Activity Inventory
November 2007



THE CHEDOKE ARM AND HAND ACTIVITY INVENTORY

OPEN JAR OF COFFEE

Instructions: "Open this jar using both of your hands."
Positioning: Standard starting position with jar placed at extended arm distance.
Unacceptable: To place jar between knees to stabilize
Required: To use both hands.

Please score the above task as follows:

7 **COMPLETE INDEPENDENCE** - Able to hold jar off the table and use the other hand to open the jar, without resting arms on the table.

6 **MODIFIED INDEPENDENCE** - Requires use of assistive device (e.g. dycem) OR requires more than reasonable time OR there are safety considerations.

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing).

4 **MINIMAL ASSISTANCE** - The weak upper limb requires light touch assistance to manipulate or stabilize during the task. Client performs 75% or more of the effort to complete the task.

3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance (e.g. hand over hand technique OR uses table or body as support). Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task. Requires assistance (e.g. hand over hand technique). Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client performs less than 25% of the effort to complete the task.

TASK COMPONENT CHART

Task 1: Open jar of coffee

If affected hand is holding the jar	If affected hand is holding the jar lid
Components of arm mobility and hand manipulation • Reaches and grasps jar • Lifts jar off the table **Components of stabilization** • Maintains grasp on jar • Maintains jar off the table	**Components of arm mobility and hand manipulation** • Turns and removes lid **Components of stabilization** • Maintains grasp on lid while it is removed

CALL 911

Instructions: " Call 911 using both of your hands"
Positioning: Standard, phone placed at extended arm distance in front of client.

Please score the above task as follows:

7 **COMPLETE INDEPENDENCE** - Able to pick up receiver and hold to ear with one hand while using other hand to dial the above listed number, without resting arms on table.

6 **MODIFIED INDEPENDENCE** - Requires use of assistive device (e.g. splint) OR requires more than reasonable time to complete task OR there are safety considerations.

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing).

4 **MINIMAL ASSISTANCE** - Requires light touch assistance (e.g. to maintain phone at ear, OR to place phone in hand, OR to guide finger towards number pads). Client performs 75% or more of the effort to complete the task.

3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance (e.g. to bring the receiver to ear OR uses table as support). Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task. Requires assistance (e.g. to pick up the receiver, hold it to the ear and dial). Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client performs less than 25% of the effort to complete the task.

Task 2: Call 911

If affected hand is holding receiver	If affected hand is dialing 911
Components of arm mobility and hand manipulation • Reaches and grasps ear/mouth piece • Brings phone to ear **Components of stabilization** • Maintains sufficient grasp on phone and holds to ear	**Components of arm mobility and hand manipulation** • Reaches for buttons • Pushes individual buttons clearly

DRAW A LINE WITH A RULER

Instructions: "Draw a straight line the length of the ruler using both of your hands."
Required: Not to rest forearms on table
Positioning: Standard, pencil and ruler set at top edge of paper. Paper placed horizontally at the edge of the table.

Please score the above task as follows:

7 **COMPLETE INDEPENDENCE** - Able to pick up pencil and ruler,correctly position ruler across the page, hold ruler in place and draw a straight line the length of the ruler, without resting arms on the table.

6 **MODIFIED INDEPENDENCE** - Requires use of assistive device (e.g. splint or built up handle) OR requires more than reasonable time.

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing)

4 **MINIMAL ASSISTANCE** - Requires light touch assistance (e.g. to stabilize proximal or distal segment of upper limb) OR uses strong hand to pick up pencil or ruler and place in weak hand OR able to complete task but while drawing line with weak hand, produces an uneven line. Client performs 75% or more of the effort to complete the task.

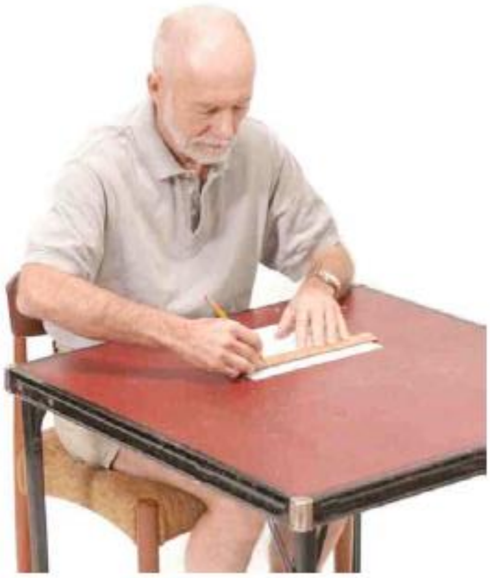
3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance (e.g. to place pencil in hand appropriately, but then able to complete task but not smoothly OR uses table as support). Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task. Requires assistance (e.g. hand over hand to maintain position of pencil in hand and then able to complete task) OR uses weak hand to stabilize ruler but not able to hold sufficiently to draw half of the line. Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client performs less than 25% of the effort to complete the task.

Task 3: Draw a line with a ruler

If affected hand is holding the ruler	If affected hand is holding the pencil
Components of arm mobility and hand manipulation • Reaches and picks up ruler • Places ruler horizontally on paper **Components of stabilization** • Places fingers on ruler • Applies sufficient force to keep ruler in place	**Components of arm mobility and hand manipulation** • Reaches and picks up pencil • In-hand manipulation to allow for writing with pencil • Drawing action along ruler **Components of stabilization** • Maintains grip on pencil



POUR A GLASS OF WATER

Instructions: "Pour a full glass of water using both of your hands."
Positioning: Standard position, 250 ml glass beside 2.3L pitcher full with water placed at extended arm length distance.

Please score the above task as follows:

7 **COMPLETE INDEPENDENCE** - Able to pick up glass and pitcher, then fill the glass with water to 2 cm. from the top without resting glass, pitcher or arms on the table.

6 **MODIFIED INDEPENDENCE** - Requires assistive device (e.g. splint) OR client stabilizes elbows only on table OR takes more than reasonable time to complete task OR there are safety considerations.

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing) Any spillage is scored as a 5.

2 **MINIMAL ASSISTANCE** - The weak upper limb requires light touch assistance (e.g. with either the glass or the pitcher in order to fill the glass with water). Client performs 75% or more of the effort to complete the task.

3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance OR client reaches for glass and holds it on table while lifting pitcher to fill glass with water. Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task. Requires assistance (e.g. hand over hand technique throughout all the components of the task). Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client initiates reaching for glass or pitcher, but unable to complete task even with hand over hand assistance. Client performs less than 25% of the effort to complete the task.

Task 4: Pour a glass of water

If affected hand is holding the glass	If affected hand is holding the pitcher
Components of arm mobility and hand manipulation • Reaches and grasps glass • Lift glass off the table **Components of stabilization** • Maintain sufficient grasp to hold the glass away from table • Maintain glass steady while pouring	**Components of arm mobility and hand manipulation** • Reaches and grasps pitcher • Lifts picture off the table • Pours water from pitcher **Components of stabilization** • Maintain sufficient grasp to hold the pitcher off the table • Maintain pitcher steady while pouring

WRING OUT WASHCLOTH

Instructions: "Wring out the washcloth using both of your hands"
Positioning: Standard position, washcloth placed in basin half full of water at table's edge.
Unacceptable: To squeeze washcloth, must use wringing action.

Please score the above task as follows:

7 **COMPLETE INDEPENDENCE** - Able to pick up washcloth from basin and wring out washcloth completely, without resting arms on the table. Therapist wrings out washcloth to ensure task is complete.

6 **MODIFIED INDEPENDENCE** - Requires more than reasonable time

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing). Any spillage is scored as a 5.

4 **MINIMAL ASSISTANCE** - The weak upper limb requires light touch assistance OR client able to wring out 75% of water from washcloth. Client performs 75% or more of the effort to complete the task.

3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance (e.g. hand over hand technique to complete the task but client able to wring out at least 50% of the water out of the washcloth OR uses table as support). Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task. Requires assistance (e.g. hand over hand) OR client holds washcloth and squeezes with the other hand (i.e. client does not perform wringing action). Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client performs less than 25% of the effort to complete the task.

Task 5: Wring out washcloth

Score the affected hand on ability to:
Components of arm mobility and hand manipulation • Reaches and grasps washcloth • Hand in wringing action **Components of stabilization** • Holds washcloth in place • Holds washcloth to permit wringing action

DO UP FIVE BUTTONS

Instructions: "Do up five buttons using both of your hands, starting at the top"
Positioning: Sitting away from table, client wearing shirt

Please score the above task as follows:

7 **COMPLETE INDEPENDENCE** - Able do up five buttons on the shirt.

6 **MODIFIED INDEPENDENCE** - Requires use of assistive device OR requires more than reasonable time OR there are safety considerations.

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing)

4 **MINIMAL ASSISTANCE** - The weak upper limb requires light touch assistance to manipulate or stabilize during the task OR client is able to fasten four buttons. Client performs 75% or more of the effort to complete the task.

3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance OR client able to fasten three buttons. Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task. Requires assistance OR able to fasten two buttons. Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client unable to fasten more than one button. Client performs less than 25% of the effort to complete the task.

Task 6: Do up five buttons

If the affected hand is holding the material	If the affected hand is holding the buttons
Components of arm mobility and hand manipulation • Reaches and grasps material • Brings sides of material together • Assists in threading the button through the holes • Releases material **Components of stabilization** • Holds and maintains grasp on material	**Components of arm mobility and hand manipulation** • Reaches and grasps buttons • Brings sides of material together • Assists in threading the button through the holes • Releases buttons **Components of stabilization** • Holds and maintains grasp on buttons

DRY BACK WITH TOWEL

Instructions: "Dry your entire back with the towel using both of your hands"
Positioning: Sitting away from table. Towel is placed on the table at extended arm distance.

Please score the above task as follows:

7 **COMPLETE INDEPENDENCE** - Able to take towel, place it over back and use both hands to maneuver towel to dry entire back.

6 **MODIFIED INDEPENDENCE** - Requires more than reasonable time OR there are safety considerations (e.g. balance).

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing)

4 **MINIMAL ASSISTANCE** - Weak upper limb requires light touch assistance to manipulate or stabilize during the task OR only dries half of back. Client performs 75% or more of the effort to complete the task.

3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance. Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task. Requires assistance. Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client performs less than 25% of the effort to complete the task.

Task 7: Dry back with towel

If the affected hand is reaching and grasping for towel	If the affected hand is grasping the towel end
Components of arm mobility and hand manipulation • Reaches and grasps towel • Manipulates towel in hand to place on back • Rubbing motion along upper and lower back **Components of stabilization** • Maintains grasp on towel sufficient to complete task	**Components of arm mobility and hand manipulation** • Grasps towel end • Manipulates towel in hand to place on back • Rubbing motion along upper and lower back **Components of stabilization** • Maintains grasp on towel sufficient to complete task

PUT TOOTHPASTE ON TOOTHBRUSH

Instructions: "Put the toothpaste on the toothbrush using both of your hands."
Positioning: Standard position, toothbrush and toothpaste positioned horizontally on table at extended arm distance.
*note: The new tube of toothpaste should be marked at half its length and the tube rolled up, as it is used, until it reaches this point. It should not be used for testing after that.

Please score the above task as follows:

7 **COMPLETE INDEPENDENCE** - Able to pick up toothpaste, undo cap, pick up toothbrush in opposite hand and apply toothpaste to toothbrush, without resting arms on the table.

6 **MODIFIED INDEPENDENCE** - Requires the use of assistive device (e.g. splint or built up handle) OR requires more than reasonable time.

5 **SUPERVISION** - Requires supervision (e.g. standby, cueing or coaxing)

4 **MINIMAL ASSISTANCE** - Requires light touch assistance (e.g. to remove cap from toothpaste OR steadying assistance while applying toothpaste). Client performs 75% or more of the effort to complete the task.

3 **MODERATE ASSISTANCE** - Weak upper limb partially **manipulates and stabilizes during task.** Requires assistance (e.g. either to place toothbrush and/or tube in hands OR unscrew cap and initiate the squeezing of the toothpaste OR uses table as support). Client performs 50 - 74% of the effort to complete the task.

2 **MAXIMAL ASSISTANCE** - Weak upper limb **stabilizes** during task.Requires assistance (e.g. hand over hand technique). Client performs 25 - 49% of the effort to complete the task.

1 **TOTAL ASSISTANCE** - Client performs less than 25% of the effort to complete the task.

Task 8: Put toothpaste on toothbrush

If affected hand is holding toothpaste	If affected hand is holding toothbrush
Components of arm mobility and hand manipulation • Reaches and grasps toothpaste • Squeezes toothpaste with enough force to get toothpaste on brush **Components of stabilization** • With sufficient force holds toothpaste while manipulating lid	**Components of arm mobility and hand manipulation** • Unscrews lid • Reaches and grasps toothbrush **Components of stabilization** • Sufficient force holding toothbrush

Université catholique de Louvain
Laboratory of Rehabilitation
and Physical Medicine

Instructions for the ABILHAND questionnaire

The ABILHAND questionnaire

The ABILHAND questionnaire was developed as a measure of manual ability as perceived by the patient. It explores the most representative inventory of manual activities. Some items were selected from existing scales; others were devised to extend the range of activities. The first application of the questionnaire in a sample of rheumatoid arthritis patients (*Arch Phys Med Rehabil 1998; 79: 1038-42*) showed that the items defined a valid manual ability scale. A second application of the questionnaire in a larger sample of chronic stroke patients showed that the unimanual activities (usually realized with one hand) were too easy for the patients. So, a subset of 23 bimanual activities (usually realized with two hands) has been retained and calibrated for chronic stroke patients (*Stroke 2001; 32: 1627-34*). ABILHAND was originally developed using the Rasch measurement model. It allows to convert ordinal scores into linear measures located on a unidimensional scale.

Procedures

The ABILHAND questionnaire is administered on an interview basis (patients do not realize the activities). Patients are asked to estimate the ease or difficulty in performing each activity, when the activities are done:
- Without other technical or human help (even if the patient actually uses help in daily life);
- Irrespective of the limb(s) actually used to do the activity;
- Whatever the strategy used (any compensation is allowed).

During the evaluation, a 3-level response scale is presented to the patients. Patients are asked to rate their perception on the response scale as either "Impossible", "Difficult" or "Easy". Activities not attempted in the last 3 months are not scored and are entered as missing responses (tick the question mark). For any activity the four potential answers are:

- ***Impossible***: the patient is unable to perform the activity without using any other help;
- ***Difficult***: the patient is able to perform the activity without any help but experiences some difficulty;
- ***Easy***: the patient is able to perform the activity without any help and experiences no difficulty;
- ***Question mark***: the patient cannot estimate the difficulty of the activity because he/she has never done the activity. Note that when a patient has never attempted the activity, the rater needs to make sure why it is so. If an activity was never attempted because it is impossible, then it must be scored as "Impossible" rather than "Question mark".

The instructions are given to the patient only at the beginning of the test. Five items are used for training in order to help the patient in feeling each level of the rating scale and in using the whole amplitude of the response scale. The subsequent activities are neither preceded nor followed by any instruction. The examiner can repeat the instructions whenever the patient shows some hesitation in answering.

Activities order

The activities of the ABILHAND questionnaire are presented in a random order to avoid any systematic effect. Ten different random orders of presentation are used. The rater must select the next one of the 10 orders for each new assessment, no matter which patient is tested.

Package content

- 1 instruction sheet;
- Testing forms in 10 random orders (10 sheets);
- Response scale presented to the patient during the evaluation (1 sheet).

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** ______________

	How DIFFICULT are the following activities?	Impossible	Difficult	Easy	?
1.	Pulling up the zipper of trousers				
2.	Peeling onions				
3.	Sharpening a pencil				
4.	Taking the cap off a bottle				
5.	Filing one's nails				
6.	Peeling potatoes with a knife				
7.	Buttoning up trousers				
8.	Opening a screw-topped jar				
9.	Cutting one's nails				
10.	Tearing open a pack of chips				
11.	Unwrapping a chocolate bar				
12.	Hammering a nail				
13.	Spreading butter on a slice of bread				
14.	Washing one's hands				
15.	Buttoning up a shirt				
16.	Threading a needle				
17.	Cutting meat				
18.	Wrapping up gifts				
19.	Fastening the zipper of a jacket				
20.	Fastening a snap (jacket, bag, ...)				
21.	Shelling hazel nuts				
22.	Opening mail				
23.	Squeezing toothpaste on a toothbrush				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 1

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** _____________

	How DIFFICULT are the following activities?	Impossible	Difficult	Easy	?
1.	Tearing open a pack of chips				
2.	Opening mail				
3.	Fastening a snap (jacket, bag, ...)				
4.	Taking the cap off a bottle				
5.	Filing one's nails				
6.	Squeezing toothpaste on a toothbrush				
7.	Peeling onions				
8.	Opening a screw-topped jar				
9.	Pulling up the zipper of trousers				
10.	Spreading butter on a slice of bread				
11.	Hammering a nail				
12.	Sharpening a pencil				
13.	Cutting one's nails				
14.	Shelling hazel nuts				
15.	Threading a needle				
16.	Washing one's hands				
17.	Buttoning up trousers				
18.	Peeling potatoes with a knife				
19.	Fastening the zipper of a jacket				
20.	Unwrapping a chocolate bar				
21.	Buttoning up a shirt				
22.	Wrapping up gifts				
23.	Cutting meat				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 2

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** _____________

	How DIFFICULT are the following activities?	Impossible	Difficult	Easy	?
1.	Wrapping up gifts				
2.	Unwrapping a chocolate bar				
3.	Filing one's nails				
4.	Spreading butter on a slice of bread				
5.	Cutting meat				
6.	Buttoning up trousers				
7.	Opening a screw-topped jar				
8.	Peeling potatoes with a knife				
9.	Pulling up the zipper of trousers				
10.	Sharpening a pencil				
11.	Threading a needle				
12.	Fastening a snap (jacket, bag, ...)				
13.	Washing one's hands				
14.	Tearing open a pack of chips				
15.	Buttoning up a shirt				
16.	Taking the cap off a bottle				
17.	Fastening the zipper of a jacket				
18.	Cutting one's nails				
19.	Hammering a nail				
20.	Opening mail				
21.	Peeling onions				
22.	Squeezing toothpaste on a toothbrush				
23.	Shelling hazel nuts				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 3

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** _____________

	How DIFFICULT are the following activities?	Impossible	Difficult	Easy	?
1.	Hammering a nail				
2.	Buttoning up a shirt				
3.	Tearing open a pack of chips				
4.	Threading a needle				
5.	Fastening a snap (jacket, bag, ...)				
6.	Fastening the zipper of a jacket				
7.	Cutting meat				
8.	Filing one's nails				
9.	Wrapping up gifts				
10.	Spreading butter on a slice of bread				
11.	Washing one's hands				
12.	Unwrapping a chocolate bar				
13.	Peeling potatoes with a knife				
14.	Pulling up the zipper of trousers				
15.	Buttoning up trousers				
16.	Squeezing toothpaste on a toothbrush				
17.	Shelling hazel nuts				
18.	Peeling onions				
19.	Opening a screw-topped jar				
20.	Taking the cap off a bottle				
21.	Opening mail				
22.	Cutting one's nails				
23.	Sharpening a pencil				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 4

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** _____________

	How **DIFFICULT** are the following activities?	**Impossible**	**Difficult**	**Easy**	**?**
1.	Tearing open a pack of chips				
2.	Filing one's nails				
3.	Unwrapping a chocolate bar				
4.	Squeezing toothpaste on a toothbrush				
5.	Pulling up the zipper of trousers				
6.	Spreading butter on a slice of bread				
7.	Fastening the zipper of a jacket				
8.	Taking the cap off a bottle				
9.	Threading a needle				
10.	Opening a screw-topped jar				
11.	Hammering a nail				
12.	Cutting one's nails				
13.	Buttoning up a shirt				
14.	Washing one's hands				
15.	Cutting meat				
16.	Wrapping up gifts				
17.	Peeling potatoes with a knife				
18.	Sharpening a pencil				
19.	Opening mail				
20.	Fastening a snap (jacket, bag, ...)				
21.	Peeling onions				
22.	Buttoning up trousers				
23.	Shelling hazel nuts				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 5

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** _____________

	How **DIFFICULT** are the following activities?	**Impossible**	**Difficult**	**Easy**	**?**
1.	Tearing open a pack of chips				
2.	Filing one's nails				
3.	Unwrapping a chocolate bar				
4.	Squeezing toothpaste on a toothbrush				
5.	Pulling up the zipper of trousers				
6.	Spreading butter on a slice of bread				
7.	Fastening the zipper of a jacket				
8.	Taking the cap off a bottle				
9.	Threading a needle				
10.	Opening a screw-topped jar				
11.	Hammering a nail				
12.	Cutting one's nails				
13.	Buttoning up a shirt				
14.	Washing one's hands				
15.	Cutting meat				
16.	Wrapping up gifts				
17.	Peeling potatoes with a knife				
18.	Sharpening a pencil				
19.	Opening mail				
20.	Fastening a snap (jacket, bag, ...)				
21.	Peeling onions				
22.	Buttoning up trousers				
23.	Shelling hazel nuts				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 5

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** ______________

	How **DIFFICULT** are the following activities?	Impossible	Difficult	Easy	?
1.	Taking the cap off a bottle				
2.	Buttoning up a shirt				
3.	Sharpening a pencil				
4.	Opening mail				
5.	Fastening a snap (jacket, bag, ...)				
6.	Washing one's hands				
7.	Tearing open a pack of chips				
8.	Wrapping up gifts				
9.	Opening a screw-topped jar				
10.	Shelling hazel nuts				
11.	Filing one's nails				
12.	Fastening the zipper of a jacket				
13.	Squeezing toothpaste on a toothbrush				
14.	Pulling up the zipper of trousers				
15.	Peeling onions				
16.	Spreading butter on a slice of bread				
17.	Cutting one's nails				
18.	Threading a needle				
19.	Cutting meat				
20.	Unwrapping a chocolate bar				
21.	Peeling potatoes with a knife				
22.	Buttoning up trousers				
23.	Hammering a nail				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 6

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** ______________

	How DIFFICULT are the following activities?	Impossible	Difficult	Easy	?
1.	Unwrapping a chocolate bar				
2.	Cutting one's nails				
3.	Filing one's nails				
4.	Shelling hazel nuts				
5.	Hammering a nail				
6.	Fastening the zipper of a jacket				
7.	Peeling potatoes with a knife				
8.	Squeezing toothpaste on a toothbrush				
9.	Sharpening a pencil				
10.	Buttoning up trousers				
11.	Fastening a snap (jacket, bag, ...)				
12.	Washing one's hands				
13.	Threading a needle				
14.	Opening mail				
15.	Pulling up the zipper of trousers				
16.	Opening a screw-topped jar				
17.	Taking the cap off a bottle				
18.	Peeling onions				
19.	Tearing open a pack of chips				
20.	Cutting meat				
21.	Wrapping up gifts				
22.	Spreading butter on a slice of bread				
23.	Buttoning up a shirt				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 7

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** _____________

	How DIFFICULT are the following activities?	Impossible	Difficult	Easy	?
1.	Washing one's hands				
2.	Tearing open a pack of chips				
3.	Opening mail				
4.	Shelling hazel nuts				
5.	Fastening the zipper of a jacket				
6.	Taking the cap off a bottle				
7.	Buttoning up a shirt				
8.	Cutting one's nails				
9.	Fastening a snap (jacket, bag, ...)				
10.	Threading a needle				
11.	Buttoning up trousers				
12.	Cutting meat				
13.	Unwrapping a chocolate bar				
14.	Wrapping up gifts				
15.	Hammering a nail				
16.	Pulling up the zipper of trousers				
17.	Filing one's nails				
18.	Peeling onions				
19.	Spreading butter on a slice of bread				
20.	Opening a screw-topped jar				
21.	Squeezing toothpaste on a toothbrush				
22.	Sharpening a pencil				
23.	Peeling potatoes with a knife				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 8

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** _____________

	How DIFFICULT are the following activities?	Impossible	Difficult	Easy	?
1.	Peeling potatoes with a knife				
2.	Washing one's hands				
3.	Peeling onions				
4.	Taking the cap off a bottle				
5.	Hammering a nail				
6.	Tearing open a pack of chips				
7.	Shelling hazel nuts				
8.	Filing one's nails				
9.	Buttoning up trousers				
10.	Spreading butter on a slice of bread				
11.	Squeezing toothpaste on a toothbrush				
12.	Wrapping up gifts				
13.	Pulling up the zipper of trousers				
14.	Sharpening a pencil				
15.	Threading a needle				
16.	Fastening the zipper of a jacket				
17.	Cutting meat				
18.	Cutting one's nails				
19.	Unwrapping a chocolate bar				
20.	Opening mail				
21.	Buttoning up a shirt				
22.	Fastening a snap (jacket, bag, ...)				
23.	Opening a screw-topped jar				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 9

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** ______________

	How **DIFFICULT** are the following activities?	Impossible	Difficult	Easy	?
1.	Buttoning up a shirt				
2.	Squeezing toothpaste on a toothbrush				
3.	Tearing open a pack of chips				
4.	Fastening a snap (jacket, bag, ...)				
5.	Opening a screw-topped jar				
6.	Opening mail				
7.	Peeling potatoes with a knife				
8.	Sharpening a pencil				
9.	Buttoning up trousers				
10.	Washing one's hands				
11.	Threading a needle				
12.	Taking the cap off a bottle				
13.	Pulling up the zipper of trousers				
14.	Cutting one's nails				
15.	Unwrapping a chocolate bar				
16.	Shelling hazel nuts				
17.	Peeling onions				
18.	Hammering a nail				
19.	Filing one's nails				
20.	Spreading butter on a slice of bread				
21.	Wrapping up gifts				
22.	Fastening the zipper of a jacket				
23.	Cutting meat				

Université catholique de Louvain, Laboratory of Rehabilitation and Physical Medicine order 10

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.