

Neurorehabilitation & Neural Repair

Phase II pragmatic randomized controlled trial of patient-led mirror therapy and lower limb exercises in acute stroke

Journal:	<i>Neurorehabilitation & Neural Repair</i>
Manuscript ID:	NNR-14-0293
Manuscript Type:	Original Research Articles
Date Submitted by the Author:	22-Aug-2014
Complete List of Authors:	Tyson, Sarah; University of Manchester, School of Nursing, Midwifery & Social Work Wilkinson, Jack; University of Manchester, Centre for Biostatistics ; Salford Royal NHS Foundation Trust, Thomas, Nessa; University of Manchester, School of Nursing, Midwifery & Social Work Selles, Ruud; Erasmus MC, Department of Rehabilitation Medicine McCabe, Candy; University of West England, ; Royal National Hospital for Rheumatic Diseases NHS Foundation Trust, Tyrrell, Pippa; University of Manchester, Stroke Research Centre, School of Nursing Midwifery & Social Work; Salford Royal NHS Foundation Trust, Vail, Andy; University of Manchester, Centre for Biostatistics ; Salford Royal NHS Foundation Trust,
Keyword:	stroke, patient-led, mirror therapy, exercise
Abstract:	<p>Background and objective: Patient-led therapy has the potential to increase the amount of therapy patients undertake during stroke rehabilitation and to enhance recovery. Our objective was to assess the feasibility and acceptability of two patient led therapies during the acute stages of stroke care: Mirror therapy for the upper limb and lower limb exercises for the lower limb.</p> <p>Methods: A blind assessed, multicentre, pragmatic randomised controlled trial of patient-led upper limb mirror therapy and patient-led lower leg exercises.</p> <p>Results: Both interventions proved feasible with >90% retention. No serious adverse events were reported. Both groups did less therapy than recommended; typically 5-15 minutes for 7 days or less. Participants receiving mirror therapy (n=63) tended to do less practise than doing lower limb exercises (n=31). Those with neglect did 69% less mirror therapy than those without, which was not observed in the exercise group (p=0.02). Observed between-group differences were modest but neglect, upper limb strength and dexterity showed some improvement in the mirror therapy group. No changes were seen in the lower limb group</p> <p>Conclusions: Both patient-led mirror therapy and lower limb exercises during in-patient stroke care are safe, feasible and acceptable and warrant further investigation. 5 to 15 minutes practise for seven days is a realistic prescription unless strategies to enhance adherence are included.</p>

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



SCHOLARONE™
Manuscripts

For Peer Review

1
2
3
4 **Phase II pragmatic randomized controlled trial of patient-led mirror therapy and lower**
5 **limb exercises in acute stroke**
6

7 ^{1,2}Sarah Tyson PhD, ^{1,3}Jack Wilkinson PhD, ^{1,2}Nessa Thomas MSc, ⁴Rudd Selles PhD,
8

9 ⁵Candy McCabe PhD, ^{1,3}Pippa Tyrrell MD, ^{1,3}Andy Vail MSc
10
11

12 ¹ Stroke Research Centre, Manchester Academic Health Sciences Centre, University of
13 Manchester, ²School of Nursing Midwifery & Social Work, ³Salford Royal NHS Foundation
14

15 Trust, ⁴Department of Plastic, Reconstructive and Hand Surgery and Department of
16
17 Rehabilitation Medicine & Physical Therapy, Erasmus MC, Rotterdam, the Netherlands,
18
19

20 ⁵University of the West England, Bristol and Royal National Hospital for Rheumatic
21
22 Diseases NHS Foundation Trust, Bath
23
24
25
26
27
28

29 **Address for correspondence:** Sarah Tyson, Stroke Research Centre, Jean McFarlane
30 Building, University of Manchester, Oxford Rd, Manchester M13 9PL.
31

32 Sarah.tyson@manchester.ac.uk
33

34 **Tel:** (0)441613067781
35

36 **Running title:** Patient led therapy in acute stroke
37

38 **4 tables and 4 figures**
39
40
41

42 **Word Count of text:** 2857
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Abstract

Background and objective: Patient-led therapy has the potential to increase the amount of therapy patients undertake during stroke rehabilitation and to enhance recovery. Our objective was to assess the feasibility and acceptability of two patient led therapies during the acute stages of stroke care: Mirror therapy for the upper limb and lower limb exercises for the lower limb.

Methods: A blind assessed, multicentre, pragmatic randomised controlled trial of patient-led upper limb mirror therapy and patient-led lower leg exercises.

Results: Both interventions proved feasible with >90% retention. No serious adverse events were reported. Both groups did less therapy than recommended; typically 5-15 minutes for 7 days or less. Participants receiving mirror therapy (n=63) tended to do less practise than doing lower limb exercises (n=31). Those with neglect did 69% less mirror therapy than those without, which was not observed in the exercise group (p=0.02). Observed between-group differences were modest but neglect, upper limb strength and dexterity showed some improvement in the mirror therapy group. No changes were seen in the lower limb group

Conclusions: Both patient-led mirror therapy and lower limb exercises during in-patient stroke care are safe, feasible and acceptable and warrant further investigation. 5 to 15 minutes practise for seven days is a realistic prescription unless strategies to enhance adherence are included.

Clinical Trial Registration Information

URL: <http://www.controlled-trials.com> Unique identifier: ISRCTN29533052.

Introduction

Rehabilitation of the upper limb after stroke is a challenge as many survivors suffer long-term upper limb deficits and few regain dexterity. Mirror therapy has been suggested as a treatment to improve upper limb function¹⁻³. It involves the seated patient placing their sound arm in front of a table mounted mirror with their weak hand behind it. When the patient looks in the mirror, the reflected image of their sound arm moving gives the visual illusion they are watching their weak hand move. This illusion is thought to enable the patient to move their weak limb more easily although the mechanism is unclear. A recent Cochrane Review of mirror therapy for people with stroke⁴ involving 14 studies and 567 participants concluded that it can improve upper limb motor function, activities of daily living, neglect and pain as an adjunct to normal rehabilitation. However most participants were in the chronic stages of stroke and there are limited data on the value of mirror therapy soon after stroke. Furthermore details of how the mirror therapy was delivered are often lacking.

These details are important when it comes to implementation in clinical practice. It is well established that most upper limb recovery occurs in the first month after stroke⁵, that rehabilitation should start as early as possible⁶ and intensity of the intervention is key to regain motor skills⁷. However UK stroke therapy typically involves low intensity, one-to-one interactions⁸ and patients rarely receive more than 45 minutes of daily therapy per discipline⁶. Consequently intensively-supervised interventions are infeasible. The challenge to improve upper limb rehabilitation is to develop interventions that can be used in the acute stages of rehabilitation, which enable patients to work intensively without direct therapist supervision.

We undertook a pragmatic phase II feasibility trial of patient-led mirror therapy during inpatient stroke care to gather information to inform a possible Phase III trial.

1
2
3 Specifically we assessed completion rates, adverse events, patient adherence and gathered
4
5 preliminary data concerning any impact on impairment and activity.
6
7
8
9

10 11 **Methods**

12
13
14 *Design:* A pragmatic assessor-blinded multi-centre controlled trial with stratified
15 imbalanced randomisation (allocation ratio 2:1) was approved by the National Ethics Service
16 and University Committees. Participants were recruited through the North-West Stroke Local
17 Research Network from in-patient stroke rehabilitation services in 12 hospitals across North-
18 West England. Eligible participants had experienced a stroke at least one week previously
19 with no pre-morbid conditions limiting upper or lower limb function, sufficient cognitive and
20 communication skills to give informed consent, and upper and lower limb weakness that
21 limited activity.
22
23
24
25
26
27
28
29
30
31

32
33 As there were no previously reported data for patient-led mirror therapy during acute
34 stroke a formal power calculation was not appropriate. Instead, we recruited sufficient
35 numbers to enable a sufficiently precise estimate of the variability (standard deviation) of
36 study endpoints for future sample size calculations and sufficient replications of the protocol
37 to assess feasibility. At least 55 participants recruited to the mirror therapy would enable
38 these objectives including a 10% drop-out. As randomisation to a control may be problematic
39 and to allow initial evaluation of effect, we also included a control group using a 2:1
40 allocation ratio (mirror: control).
41
42
43
44
45
46
47
48
49
50

51 Following informed consent, participants undertook baseline assessments before
52 randomisation using an independent web-based randomisation service so that allocation was
53 concealed. The strata for randomisation were defined by upper limb weakness (Motricity
54
55
56
57
58
59
60

1
2
3 Index <48 or 48+) and the presence of neglect (<44 on the Star Cancellation Test). Random
4
5 block sizes preserved allocation concealment. A blinded assessor repeated the assessments at
6
7 the end of the treatment period (4 weeks) and at follow up (4 weeks after the end of
8
9 treatment).

10
11
12
13
14
15
16 *Interventions:* All participants received usual care and were randomised to also
17
18 receive either patient-led mirror therapy or attentional control (patient-led lower limb
19
20 exercise without a mirror). Lower limb exercises were selected as the control to ensure both
21
22 groups received similar attention from the trial and clinical teams, thereby balancing placebo
23
24 effects. As the effects of exercise are specific to the areas exercised, exercising the lower
25
26 limb would not affect the upper limb, and vice versa. Additionally, this allowed us to make a
27
28 preliminary evaluation of a patient-led exercise as an intervention for lower limb deficits.

29
30
31
32 The mirror therapy intervention was based on that used by Michielsen et al⁹ (Figure 1)
33
34 but as the interventions needed to be ‘fit-for-purpose’ for acute care settings, the trial team
35
36 worked with consultation groups of stroke survivors and stroke therapists throughout the trial
37
38 to ensure the treatment and trial protocols were feasible and acceptable for the patients and to
39
40 fit within every-day clinical practice. It is well-established that exercise needs to be feasible
41
42 yet challenging to improve strength and motor control, so the therapies were individualised to
43
44 each patient to accommodate the wide range of abilities. For each intervention there were
45
46 four levels of exercises. For the mirror therapy the fingers, wrist and elbow movements,
47
48 reaching, and at the highest level, functional activities were exercised. The lower limb
49
50 exercises involved the ankles, knees and hips.

- 51
52
53
54
55 • Level 1 involved flexion, extension, abduction and adduction movements with limb fully
56
57 supported.
58
59
60

- Level 2 involved multi-planar multiple joint movements, some against gravity
- Level 3 involved movements against gravity
- Level 4 involved functional activities.

The most appropriate exercises were selected for each patient and instructions (with aphasia-friendly photos and written instruction) on how to perform them were put in free-standing ring binder folder which the patient kept to act as an aide-memoire (Figure 2). As the patient progressed, the redundant exercises were removed and new ones were added.

For each participant a 'local clinician' was identified to take day-to-day responsibility for supervising the interventions. The trial therapists initially taught each participant and local clinician how to do the interventions through instruction and demonstrations and selected the initial exercises with them. Participants were asked to undertake up to 30 minutes of daily practice. It was unlikely that 30 minutes of concentrated practice would be tolerable and so ways in which the practice could be undertaken "a little and often" and fitted into the routine of the rehabilitation unit (e.g. identifying times in the day/ timetable for the patient to practice) were negotiated. The local clinician checked on, and encouraged the patient's practice, dealt with any problems and progressed the exercises as necessary. They also encouraged the participants to complete the practice log sheet and completed a log of their own input. Patients who were discharged before the end of the 4 week treatment were encouraged to continue with their allocated intervention. The trial therapist rang or visited the patient twice a week to monitor adherence and the patient's progression on to more advanced exercises, as necessary. Wherever possible a carer or relative was also taught about the treatment and encouraged to assist the patient as necessary and able.

Outcome Measures: We measured the upper limb to assess the mirror therapy and the lower limb to assess the lower-limb exercises as follows:

- Upper and lower limb weakness (Motricity Index¹⁰ and grip strength¹¹)
- Upper and lower limb sensation (Rivermead Assessment of Sensory Perception, RASP¹²)
- Spasticity of biceps and gastrocnemius for the upper and lower limb respectively (Modified Ashworth Scale¹³)
- Neglect (Star Cancellation test¹⁴)

Specifically for the upper limb we measured dexterity (Box and Block¹⁵) and activity (Action Research Arm Test¹⁵). For lower limbs, we also measured mobility (Rivermead Mobility Index¹⁶) and balance (Brunel Balance Assessment¹⁷). We monitored participants' adherence using a daily self-reported exercise log. Adverse events were monitored during the treatment phase and reported using standardised forms. We also intended to record activity in everyday life (Motor Activity Log) but human error led to uninterpretable data.

Analysis: In addition to descriptive analyses, we undertook exploratory comparisons of outcome using t-tests and 95% confidence intervals for the difference in mean change from baseline to 4 and 8 weeks. To explore whether potential responders could be identified, plausible exploratory subgroup analyses of neglect, sensory impairment, weakness and balance at each time point were undertaken. Patients were excluded from a given analysis if their corresponding measurement was missing; in other respects we employed an intention to treat analysis. Multiple linear regression identified factors influencing treatment adherence. Treatment time was log transformed to satisfy the assumptions of the regression model. The included predictors were age, side of weakness, time since stroke, treatment group, neglect and sensation.

Results

Ninety-four participants were recruited; 63 and 31 to the mirror therapy and lower limb exercises respectively. Retention rate was high (90%), detailed in Figure 3. Demographic, clinical characteristics and baseline assessments are shown in Tables 1 and 2. The cohort was representative of patients in inpatient stroke care with a wide range of abilities and no major differences between groups. No serious adverse events were reported. There were eight reports of short-lived upper and lower limb aches or limb tightness.

1801 treatment sessions were recorded. Eighty-two participants (87%) recorded at least one session; 51 (81%) in the mirror therapy and 30 (97%) in the lower limb exercises group. It is not known whether participants who did not complete the exercise logs did not do any exercise or just did not complete the log. The mean (SD) number of days when the patient-led therapies were performed was 14 (sd 10, range 1- 41) days; 12.9 days (sd =9.3) for the mirror group, and 15.2 days (sd =9.5) for the lower limb group, but this difference was not significant ($p=0.294$ 95%CI = -6.64, 2.04). Twenty-one (26%) patients continued to exercise and record beyond the designated 28 day period but most practised for 7 days or fewer ($n=29$, 35%). This was slightly higher in the mirror therapy group ($n= 20$, 39%) than the lower limb exercises ($n=10$, 30%). Only two (1%) mirror therapy participants exercised for the recommended 28 days while five (15%) lower limb exercise participants achieved this. The most common duration of exercise was 5-15 minutes ($n=1054$, 59%) per session. Only 1% ($n=21$) of mirror therapy sessions and 3% ($n=40$) of lower limb exercise sessions lasted for the recommended 30 minutes.

Linear regression suggested participants with neglect in the mirror therapy group practised less than those without neglect. After adjusting for the other factors, mirror therapy group participants with neglect achieved only 31% ($p = 0.02$, 95%CI: 12, 82%) of the

1
2
3 practice time of those without neglect. There was an interaction between treatment group and
4
5 neglect ($p=0.052$) indicating that this disadvantage was not present in the lower limb exercise
6
7 group.
8
9

10 Outcome assessments at 4 and 8 weeks are shown in Tables 2, 3 and 4, and as
11
12 standardised mean differences in Figure 4. Neglect, upper limb weakness and dexterity
13
14 showed some improvement for the mirror therapy group compared to the control at the end of
15
16 treatment, which was sustained at follow up. The mirror therapy group showed less
17
18 improvement in upper limb sensation and activity than the control group. All between-group
19
20 differences were small relative to the variability of the endpoints. There was no evidence of
21
22 differences in the lower limb outcome measures (Table 4, figure 4).
23
24
25

26
27 The exploratory subgroup analyses suggested that people with neglect who received
28
29 mirror therapy had less neglect at follow up than those whom received the lower limb
30
31 exercises. The mean change (in Star Cancellation Test) was 23.5 (sd 11.3) and 10.0 (sd 8.0)
32
33 stars respectively and the difference in means was 13.5 stars ($p = 0.03$, 95% CI 1.7, 25.2). All
34
35 other explorations were non-significant.
36
37
38
39
40

41 Discussion

42
43 This study shows that patient-led mirror therapy and lower limb exercises are safe,
44
45 feasible and acceptable to patients during inpatient stroke care. Few participants achieved the
46
47 recommended 30 minutes of daily practise for 28 days. Most practised for 5-15 minutes for 7
48
49 days. The presence of neglect neglected on the amount of patient-led mirror undertaken.
50
51 Differences between groups were small but neglect, upper limb strength and dexterity
52
53 showed some greater improvement the mirror therapy group than the controls, while
54
55 sensation and upper limb activity improved less than the control group.
56
57
58
59
60

1
2
3 As an unpowered trial, significant results would not be expected. However our sample
4 size was larger than most previous trials, some of which have reported positive results⁴. The
5 current trial differs from previous reports in several other methodological details. This is the
6 first trial to specifically involve people in the acute stages of stroke. A definitive study in this
7 population may require a large sample size as any 'signal' from the mirror therapy may be
8 subsumed by the 'noise' of spontaneous recovery and standard care. Using the data from this
9 trial, we calculate that a sample size of 250 patients would be required to detect clinically
10 meaningful differences in a phase III trial.
11
12
13
14
15
16
17
18
19

20
21 Another methodological difference with previous studies is that most appear to
22 involve direct supervision from trial therapists⁴. We used patient-led mirror therapy with
23 light-touch supervision from the clinical therapy team. This provides a pragmatic indication
24 of the potential impact of mirror therapy in every-day clinical life but meant that we had little
25 control over clinicians' and participants' fidelity to the treatment protocol. There is a growing
26 recognition that this is a neglected, but crucial, element of complex intervention trials¹⁸. Clear
27 strategies to ensure fidelity is maintained and monitored in future trials are needed.
28
29
30
31
32
33
34
35
36
37

38 Participants' adherence to the intervention was less than expected, but perhaps not
39 surprising as it was largely up to the patient when to practise. In the process evaluation
40 accompanying this trial, some participants described how adherence tailed off as they became
41 bored or demotivated by lack of obvious improvement. Others, particularly those with more
42 severe strokes, struggled to complete the mirror therapy without additional help. Thus an
43 insufficient dose of therapy may be a factor. Adherence has rarely been reported to date in
44 mirror therapy trials and is generally assumed to be high, given that most trials use directly
45 supervised therapy. Future trials should comment on adherence. Our therapy delivery was
46 based on Michielsen and colleagues⁸, who used patient-led mirror therapy for people with
47 chronic stroke at home, with telephone support and weekly face-to-face contact from trial
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 therapists. They had excellent (self-reported) adherence. It may be that participants found
4
5 mirror therapy easier to undertake at home, than the cramped and busy environment of acute
6
7 stroke care, particularly while they are still very fatigued and over-whelmed by the emotional
8
9 shock of the stroke. This point was highlighted by some of our participants who continued the
10
11 mirror therapy after discharge from hospital. Additionally, a few of our participants raised
12
13 concerns that patient-led therapy may interfere with 'main-stream' rehabilitation.
14
15 Michielsens's⁹ participants had completed their rehabilitation so participation was a welcome
16
17 opportunity to access further therapy. This could have increased motivation and adherence.
18
19

20
21 The choice of control is another methodological difference from previous trials. Most
22
23 trials chose other upper limb therapies (most commonly exercises without a mirror or a sham
24
25 mirror) as the control. This provides information about whether the mirror provides an
26
27 additional benefit to exercise alone, but does not indicate the potential advantage of adding
28
29 mirror therapy to standard clinical care. As this was our primary interest, we chose an
30
31 attentional control which did not involve the upper limb. As evaluation of mirror therapy
32
33 moves from efficacy to clinical effectiveness, clinically relevant control interventions are
34
35 needed.
36
37
38
39

40 Surprisingly, although participants with neglect undertook less mirror therapy than
41
42 others, there was still a positive effect. Two recent trials have also reported a positive impact
43
44 of mirror therapy on neglect (as secondary outcomes)^{19,20}. This raises an interesting question
45
46 about the potential mechanism of mirror therapy. Trials of intensive upper limb exercises
47
48 with mirror therapy are based on motor learning theory in which intensive practice of
49
50 functional tasks is key to restoring movement and function²¹. It is hypothesised that the
51
52 mirror therapy promotes the neuroplasticity that underlies this process, possibly through
53
54 visually guided motor imagery and the mirror neuron system. Imaging studies of healthy
55
56 individuals demonstrate promotion of motor cortical activity and cortico-spinal excitation
57
58
59
60

1
2
3 with mirror therapy¹⁻³ (although a more recent fMRI study could not confirm this²², and it has
4
5 been assumed to occur in stroke survivors. However, the first imaging based evaluation of
6
7 mirror therapy involving movements of both hands in people following stroke²³ found
8
9 increased activity in the precuneus and the posterior cingulate cortex (which are associated
10
11 with body perception and spatial attention) but not in the motor cortex or mirror neuron
12
13 system, suggesting a perceptual rather than motor effect. A more recent study supports these
14
15 findings finding that mirror therapy primarily affects the sensorimotor cortex in stroke
16
17 survivors²⁴.

20
21 It is noteworthy that mirror therapy in complex regional pain syndrome (in which
22
23 neglect-like symptoms may be found²⁵) is thought to act in a similar way on the dysfunctional
24
25 somatosensory processing that underlies the condition, possibly by reversing learned disuse
26
27 and dissociation by training sustained attention to the affected limbs and/or reconciling
28
29 sensory-motor incongruence^{26,27}. A similar perception-based mechanism may be possible in
30
31 stroke, particularly those with neglect. Further work is needed to understand the mechanisms
32
33 of mirror therapy so the most appropriate patients can be targeted and treatment protocols
34
35 developed
36
37
38
39
40

41 **Conclusion:** Patient led mirror therapy and lower limb exercises are safe, feasible and
42
43 acceptable during acute stroke care and warrant further investigation. 5 to 15 minutes practise
44
45 for seven days is a realistic prescription unless strategies to enhance adherence are included.
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Garry MI, Loftus A, Summers JJ. Mirror, mirror on the wall: viewing a mirror reflection of unilateral hand movement facilitates ipsilateral M1 excitability. *Exp Brain Res* 2005;163:118-122.
2. Butefisch CM, Davis BC, Wise SP et al. Mechanisms of use-dependent plasticity in the human motor cortex. *Proc Nat Acad Sci USA* 2000;97:3661–3665
3. Muellbacher W, Facchini S, Boroojerdi B et al. Changes in motor cortex excitability during ipsilateral hand muscle activation in humans. *Clin Neurophysiol* 2000;111:344–349
4. Thieme H, Mehrholz J, Pohl M et al. Mirror therapy for improving motor function after stroke. *Cochrane Database of Systematic Reviews* 2012; 3; CD008449.
5. Nakayama H, Jørgensen HS, Raaschou HO et al. Recovery of upper extremity function in stroke patients: the Copenhagen Stroke Study. *Arch Phys Med Rehabil* 1995;76:27–32
6. Intercollegiate Stroke Working Party. *National Clinical Guideline for stroke, 4th Ed.* London: Royal College of Physicians; 2012.
7. Dept of Health (2007). *National Stroke Strategy*. www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyandguidance/dh_081062 Last accessed 10th June 2014
8. Royal College of Physicians (2007). *National Sentinel Stroke Audit. Phase I (Organisational Audit) and Phase II (Clinical Audit)* 2006. Prepared on behalf of the Intercollegiate Stroke Working Party. Royal College of Physicians, London

- 1
2
3 9. Michielsen ME, Selles RW, van der Geest JN et al. Motor recovery and cortical
4 reorganization after mirror therapy in chronic stroke patients: A phase II randomized
5 controlled trial. *Neurorehabil Neur Repair* 2011;25:223–33
6
7
- 8
9
10 10. Demeurisse G, Demol O, Robaye E. Motor evaluation in vascular hemiplegia. *Eur*
11 *Neurol* 1980;19:382-9.
12
- 13
14
15 11. Sunderland A, Tinson D, Bradley L et al. Arm function after stroke. An evaluation of
16 grip strength as a measure of recovery and a prognostic indicator. *JNNP* 1989;52:1267-
17 1272
18
- 19
20
21
22 12. Winward C, Halligan P, Wade D. The Rivermead Assessment of somatosensory
23 performance: standardisation and reliability data. *Clin Rehab* 2002;16:523-533
24
- 25
26
27
28 13. Bohannon R, Smith M. Inter-rater Reliability of a Modified Ashworth Scale of Muscle
29 Spasticity. *Phys Ther* 1987;67; 206-207
30
- 31
32
33 14. Wilson B, Cockburn J, Halligan P. Development of a behavioral test of visuo-spatial
34 neglect. *Arch Phys Med & Rehab* 1987;68:98-102
35
- 36
37
38 15. Platz T, Pinkowski C, van Wijck F et al. Reliability and validity of arm function
39 assessment with standardized guidelines for the Fugl-Meyer Test, Action Research Arm
40 Test and Box and Block Test: a multicentre study. *Clin Rehab* 2005;19; 404-411
41
42
- 43
44
45 16. Collen FM, Wade DT, Robb GF et al. The Rivermead Mobility Index: a further
46 development of the Rivermead Motor Assessment. *Int Disabil Stud* 1991;13:50–54
47
- 48
49
50 17. Tyson SF, DeSouza LH. Development of the Brunel Balance Assessment: a new
51 measure of balance disability post stroke. *Clin Rehabil* 2004;18:801–10.
52
- 53
54
55 18. Hennessey ML & Rumrill PD. Treatment fidelity in rehabilitation research. *J Voc*
56 *Rehabil* 2003;19;123–126
57
58
59
60

- 1
2
3 19. Thieme H, Bayn M, Wurg M et al. Mirror therapy for patients with severe arm paresis
4 after stroke. *Clin Rehab* 2012;27:314–324
5
6
7 20. Dohle C, Püllen J, Nakaten A et al. Mirror therapy promotes recovery from severe
8 hemiparesis. *Neurorehabil Neural Repair* 2009;23:209–217.
9
10
11 21. Van Peppen RPS, Kwakkel G, Wood-Dauphinee S et al. The impact of physical therapy
12 on functional outcomes after stroke: what's the evidence? *Clin Rehab* 2004;18:833-862
13
14
15 22. Matthys K, Smits M, Van der Geest JN et al. Mirror-induced visual illusion of hand
16 movements: a functional magnetic resonance imaging study. *Arch Phys Med Rehabil*
17 2009;90:675-81
18
19 23. Michielsen ME, Smits M, Ribbers GM et al. The neuronal correlates of mirror therapy:
20 an fMRI study on mirror induced visual illusions in patients with stroke. *J Neurol*
21 2009;217:393-398
22
23
24 24. Saleh S, Adamovich SV, Tunik E. Mirrored Feedback in Chronic Stroke Recruitment
25 and Effective Connectivity of Ipsilesional Sensorimotor Networks. *Neurorehab Neural*
26 *Repair* 2014;28:344–354
27
28
29 25. Lewis J, Kersten P, McCabe C et al. Body perception disturbance: A contribution to
30 pain in complex regional pain syndrome. *Pain* 2007;133:111-119.
31
32
33 26. McCabe C, Cohen H, Hall J et al. Somatosensory conflicts in complex regional pain
34 syndrome and fibromyalgia syndrome. *Curr Rheumat Reports* 2009;11:461-465
35
36
37 27. Maihofner C, Handwerker HO, Neundorfer B et al. Patterns of cortical reorganization in
38 complex regional pain syndrome. *Neurol* 2003;61:1707–15
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1: Baseline demographic and clinical characteristics

Characteristic		Total group (n=94)	Mirror therapy (n=62)	Lower limb exercises (n=31)
Age (years)	Median (range)	66 (26 to 92)	66 (26 to 88)	65 (40 to 91)
	Mean (sd)	64 (14)	64 (15)	64 (13)
Sex	Male	60 (65%)	37 (60%)	23 (74%)
Time since stroke (days)	Median (range)	19 (7 to 133)	18 (7 to 76)	29 (7 to 133)
	Mean (sd)	28.8 (22)	26 (18)	35 (27)
Stroke type	Ischaemic	76 (82%)	50 (81%)	26 (84%)
Side of weakness	Dominant	35 (38%)	25 (40%)	10 (32%)
Side of weakness	Right	38 (41%)	27 (44%)	11 (35%)

Patient led therapy in acute stroke

Table 2: Baseline assessments of the recruited participants

Assessment		Total group (n=94)	Mirror therapy (n=62)	Lower leg exercises (n=31)
Upper limb				
Neglect (Star Cancellation)	Median (range)		55 (9-56)	54 (8 to 56)
	Mean (SD)	47 (14)	47 (15)	48 (12)
Weakness (Motricity Index)	Median (range)	43 (1 to 93)	44 (1-93)	43 (1 to 85)
	Mean (SD)	40 (30)	40 (32)	39 (29)
Weakness (Grip strength)	Median (range)	0 (0 to 20)	0 (0-20)	0 (0 to 12)
	Mean (SD)	3 (6)	4 (7)	2 (3)
Sensation (Rivermead Assessment of Sensory Perception)	Median (range)	19 (0 to 24)	22 (0-24)	16 (0 to 24)
	Mean (SD)	16 (9)	17 (9)	14 (8)

Patient led therapy in acute stroke

Spasticity (Modified Ashworth Scale of biceps)	Median (IQR)	0 (0 to 2)	0 (0-1)	0 (0 to 2)
	Mean (SD)	1 (1)	1 (1)	1 (1)
Dexterity (Box & Block)	Median (range)	0 (0 to 36)	0 (0-36)	0 (0 to 29)
	Mean (SD)	5 (9)	5 (9)	4 (9)
Activity (Action Research Arm Test)	Median (range)	0 (0 to 57)	0 (0-57)	0 (0 to 48)
	Mean (SD)	12 (17)	13 (18)	10 (15)
Lower limb				
Weakness (Motricity Index)	Median (range)	54 (1 to 92)	59 (1-92)	48 (1 to 92)
	Mean (SD)	50 (27)	52 (27)	46 (28)
Sensation (Rivermead Assessment of Sensory Perception)	Median (range)	19 (0 to 24)	20 (0-24)	19 (0 to 24)
	Mean (SD)	16 (8)	17 (8)	15 (9)

Patient led therapy in acute stroke

Spasticity (Modified Ashworth Scale of tibialis anterior)	Median (IQR)	0 (0 to 2)	0 (0-1)	0 (0 to 2)
	Mean (SD)	1 (1)	1 (1)	1 (1)
Balance (Brunel Balance Assessment)	Median (IQR)	4 (0 to 12)	4 (3- 5)	3 (1 to 4)
	Mean (SD)	4 (3)	4 (3)	4 (3)
Mobility (Rivermead Mobility Index)	Median (range)	1 (0 to 14)	1 (0-14)	1 (0 to 7)
	Mean (SD)	3 (3)	3 (3)	2 (3)

Patient led therapy in acute stroke

Table 3: Change in upper limb outcomes at end of intervention and follow-up

Measure	Mirror therapy mean (SD)	Lower limb exercises mean (SD)	Difference (95% CI)	P value
At the end of the intervention (4 weeks)				
Neglect (Star Cancellation)	4.4 (10.8)	2 (7.4)	2.4 (-2.1, 6.8)	0.30
Weakness (Motricity Index)	9.1 (18.3)	6.8 (16.8)	2.4 (-5.8, 10.6)	0.57
Weakness (Grip strength)	1.7 (4.9)	2.8 (5.7)	-1.0 (-3.4, 1.4)	0.41
Sensation (Rivermead Assessment of Sensory Perception)	0.3 (7.7)	2.4 (6.2)	-2.1 (-5.4, 1.2)	0.21
Spasticity (Modified Ashworth Scale of biceps)	-0.0 (1.0)	-0.3 (1.1)	0.2 (-0.3, 0.7)	0.36
Dexterity (Box & Block Test)	8.2 (12.7)	6.0 (11.1)	2.2 (-3.3, 7.8)	0.42
Activity (Action Research Arm Test)	6.9 (13.9)	8.3 (12.1)	-1.4 (-7.6, 4.7)	0.64
At the end of follow up (8 weeks)				

Patient led therapy in acute stroke

Neglect (Star Cancellation)	5.9 (11.3)	3.2 (5.4)	2.7 (-1.9, 7.4)	0.24
Weakness (Motricity Index)	12.9 (20.8)	10.5 (19.9)	2.3 (-7.2, 12.0)	0.63
Weakness (Grip strength)	2.3 (6.8)	3.6 (5.4)	-1.3 (-4.4, 1.7)	0.40
Sensation (Rivermead Assessment of Sensory Perception)	2.4 (6.5)	3.3 (7.4)	-0.9 (-4.1, 2.3)	0.56
Spasticity (Modified Ashworth Scale of biceps)	-0.1 (1.1)	0.1 (1.6)	-0.2 (-0.8, 0.4)	0.51
Dexterity (Box & Block Test)	9.3 (14.9)	7.0 (12.3)	2.4 (-4.3, 9.0)	0.48
Activity (Action Research Arm Test)	8.5 (14.5)	8.8 (13.8)	-0.3 (-7.0, 6.4)	0.93

Patient led therapy in acute stroke

Table 4: Change in lower limb outcomes at end of intervention and follow-up.

Measure	Lower limb exercises (n=29)	Control (n=57)	Difference (95% CI)	P value
At the end of the intervention (4 weeks)				
Weakness (Motricity Index)	13.5 (15.4)	10.5 (16.4)	3.0 (-4.5, 10.4)	0.43
Spasticity (Modified Ashworth Scale of gastrocnemius)	0.1 (2.0)	-0.5 (1.6)	0.6 (-0.1, 1.4)	0.11
Sensation (Rivermead Assessment of Sensory Perception)	1.7 (9.1)	0.4 (8.0)	1.3 (-2.5, 5.1)	0.51
Mobility (Rivermead Mobility Index)	2.4 (2.8)	3.1 (2.9)	- 0.7 (-2.0, 0.7)	0.32
Balance (Brunel Balance Assessment)	1.9 (1.9)	2.4 (3.1)	-0.4 (-1.7, 0.8)	0.48
At the end of follow up (8 weeks)				
Motricity Index (Motricity Index)	20.3 (12.5)	16.6 (15.0)	3.7 (-3.1, 10.4)	0.28
Sensation (Rivermead Assessment of Sensory Perception)	1.9 (10.6)	1.7 (6.7)	0.2 (-3.6, 4.0)	0.93

Patient led therapy in acute stroke

Spasticity (Modified Ashworth Scale of gastrocnemius)	0.1 (1.8)	-0.3 (1.7)	0.4 (-0.4, 1.2)	0.29
Mobility (Rivermead Mobility Index)	3.0 (2.7)	3.5 (3.0)	-0.4 (-1.8, 0.9)	0.52
Balance (Brunel Balance Assessment)	3.7 (4.1)	4.1 (3.7)	-0.4 (-2.2, 1.4)	0.65

For Peer Review

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review

1
2
3 **Figure 1. The mirror in use**
4
5
6



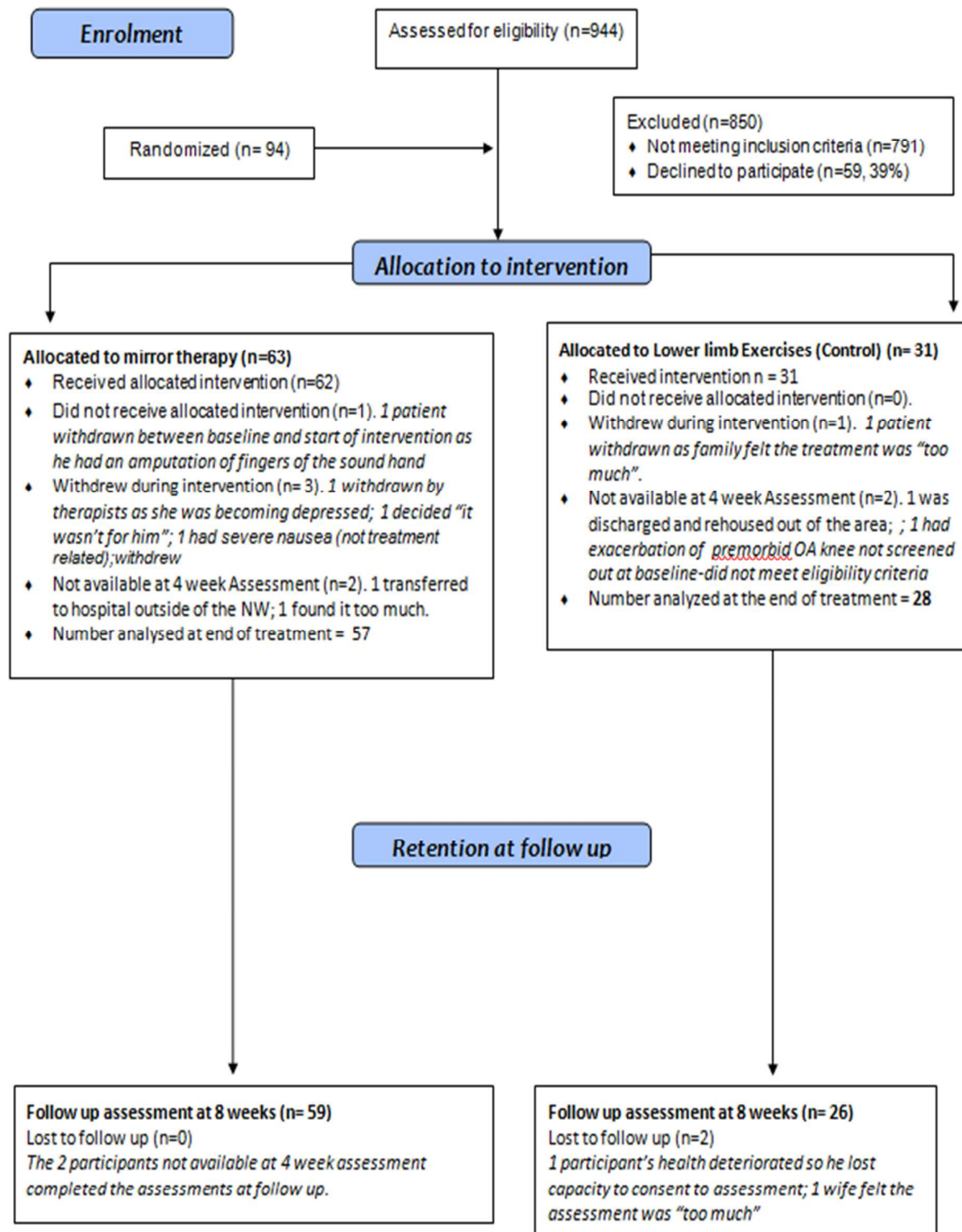
Figure 2. The exercise booklets: a) example of the exercise sheets and b) the free standing folder



Or Peer Review

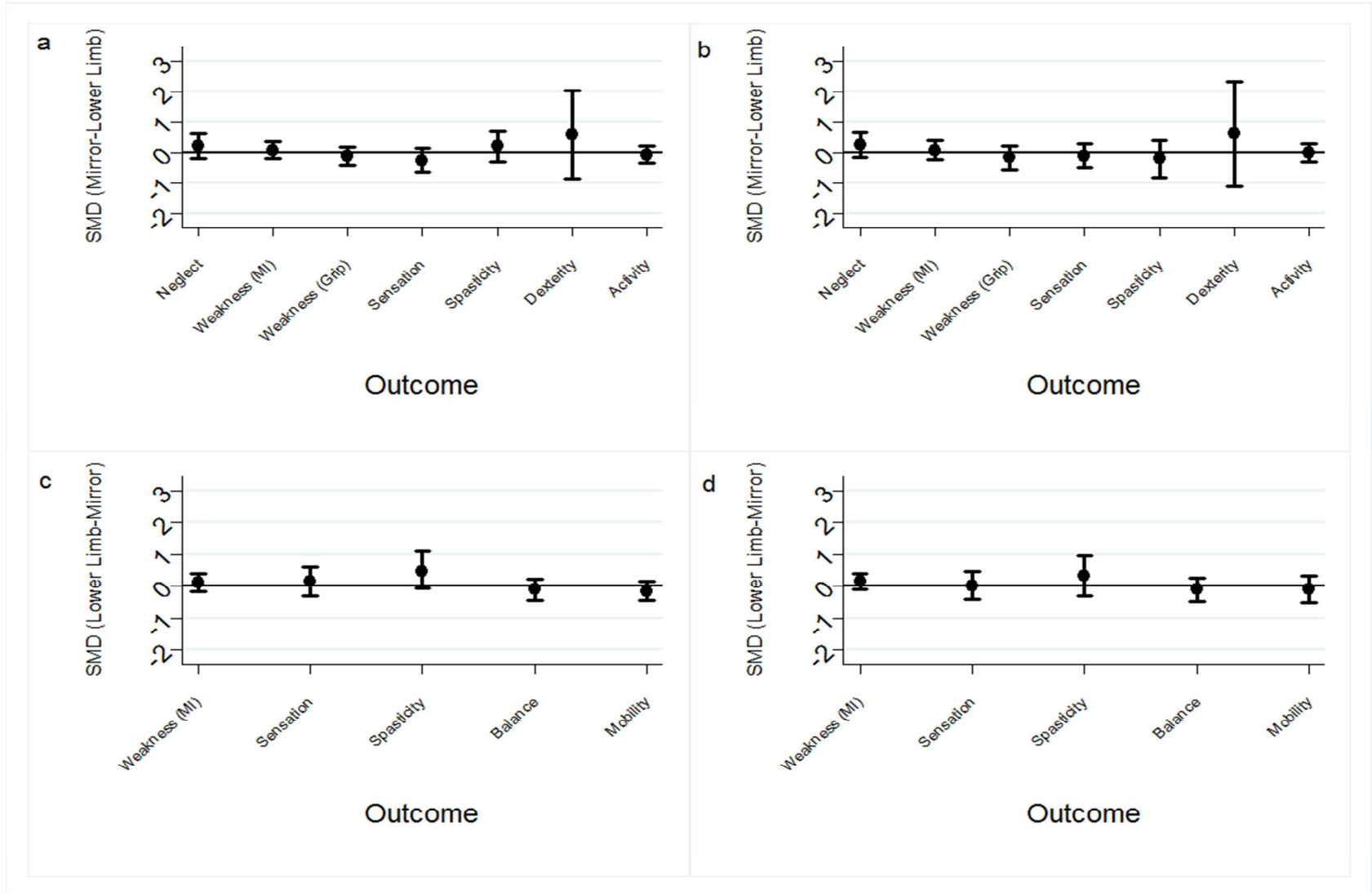
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 3. Consort Flow Diagram



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Figure 4: Standardised mean differences for upper limb outcomes (mirror therapy minus control) at A) 4 weeks and B) 8 weeks. Lower limb outcomes (lower limb exercises minus mirror therapy) at C) 4 weeks and D) 8 weeks.



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

For Peer Review