Upper Extremity Interventions

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Last Updated: March 2018

Abstract

Upper extremity complications are common following stroke and may be seriously debilitating. Regaining mobility in the upper extremities is often more difficult than in lower extremities, which can seriously impact the progress of rehabilitation. A large body of research exists around upper extremity complications but debate continues regarding the timing of treatment and adequate prognostic factors. This review provides current information regarding upper extremity interventions. Topics include robotic devices for movement therapy, virtual reality technology, spasticity treatment, EMG/biofeedback, electrical stimulation, brain stimulation, drugs and medical interventions, alternative and complementary medicine, hyperbaric oxygen therapy, and hand edema treatment. Neurodevelopmental upper extremity therapy techniques are reviewed along with other therapy options including repetitive/task-specific training, sensorimotor interventions, splinting, and constraint-induced movement therapy.
Key Points

- Attempts to regain function in the affected upper extremity should be limited to those individuals already showing signs of some recovery.
- Neurodevelopmental techniques are not superior or inferior compared with other therapeutic approaches in treatment of the hemiparetic upper extremity.
- Motor relearning programs may be superior to the Bobath method, while Brunnstrom hand manipulation treatment may be superior to motor relearning programs for patients post stroke.
- Bilateral arm training on its own or in combination with other therapies is likely not more effective for improving upper limb motor function than unilateral arm training or other conventional therapies.
- Arm training is likely more effective than leg training for improving arm function after stroke.
- Additional upper limb therapy does not appear to be superior to conventional therapy for improving upper limb motor function or functional independence.
- Strength training likely helps improve grip strength, motor function, and shoulder range of motion following stroke.
- Due to the variation of the treatment protocols, it is unclear whether repetitive task-specific training in combination with additional treatments improves upper extremity function.
- Trunk restraint may improve some aspects of upper limb motor function but not others (i.e. elbow extension, reaching trajectory, trunk displacement).
- Transcutaneous electrical nerve stimulation, vibration therapy, mesh glove, and thermal stimulation may improve upper limb motor function.
- Peripheral nerve stimulation and electroacupuncture may not improve upper limb motor function.
- Mental practice may improve upper limb motor function after stroke, while motor imagery likely does not.
- Splinting, taping, and orthoses likely do not improve upper limb motor function.
- Constraint-induced movement therapy (CIMT) may be ineffective in the acute stage of stroke, but likely effective in the chronic phase for improving upper extremity motor function.
- Modified constraint-induced movement therapy (mCIMT) may improve adaption to preserved function, but not neurological impairment in the early stage of stroke. However, mCIMT may improve upper limb motor function in the chronic phase.
- Mirror therapy is likely effective for improving upper limb motor function.
- Feedback may improve upper limb motor function post stroke.
• Evidence for the use of action observation is conflicting, although the combination of action observation with brain-computer interface-based functional electrical stimulation may be effective for upper limb motor rehabilitation.

• Music therapy may improve upper limb motor function but not muscle strength.

• Home-based rehabilitation interventions are likely not effective for improving upper limb motor function.

• Additional research is needed to evaluate the effectiveness of additional exercise therapy for upper limb motor function.

• There is conflicting evidence as to whether the use of robotic devices is effective for improving upper limb motor function.

• Virtual reality therapy may not improve upper limb motor function in chronic stroke patients.

• Computer-brain-interface technology is likely not effective for improving upper limb motor function although more research is required to come to a more definitive result.

• Hand splints alone likely do not reduce spasticity or prevent contracture.

• Stretching programs may improve upper limb spasticity.

• Botulinum toxin likely decreases spasticity, but likely does not improve upper limb motor function.

• Botulinum toxin in combination with electrical stimulation or modified constraint induced movement therapy likely improves muscle tone in the upper extremity.

• More research is needed to determine whether nerve block treatment decreases spasticity in the upper extremity.

• Physical therapy may not decrease spasticity, or pain, or contracture, or improve upper extremity motor function.

• Neuromuscular electrical stimulation (NMES) may not reduce wrist or elbow spasticity.

• Extracorporeal shockwave therapy likely improves upper limb spasticity.

• Further research is needed to determine the benefits of tolperisone on upper limb muscle tone.

• EMG/biofeedback therapy is likely not effective for improving upper limb motor function or spasticity.

• Both functional electrical stimulation (FES) and neuromuscular electrical stimulation (NMES) may help improve impaired upper extremity motor function during all phases of stroke (i.e. from acute to chronic).

• FES may be more beneficial at improving impaired motor function when delivered early (<6 months) than late (>6 months).
• There is no significant difference in the benefits observed following different NMES delivery modalities (i.e. cyclic, EMG-triggered, and passive).

• Motor Cortex Stimulation via implanted electrodes may not improve upper limb function in patients post-stroke. More studies are needed to conclude on the effectiveness of vagus nerve stimulation for upper limb motor function.

• It is unclear whether low-frequency (1 Hz) Repetitive Transcranial Magnetic Stimulation (RTMS) is effective, while high-frequency (5 Hz) and Dual RTMS Repetitive Transcranial Magnetic Stimulation is likely effective for improving upper limb motor function.

• Intermittent Theta Burst Stimulation (iTBS) may improve upper limb motor function in the acute/subacute phase as well as during the chronic phase post stroke. While iTBS may not be effective for improving dexterity in the acute/subacute phase, it is likely effective during the chronic phase.

• Continuous Theta Burst Stimulation (cTBS) may not be effective for improving upper limb motor function or dexterity after stroke.

• Anodal Transcranial Direct Current Stimulation (tDCS) is likely not effective for improving upper limb motor function, spasticity, and grip strength, with uncertainty regarding its effectiveness for dexterity.

• The effectiveness of Cathodal Transcranial Direct Current Stimulation (tDCS) remains uncertain for upper limb motor function, dexterity, and activities of daily living.

• Dual Transcranial Direct Current Stimulation is likely effective for dexterity.

• Stimulants may help improve impaired upper limb function; however, the effects may not be observed in the long term.

• More research is needed to determine the effects of Levodopa on impaired upper limb motor function.

• Stimulants may help improve impaired upper limb function; however, the effects may not be observed in the long term.

• Antidepressants may help improve impaired upper extremity motor function following a stroke.

• Further research is needed to determine if steroid injections are beneficial at reducing upper limb pain and improving range of motion following a stroke.

• Further research is needed to determine the effects of d-cycloserine on post-stroke upper extremity motor function.

• Evidence for the use of the ozonated autohemotherapy for improving post-stroke upper limb motor function is currently limited.

• Cerebrolysin may improve upper limb motor function, dexterity, and measures of independence/daily living.
• NeuroAid may not improve upper limb motor function and phosphodiesterase-5 inhibitor may not improve dexterity, grip strength, or level of independence/daily living.

• Evidence for the use of Atorvastatin for improving outcomes after stroke is limited.

• Acupuncture likely does not improve upper limb motor function or level of independence.

• Limited evidence indicates a potential benefit of meridian acupuncture on upper limb motor function, performance of activities of daily living, and pain post-stroke.

• Limited evidence regarding the use of Traditional Chinese Herbal Medicine suggests potential benefits of improved functional independence after stroke.

• Massage Therapy likely does not improve functional independence, spasticity, hand dexterity, or quality of life after stroke.

• Intermittent pneumatic compression does not appear to reduce hand edema or improve upper limb strength post stroke.
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Introduction

Impaired upper extremity function is a common and often devastating problem for stroke survivors. In the population-based Copenhagen Stroke Study (Nakayama, Jorgensen, Raaschou, & Olsen, 1994), 32% of stroke patients had severe arm paresis at admission and 37% had mild paresis. In 64 out of 491 (13%) stroke survivors, the arm remained entirely non-functional despite comprehensive rehabilitation efforts. Regaining lost function in the upper extremities may be more difficult to achieve than return of normal function (ambulation) in the lower extremities (Hiraoka, 2001). Similarly, Barecca (2001) noted that “Rehabilitation of the hemiplegic upper limb remains difficult to achieve, with only 5% of stroke survivors who have complete paralysis regaining functional use of their impaired arm and hand (Dombovy, 1993; Gowland, 1982; Kwakkel, van Dijk, & Wagenaar, 2000). Limited rehabilitation resources, time constraints, and a lack of early motor recovery in the arm and hand tend to focus therapy on improving balance, gait and general mobility.”

There is much discussion regarding which patients benefit the most from therapy. Kwakkel et al. (2003) reported that 11.6% of patients had achieved complete functional recovery at 6 months, while 38% had some dexterity. There is also evidence that motor rehabilitation of chronic stroke patients remains successful several months or years after the acute stroke (Hummelsheim & Eickhof, 1999; Kraft, Fitts, & Hammond, 1992). In terms of patients with less severe initial impairment (defined as a Chedoke-McMaster Stroke Assessment (CMSA) score of stage 4 or greater), Barecca (2001) recommended that an aggressive restorative program geared towards regaining function in the affected upper extremity be adopted (See Table 10.1.1 for the CMSA stages of motor recovery).

Table 10.1.1 Stages of Motor Recovery of the Chedoke-McMaster Stroke Assessment (Gowland et al., 1993):

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Flaccid paralysis is present. Phasic stretch reflexes are absent or hypoactive. Active movement cannot be elicited reflexly with a facilitatory stimulus or volitionally.</td>
</tr>
<tr>
<td>2</td>
<td>Spasticity is present and is felt as a resistance to passive movement. No voluntary movement is present, but a facilitatory stimulus will elicit primitive movement patterns reflexly. These primitive patterns are the stereotyped flexion and extension synergies.</td>
</tr>
<tr>
<td>3</td>
<td>Spasticity is marked. The primitive synergistic movement patterns can be elicited voluntarily, but are obligatory. In most cases, the flexion synergy dominates the arm, the extension synergy the leg. There are strong and weak components within each synergy.</td>
</tr>
<tr>
<td>4</td>
<td>Spasticity decreases. Synergy patterns can be reversed if movement takes place in the weaker synergy first. Movements combining antagonistic synergies can be performed when the prime movers are the strong components of the synergy.</td>
</tr>
<tr>
<td>5</td>
<td>Spasticity wanes, but it is evident with rapid movement and at the extremes of range. Synergy patterns can be reversed even if the movement takes place in the stronger synergy first. Movements utilizing the weak components of both synergies acting as prime movers can be performed. Most movements become environmentally specific.</td>
</tr>
<tr>
<td>6</td>
<td>Coordination and patterns of movement are near normal. Spasticity as demonstrated by resistance to passive movement is no longer present. A great variety of environmentally specific patterns of movement are now possible. Abnormal patterns of movement with faulty timing emerge when rapid or complex actions are requested.</td>
</tr>
<tr>
<td>7</td>
<td>Normal. A “normal” variety of rapid, age-appropriate complex movement patterns are possible with normal timing, coordination, strength, and endurance. There is no evidence of functional impairment compared with the normal side. There is a “normal” sensory-perceptual-motor system.</td>
</tr>
</tbody>
</table>
Previous Reviews
Two reviews pooled the results of RCTs quantitatively (Barecca et al., 2001; Hiraoka, 2001). Barecca (2001) reported the following pooled effect sizes associated with upper extremity treatments: $Z=4.87$ for sensorimotor training (including 4 RCTs); $Z=3.43$ for EMG-electrical stimulation (including 3 RCTs); and $Z=4.44$ for electrical stimulation (including 2 RCTs). Hiraoka (2001) included 14 RCTs evaluating upper extremity therapies and found an overall effect size ($d$) of 0.33, suggestive of a small to medium impact of therapy. Subgroup analyses suggested that there was no treatment effect of neurodevelopmental treatment compared with conventional physical therapy ($d=-0.01$); there was a medium effect of conventional physical therapy compared to no therapy ($d=0.51$) and a large effect of EMG biofeedback treatment compared to conventional physical therapy ($d=0.85$).

10.1 Consensus Panel Treatment and Recommendations
Barecca et al. (2001) provided consensus treatment recommendations for management of the post-stroke arm and hand, based on a synthesis of best evidence. After reviewing the evidence, the panel came to a consensus agreement that a hemiplegic upper extremity must be at least at CMSA stage 4 before full rehabilitation efforts designed to restore function in the arm are attempted. The panel concluded that attempts to rehabilitate the upper extremity of a person with a score of less than 4 will not succeed. A more palliative compensatory approach is recommended in such cases.

2001 Consensus Panel Recommendations for Patients with Severe Impairment

“For the client with severe motor, sensory and functional deficits in the involved limb after stroke, the effectiveness literature indicates that additional treatment for the upper limb will not result in any significant neurological change. The evidence to date suggests that interventions may not lead to meaningful functional use of the affected limb at this stage of motor recovery.”

1. **Maintain a comfortable, pain-free, mobile arm and hand**
   - emphasize proper positioning, support while at rest and careful handling of the upper limb during functional activities.
   - engage in classes overseen by professional rehabilitation clinicians in an institutional or community setting that teach the client and caregiver to perform self-range of motion exercises.
   - avoid use of overhead pullies that appear to contribute to shoulder tissue injury
   - use some means of external support for the upper limb in stages 1 or 2 during transfers and mobility
   - place upper limb in a variety of positions that include placing arm and hand within the client’s visual field.
   - **Use some means of external support to protect the upper limb during wheelchair use.”**

2. **To maximize functional independence, stroke survivors with persistent motor and sensory deficits and their caregivers should be taught compensatory techniques and environmental adaptations that enable performance of important tasks and activities with the less affected arm and hand.**
There is consensus opinion that in severely impaired upper extremities (less than stage 4) the focus of treatment should be on compensation.

For those upper extremities with signs of some recovery (stage 4 or better) there is consensus that attempts to restore function through therapy should be made.

Attempts to regain function in the affected upper extremity should be limited to those individuals already showing signs of some recovery.

10.2 Upper Extremity Interventions

A variety of treatment interventions to improve motor recovery in the upper extremity have been evaluated. They are presented in sections 10.2.1 to 10.2.17.

10.2.1 Neurodevelopmental Techniques

A variety of treatment approaches are in use currently. Arguably, the Bobath concept (a neurodevelopmental technique also referred to as Neurodevelopmental Treatment (NDT) is the most commonly used approach.

There are a number of approaches that are considered to be neurodevelopmental techniques. These include Bobath/NDT, Brunnstrom’s Movement Therapy and Proprioceptive Neuromuscular Facilitations. The concept of Bobath/NDT emphasizes that abnormal muscle tone or patterns should be inhibited and normal patterns should be used in order to facilitate functional and voluntary movements, which is in direct opposition to Brunnstrom’s approach. Therapy approaches aimed at the rehabilitation of the lower extremity are also discussed in Chapter 9.

<table>
<thead>
<tr>
<th>Approach</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bobath/Neurodevelopmental</td>
<td>Aims to reduce spasticity and synergies by using inhibitory postures and movements in order to facilitate normal autonomic responses that are involved in voluntary movement (Bobath 1990).</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>Brunnstrom’s Movement Therapy</td>
<td>Emphasizes synergistic patterns of movement that develop during recovery from hemiplegia. Encourages the development of flexor and extensor synergies during early recovery, assuming that synergistic activation of the muscle will result in voluntary movement (Brunnstrom 1970).</td>
</tr>
<tr>
<td>Proprioceptive</td>
<td>Emphasizes use of the patient’s stronger movement patterns to strengthen weaker motions.</td>
</tr>
</tbody>
</table>

2001 Consensus Panel Recommendations for Patients with Moderate Impairment

“For clients with moderate impairments who demonstrate high motivation and potential for functional motor gains

1. Engage in repetitive and intense use of novel tasks that challenge the stroke survivor to acquire necessary motor skills to use the involved upper limb during functional tasks and activities.

2. Engage in motor-learning training including the use of imagery.”
Neuromuscular Facilitation (PNF)  
PNF techniques use manual stimulation and verbal instructions to induce desired movement patterns and enhance motor function (Voss et al. 1985).

In their review of neurodevelopmental techniques versus other treatment approaches, Barreca et al. (2003b) included five RCTs (Basmajian et al., 1987; Dickstein, Hocherman, Pillar, & Shaham, 1986; Gelber, Josefczyk, Herrman, Good, & Verhulst, 1995; Logigian, Samuels, Falconer, & Zagar, 1983; van der Lee et al., 1999) and concluded that neurodevelopmental techniques were not superior to other types of interventions for the paretic upper limb post stroke. Van Peppen et al. (2004) conducted a systematic review of specific neurological treatment approaches and also concluded that compared to a Bobath approach, no one particular program was favoured over another with respect to improvement in functional outcomes (activities of daily living; ADLs), muscle strength, tone, or dexterity, although motor relearning programs were associated with shorter lengths of hospital stays.

Paci (2003) conducted a review of 15 trials including six RCTs and six non-RCTs and three case series to determine the effectiveness of NDT for adults with post-stroke hemiplegia. The author concluded that there is no evidence to support NDT as being the superior type of treatment.

We found twelve studies that evaluated the effectiveness of neurodevelopmental techniques, eleven of which were RCTs. Another systematic review (Luke, Dodd, & Brock, 2004) which included the results from 8 trials (5 RCTs) came to similar conclusions.

A summary of RCTs evaluating neurodevelopmental techniques are presented in Table 10.2.1.2.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platz et al. (2005)</td>
<td>RCT (8)</td>
<td>N=62</td>
<td>E1: Augmented therapy time (Arm BASIS) E2: Augmented therapy time (Bobath) C: No augmented therapy time</td>
<td>Fugl Meyer Assessment: Arm (-)</td>
</tr>
<tr>
<td>Langhammer &amp; Stanghelle (2003)</td>
<td></td>
<td></td>
<td></td>
<td>Motor Assessment Scale (+MPR) at post, (-) at 1 and 4yr follow-up</td>
</tr>
<tr>
<td>Langhammer &amp; Stanghelle (2011)</td>
<td></td>
<td></td>
<td></td>
<td>Sodring Motor Evaluation Scale (+MPR) at post, (-) at 1 and 4yr follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Life Quality Test (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Quality of Movement (+MPR)</td>
</tr>
<tr>
<td>van Vliet et al. (2005)</td>
<td>RCT (7)</td>
<td>N=120</td>
<td>E: Motor Relearning Programme (MRP) C: Bobath</td>
<td>Rivemead Motor Assessment (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Motor Assessment Scale (-)</td>
</tr>
<tr>
<td>Timmerman et al. (2013)</td>
<td>RCT (7)</td>
<td>NStart=42 NEnd=42</td>
<td>E: Regular + Mirror therapy C: Neurodevelopmental Bobath therapy</td>
<td>Frenchay Arm Test (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Functional Assessment Scale (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Wolf Motor Function Test (-)</td>
</tr>
<tr>
<td>van der Lee et al. (1999)</td>
<td>RCT (7)</td>
<td>N=66</td>
<td>E: Neurodevelopmental Therapy C: Forced-use therapy</td>
<td>Action Research Arm Test (+) forced-use</td>
</tr>
</tbody>
</table>
Walker et al. (2012)  
RCT (7)  
N\textsubscript{Start}=70  
N\textsubscript{End}=64  
E: Neuropsychological approach to dressing  
C: Dressing without a task-oriented approach  
- Nottingham Stroke Dressing Assessment (-)  
- 10-hole peg transfer test (-)

Basmajian et al. (1987)  
RCT (6)  
N=29  
E: Physical Therapy based on neuro-facilitated techniques  
C: EMG  
- Upper Extremity Function Test (-)  
- Finger Oscillation Test (-)

Pandian et al. (2012)  
6 (RCT)  
N=30  
E: Brunstrom hand manipulation treatment (BHM)  
C: Motor relearning program (MRP)  
- Fugl-Meyer Assessment for Hand (+)

Gelder et al. (1995)  
RCT (5)  
N=20  
E: Bobath  
C: Traditional techniques  
- FIM (-)  
- Box and Block Test (-)  
- Nine Hole Peg Test (-)  
- LOS (-)

Dickstein et al. (1986)  
RCT (5)  
N=131  
E1: Proprioceptive neuromuscular facilitation  
E2: Bobath  
C: Traditional techniques  
- Barthel Index (-)  
- Muscle tone (-)  
- Active Range of Motion (-)

Logigian et al. (1983)  
RCT (4)  
N=42  
E: Facilitated therapy  
C: traditional techniques  
- Barthel Index (-)  
- Manual muscle test (-)

Hafsteinsdóttir et al. (2005)  
Hafsteinsdóttir et al. (2007)  
PCT  
No Score  
N\textsubscript{Start}=326  
N\textsubscript{End}=286  
E: Neurodevelopmental Treatment (NDT)  
C: Traditional techniques  
- Barthel Index (-)  
- Quality of Life (-)  
- Health-related Quality of Life (-)  
- Visual Analogue Scale for Depression (-)

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

Discussion

The results from two recent, high quality RCTs assessing similar treatment approaches and outcomes differed. Langhammer and Stanghelle (2000) reported improvements in upper extremity function and a shorter length of hospital stay associated with motor relearning, while van Vilet et al. (2005) did not report a significant difference between treatment approaches. van Vilet et al. (2005) speculate that earlier, more intensive training provided in the Langhammer and Stanghelle (2000) study as well as a higher (albeit non-statistically significant) baseline difference may have contributed to the differences. The content of the treatment programs within the two studies may also have differed. Platz et al. (2005) failed to demonstrate an effect of augmented arm therapy (in addition to regular rehabilitation) upon motor recovery, regardless of the treatment approach (BASIS arm training or Bobath) or following passive, conventional or impairment-oriented training.

Hafsteinsdóttir et al. (2007), Dickstein et al. (1986), and Gelder et al. (1995) reported that the Bobath approach was not superior to that of non-NDT approach. There were no differences between the groups on measures of independence or quality of life. Furthermore, Timmerman et al. (2013); van der Lee et al. (1999); and Basmajian et al. (1987) noted no significant difference between neurodevelopmental techniques and various control therapies on arm motor function. Pandian et al. (2012) found that the Brunstrom hand manipulation treatment was associated with improved Fugl-Meyer Hand Assessment scores when compared to a motor relearning program.

Conclusions Regarding Neurodevelopmental Techniques
There is level 1a evidence that neurodevelopmental techniques are not superior to other therapeutic approaches.

There is level 1b evidence that when compared to the Bobath treatment approach, Motor Relearning Programme may be associated with improvements in short-term motor functioning, shorter lengths of hospital stay and better movement quality.

There is level 1b evidence that Brunnstrom hand manipulation treatment is preferable over a motor relearning program.

**Neurodevelopmental techniques are not superior or inferior compared with other therapeutic approaches in treatment of the hemiparetic upper extremity.**

**Motor relearning programs may be superior to the Bobath method, while Brunnstrom hand manipulation treatment may be superior to motor relearning programs for patients post stroke.**

### 10.2.2 Bilateral Arm Training

The use of bilateral training techniques with the upper limb following stroke has been encouraged recently with the development of new theories regarding neural plasticity. Bilateral arm training is a technique whereby patients practice the same activities with both upper limbs simultaneously. Theoretically, the use of the intact limb helps to promote functional recovery of the impaired limb through facilitative coupling effects between the upper limbs. Practicing bilateral movements may allow the activation of the intact hemisphere to facilitate the activation of the damaged hemisphere through neural networks linked via the corpus callosum (Morris et al., 2008; Summers et al., 2007).

A Cochrane review by Coupar et al. (2010), which included the results from 18 RCTs, and 549 participants, reported that there was no significant improvement in ADL function (standardized mean difference of 0.25, 95% CI: -0.14 to 0.63), functional movement of the arm (SMD=-0.07, 95% CI -0.42 to 0.28) or hand, (SMD -0.04, 95% CI -0.50 to 0.42) of bilateral arm training compared with usual care following stroke.

Cauraugh et al. (2010) conducted a meta-analysis, including the results from 25 studies, the majority of which were RCTs. The overall treatment effect was a standardized mean difference (SMD) of 0.734, representing a large effect. The effect size was influenced by the type of treatment (pure bilateral, Bilateral Arm Training with Rhythmic Auditory Cueing (BATRAC), coupled bilateral and electromyography (EMG) -triggered neuromuscular stimulation and active/passive movement using robotics). BATRAC and EMG-triggered stimulation studies were associated with the largest SMD.

Van Delden et al. (2012) evaluated the effectiveness of bilateral versus unilateral upper limb therapy and whether or not it was affected by severity of paresis. The review included the results from 9 RCTs. Pooled analyses of 452 patients were conducted for the Fugl-Meyer Assessment (FMA), Action Research Arm test (ARAT), Motor Assessment Scale (MAS) and Motor Activity Log (MAL). Across all severity categories, unilateral training was superior when outcomes were assessed using the ARAT, but there were no differences in the scores of patients who had severe or moderate paresis. There were no significant differences in improvement between groups of either severe or moderate patients on MAS or FMA scores, suggesting both training approaches were effective. Improvements in MAL scores favored patients in the unilateral training group, although only the mild subgroup was represented.
The results of controlled trials evaluating bilateral arm training are summarized in Table 10.2.2.1.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morris et al. (2008)</td>
<td>RCT (7) N=106</td>
<td>E: Bilateral training C: Unilateral training</td>
<td>• ARAT (-) • Rivermead Motor Assessment (-) • Nine Hole Peg Test (+) • Modified Barthel Index (-)</td>
</tr>
<tr>
<td>Morris &amp; van Wijck (2012)</td>
<td>RCT (7) N=106</td>
<td>E: Bilateral training C: Unilateral training</td>
<td>• 9HPT: 6wk (+), 18wk (-) • ARAT (-)</td>
</tr>
<tr>
<td>Whitall et al. (2011)</td>
<td>RCT (7) N=111</td>
<td>E: Bilateral training C: Unilateral training</td>
<td>• Fugl Meyer (-) • Wolf Motor Function Test (-)</td>
</tr>
<tr>
<td>Wu et al. (2013)</td>
<td>RCT (7) NStart=53 NEnd=53 TPS=chronic</td>
<td>E1: Bilateral robotic training E2: Unilateral robotic training C: Conventional therapy</td>
<td>• Motor Activity Log (-) • Wolf Motor Function Test (FAS subscale) (-) • ABILHAND (-)</td>
</tr>
<tr>
<td>Brunner et al. (2012)</td>
<td>RCT (7) N=30</td>
<td>E: Bilateral training C: mCIMT</td>
<td>• ARAT (-) • 9HPT (-) • Motor Activity Log (-)</td>
</tr>
<tr>
<td>Desrosiers et al. (2005)</td>
<td>RCT (7) N=41</td>
<td>E: Symmetrical bilateral tasks C: Conventional therapy</td>
<td>• Fugl Meyer (-) • Grip strength (-) • Box and Block Test (-) • Purdue Pegboard Test (-) • Finger-to-Nose Test (-) • TEMPA (-) • Functional Independence Measure (-) • The Assessment of Motor and Process Skills (-)</td>
</tr>
<tr>
<td>Yang et al. (2012)</td>
<td>RCT (7) N=21 TPS=chronic</td>
<td>E1: Unilateral robot assisted training E2: Bilateral robot assisted training C: Standard training group</td>
<td>• Fugl Meyer Score (-) • Medical Research Council (-)</td>
</tr>
<tr>
<td>Luft et al. (2004)</td>
<td>RCT (7) N=21</td>
<td>E: Bilateral arm training + rhythmic auditory cueing C: Therapeutic exercises.</td>
<td>• Fugl Meyer (-) • Wolf Motor Arm Test (-) • University of Maryland Arm Questionnaire for Stroke (-) • Elbow and Shoulder Strength (-)</td>
</tr>
<tr>
<td>Dispa et al. (2013)</td>
<td>RCT (7) NStart=10 NEnd=10</td>
<td>E: Bilateral therapy C: Unilateral therapy</td>
<td>• Fugl Meyer (-) • Purdue pegboard Test (-) • ABIL-hand questionnaire (-) • STAIS-stroke questionnaire (-)</td>
</tr>
<tr>
<td>McCombe et al. (2014)</td>
<td>RCT (7) NStart=30 NEnd=26</td>
<td>E: Bilateral + Unilateral training C: Unilateral training</td>
<td>• Wolf Motor Function Test (+) • University of Maryland Arm Questionnaire (+) • Fugl Meyer (-) • Box and Block Test (-)</td>
</tr>
<tr>
<td>Lin et al. (2010)</td>
<td>RCT (6)</td>
<td>E: Bilateral training C: Unilateral training</td>
<td>• Fugl Meyer (+) • FIM (-)</td>
</tr>
</tbody>
</table>
| N=33 | E: Active-passive bilateral therapy  
C: Self-directed motor practice | • Motor Assessment Log (-)  
• Fugl Meyer (+)  
• Grip strength (-) |
|---|---|---|
| **Stinear et al. (2008)**  
RCT (6)  
N=32 | E: Bilateral arm training with rhythmic auditory cueing  
C: Dose matched unilateral therapeutic exercises | • Fugl Meyer Assessment (-)  
• Wolf Motor Function Test (-)  
• Stroke Impact Scale: Post-intervention (-); 4mo follow up: Emotion (-), Hand (-), Strength (-), Total score (+)  
• Isokinetic strength: Elbow extension (-)  
• Isometric strength: Shoulder extension (-); Wrist extension (+); Elbow flexion (-) |
| **Whitall et al. (2011)**  
RCT (6)  
N\text{Start}=111  
N\text{End}=92 | E: Active-passive bilateral therapy  
C: Self-directed motor practice | • Motor Function Test (+)  
• Box and Block Test (+)  
• Modified Rankin Scale (-)  
• Functional Independence Measure (-)  
• Activities of Daily Living (-)  
• Mobility (-)  
• Fatigue (-)  
• Stroke Impact Scale (+) |
| **van Delden et al. (2015)**  
RCT (6)  
N\text{Start}=60  
N\text{End}=52 | E1: Modified CIMT + unilateral training  
E2: Rhythmic movement + bilateral training  
C: Control | • Motor Assessment Log (+)  
• Unimanual reference task: E1 vs. E2 (+); E1 vs. C (+) |
| **Lee et al. (2013)**  
RCT (6)  
N\text{Start}=26  
N\text{End}=26 | E: Bilateral training + Nervous system rehabilitation  
C: Nervous system rehabilitation | • Motor Function Test (+)  
• FIM (+)  
• Affected hand amount of sedentary and moderate activity (+) |
| **Stinear et al. (2014)**  
RCT (6)  
N\text{Start}=57  
N\text{End}=51 | E: Bilateral training  
C: Cutaneous electrical stimulation (no neurophysiological effects) | • Modified Ashworth Scale (-)  
• Stroke Impact Scale (-) |
| **Shim et al. (2015)**  
RCT (6)  
N\text{Start}=20  
N\text{End}=20 | E: Bilateral training  
C: Unilateral training | • Motor Function Test (+)  
• FIM (+)  
• Affected hand amount of sedentary and moderate activity (+) |
| **van Delden et al. (2013)**  
RCT (6)  
N\text{Start}=60  
N\text{End}=55 | E1: Modified CIMT + unilateral training  
E2: Rhythmic movement + bilateral training  
C: Control | • Action Research Arm Test (-)  
• Nine Hole Peg Test (-)  
• Motricity Index (-)  
• Fugl Meyer (-)  
• Motor Activity Log (-)  
• Stroke Impact Scale: bilateral vs. control for emotion (+), strength (+)  
• Motor Activity Log - Amount of Use and Quality of Movement: E1 vs. E2/C (+); E2 vs. C (-) |
| **Hsieh et al. (2016)**  
RCT (6)  
N\text{Start}=31  
N\text{End}=31 | E: Bilateral arm priming + task-oriented training  
C: Task-oriented training alone | • Fugl-Meyer Assessment (-)  
• Box and Block Test (-)  
• Grip Strength (-)  
• Modified Rankin Scale (-)  
• Functional Independence Measure (-)  
• Activities of Daily Living (-)  
• Mobility (-)  
• Fatigue (-)  
• Stroke Impact Scale (+) |
| **Wu et al. (2011)**  
RCT (5)  
N=66 | E1: dCIT  
E2: Bilateral training  
C: Control | • Normalized Movement Unit for unilateral and bilateral tasks: E1/E2 vs. C (+); E1 v. E2 (-)  
• Peak Velocity for unilateral and bilateral tasks: E2 vs. C (+); E1 vs. E2/C (-)  
• Wolf Motor Function Test- Time and Functional Ability: E1 vs. C (+); E1/C vs. E2 (-)  
• Motor Activity Log- Amount of Use and Quality of Movement: E1 vs. E2/C (+); E2 vs. C (-) |
| **Song et al. (2015)**  
RCT (6)  
N\text{Start}=20  
N\text{End}=20 | E1: Task-oriented bilateral arm training  
C: Control | • Box and Block Test (+)  
• Motor Activity Log (+)  
• Modified Ashworth Scale (-)  
• Stroke Impact Scale (-)  
• Functional Independence Measure (-)  
• Activities of Daily Living (-)  
• Mobility (-)  
• Fatigue (-)  
• Stroke Impact Scale (+) |
RCT (5)
N<sub>Start</sub>=40
N<sub>End</sub>=40

| E2: BATRAC | • Jepsen Taylor Hand Function Test (+)
| • Modified Barthel Index (+) |

Stoykov et al. (2009)
RCT (5)
N=21

| E: Bilateral training | • Motor Assessment Scale (-)
| C: Unilateral training | • Motor Status Scale (-) |

Summers et al. (2007)
RCT (5)
N=12

| E: Bilateral training | • Modified Motor Assessment Scale (+) |
| C: Unilateral training |

Cauraugh & Kim (2002)
RCT (5)
N=25

| E1: Electrical stimulation + bilateral training | • Box and Block Test: E1 vs. E2/C (+); E2 vs. C (+) |
| E2: Electrical stimulation + unilateral training | C: Control |

Byl et al. (2013)
RCT (5)
N<sub>Start</sub>=18
N<sub>End</sub>=15

| E: Bilateral orthosis | • Upper Limb Fugl Meyer Assessment (-) |
| C: Unilateral orthosis |

Han & Kim (2016)
RCT (5)
N<sub>Start</sub>=25
N<sub>End</sub>=25

| E: Bilateral arm training | • Box and Block Test (-)
| C: Unilateral arm training | • Elbow Amplitude (-)
| | • Shoulder Amplitude (+) |

Singer et al. (2013)
RCT (4)
N<sub>Start</sub>=24
N<sub>End</sub>=21

| E: Bilateral training + EMG-ES | • Fugl Meyer (-) |
| C: Unilateral training + EMG-ES | • Arm Motor Ability Test (-) |

Kim et al. (2013)
RCT (3)
N=15

| E1: Bilateral robotic training | • Fugl-Meyer Assessment (-) |
| E2: Unilateral robotic training | C: Usual Care |

Anandabai et al. (2013)
PCT
N<sub>Start</sub>=30
N<sub>End</sub>=30

| E: Bimanual training | • Fugl Meyer (-) |
| C: Unilateral training | • Wolf Motor Function Test (-) |

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion
In a large multicentre RCT, Whitall et al. (2011) evaluated the effect of bilateral arm training on upper limb functional recovery. Results failed to show a difference between bilateral training and unilateral training, indicating that training with both arms does not provide additional benefits for improving impairment in the affected upper limb (Whitall et al., 2011). While the results of another large RCT also found no significant difference between bilateral arm training and unilateral arm training interventions in arm function, finger dexterity was improved in the bilateral arm training group (Morris et al., 2008). In addition to these, many additional studies including those by Dispa et al. (2013), Stoykov et al. (2009), Han & Kim (2016), Desrosiers et al. (2005), Byl et al. (2013), and Anandabai et al. (2013) have found no difference between bilateral arm training and unilateral training on various functional outcomes. Bilateral training was also shown to have no significant effect when compared to cutaneous electrical stimulation (Stinear et al., 2014). Some studies show conflicting evidence when comparing bilateral training to unilateral training and various other conventional therapies, with some outcomes being no different while others favoring the bilateral arm training group (K. C. Lin et al., 2010; McCombe Waller et al., 2014; Stinear et al., 2008). On the other hand, studies by Shim et al. (2015) and Summers et al. (2007) found significant differences between the groups in favour of the bilateral arm training group,
although both of these studies had very small sample sizes, indicating low validity and credibility due to insufficient power.

Coupling bilateral arm training with rhythmic auditory cueing (BATRAC) was also found to be non-superior over conventional therapy with regards to its effectiveness on upper limb motor function in both chronic and acute stroke patients (Luft et al., 2004; van Delden et al., 2015; van Delden et al., 2013). However, van Delden et al. (2013) found that the BATRAC group had a significantly more favourable score on the Stroke Impact Scale than conventional therapy. This suggests that while the BATRAC protocol may not improve functional outcomes, it may provide improvements on measures of independence.

Overall, studies reveal that in comparison with modified constraint-induced movement therapy (mCIMT) delivered alone or in combination with other treatment, bilateral arm training does not improve upper limb motor function (Brunner et al., 2012; van Delden et al., 2013). Distributed constraint-induced therapy (dCIT) has been found to evoke significantly greater changes in the Motor Activity Log measure compared to bilateral arm training and to conventional therapy in one study (Wu et al., 2011); however, the apparent lack of effectiveness of mCIMT suggests that more research is needed to come to a definitive conclusion about dCIT (van Delden et al., 2013).

In one study, when bilateral arm training was supplemented with electrical stimulation, findings revealed an improvement in manual dexterity and function when compared to a control group (Cauraugh & Kim, 2002). However, no significant difference in general arm motor function was found when this treatment was compared with unilateral arm training (Singer et al., 2013). Due to low methodological quality and statistical power, further evidence is required to come to a conclusion regarding the effectiveness of bilateral training with electrical stimulation.

According to three studies (H. Kim et al., 2013; C. Y. Wu, C. L. Yang, et al., 2013; Yang CL, 2012), bilateral robotic training did not improve motor function significantly more than unilateral robotic training or conventional therapy.

In a recent study by Hsieh et al. (2016), bilateral arm priming was coupled with task-oriented training and was compared to task-oriented training alone. The results indicated that there was no significant difference between groups in terms of motor function, although there was a significant benefit in measures of independence for the bilateral arm training group. When bilateral training was coupled with nervous system rehabilitation, it was also shown to improve independence in participants when compared to nervous system rehabilitation alone (M.-H. Lee et al., 2013).

Conclusions Regarding Bilateral Arm Training

There is level 1a evidence that bilateral training is not more effective than unilateral training for upper limb motor function outcomes.

There is level 1a evidence that bilateral training is not more effective than conventional therapies such as modified constraint induced movement therapy and cutaneous electrical stimulation.

There is level 1a evidence that bilateral arm training with rhythmic auditory cueing (BATRAC) is not more effective than unilateral arm training.
Bilateral arm training on its own or in combination with other therapies is likely not more effective for improving upper limb motor function than unilateral arm training or other conventional therapies.

10.2.3 Arm and Leg Training
In this section, we examined studies that investigated the effectiveness of providing arm training in comparison to leg training for upper limb function.

The results of controlled trials evaluating arm training versus leg training are summarized in Table 10.2.3.1.

Table 10.2.3.1 Summary of Controlled Trials Evaluating Arm and Leg Training for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blennerhassett &amp; Dite (2004b)</td>
<td>RCT (9) N=30</td>
<td>E1: Upper extremity task related practice E2: Lower extremity task-related practice (1 hour a day x 5 days x 4 weeks)</td>
<td>• Jebsen Taylor Hand Function (+) • Motor Assessment Scale (+)</td>
</tr>
<tr>
<td>Kwakkel et al. (1999)</td>
<td>RCT (8) N=101</td>
<td>E1: Arm training E2: Leg training</td>
<td></td>
</tr>
<tr>
<td>Higgins et al. (2006)</td>
<td>RCT (8) N=47</td>
<td>E1: Upper extremity task related practice E2: Lower extremity task-related practice (90 min x 3 sessions/week x 6 weeks)</td>
<td></td>
</tr>
<tr>
<td>Sanchez-Sanchez et al. (2017)</td>
<td>RCT (8) NStart=15 NEnd=14</td>
<td>E1: Upper extremity function training E2: Lower extremity function training</td>
<td></td>
</tr>
<tr>
<td>Mares et al. (2014)</td>
<td>RCT (8) NStart=52 NEnd=44</td>
<td>E1: Functional strength training for upper limb E2: Functional strength training for lower limb</td>
<td></td>
</tr>
<tr>
<td>Pang et al. (2006)</td>
<td>RCT (7) NStart=63 NEnd=60</td>
<td>E1: Arm training E2: Leg training</td>
<td></td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion
Based on the results of 5 randomized controlled trials, additional upper extremity task practice, function training or strength training offers significantly greater benefits in arm function than what is obtained from comparable leg rehabilitation (Blennerhassett & Dite, 2004a; Kwakkel et al., 1999; Mares et al., 2014; Pang et al., 2006; Sánchez-Sánchez et al., 2017). One study by Higgins et al. (2006) found no significant difference between upper extremity and lower extremity task practice on the Box and Block Test, a measure of function and dexterity for the upper body.

Conclusions Regarding Arm and Leg Training
There is level 1a evidence that arm function training, task practice, and strength training provide significant functional improvements in the arm after stroke in comparison to similar leg training.

Arm training is likely more effective than leg training for improving arm function after stroke.

10.2.4 Additional/Enhanced Therapy

In this section, we examined studies that investigated the effectiveness of providing supplementary therapy targeting the upper extremity in addition to usual care or conventional therapy.

The results of controlled trials evaluating additional/enhanced therapy are summarized in Table 10.2.4.1.

Table 10.2.4.1 Summary of Controlled Trials Evaluating Additional/Enhanced Therapy for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
</table>
| Kwakkel et al. (1999) | RCT (8) | N=101 | E1: Arm training  
E2: Leg training  
C: Conventional therapy | • Action Research Arm Test: E1 vs C (+)  
• Barthel Index: E1 vs C (-) |
| Ross et al. (2009) | RCT (8) | NStart=39  
NEnd=37 | E: Additional task-specific motor training  
C: Standard care | • Action Research Arm Test (-)  
• Summed Manual Muscle Test (-) |
| Harris et al. (2009) | RCT (8) | N=103 | E: Graded repetitive upper limb supplementary program (GRASP)  
C: Education | • Chedoke Arm and Hand Activity Inventory (+)  
• Grip Strength (+)  
• Paretic Upper Limb Use (+) |
| Duncan et al. (2003) | RCT (8) | N=92 | E: Supervised home program  
C: Usual care | • Fugl Meyer Score (-)  
• Grip Strength (-)  
• Functional Reach (-)  
• Wolf Motor Function Test (-) |
| Lincoln et al. (1999) | RCT (7) | N=282 | E: Additional physiotherapy  
C: Routine physiotherapy | • Rivermead Motor Assessment (arm) (-)  
• Action Research Arm Test (-)  
• Barthel Index (-) |
| English et al. (2015) | RCT (7) | NStart=283  
NEnd=261 | E1: Group Circuit Classes of task-specific training days a week  
E2: Usual Physiotherapy 7 days a week  
C: Individual Physiotherapy 5 days a week | • Wolf Motor Function Test (-)  
• Functional Independence Measure (-)  
• Stroke Impact Scale (-)  
• Health related quality of life (-) |
| Platz et al. (2001) | RCT(7) | N=60 | E: Arm ability training  
C: Routine therapy | • Test d’Évaluation des Membres Supérieurs d’Personnes Âgées (TEMPA) (+) |
| Liu et al. (2014) | RCT (7) | NStart=46  
NEnd=44 | E: Self-regulation  
C: Conventional functional rehabilitation | • FIM motor (+)  
• FIM: cognitive (-)  
• Fugl Meyer: upper limb (-), lower limb (-) |
| Rodgers et al. (2003) | RCT (7) | | E: Stroke unit care + enhanced upper limb rehab  
C: Conventional stroke unit care | • Action Research Arm Test (-)  
• Motricity Index (-) |
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N Start</th>
<th>N End</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donaldson et al. (2009)</td>
<td>RCT (6)</td>
<td>30</td>
<td>19</td>
<td>E: Functional strength training + conventional therapy C: Conventional therapy</td>
<td>• Frenchay Arm Test (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Upper limb pain (-)</td>
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<td></td>
<td>• Barthel Index (-)</td>
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<td></td>
<td>• Nottingham E-ADL (-)</td>
</tr>
<tr>
<td>Han et al. (2013)</td>
<td>6 (RCT)</td>
<td>32</td>
<td></td>
<td>E1: 1 hour of standard arm training per day</td>
<td>• Fugl Meyer Score: E3 vs. E1 (+); E3 vs. E2 (-); E1 vs. E2 (+)</td>
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<tr>
<td></td>
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<td></td>
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<td>E2: 2 hours of standard arm training per day</td>
<td>• Barthel Index (-)</td>
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<td></td>
<td>E3: 3 hours of standard arm training per day</td>
<td></td>
</tr>
<tr>
<td>Sunderland et al. (1992)</td>
<td>RCT (6)</td>
<td>32</td>
<td></td>
<td>E: Enhanced therapy C: Conventional therapy</td>
<td>• Extended Motricity Index: 6mo (-)</td>
</tr>
<tr>
<td>Sunderland et al. (1994)</td>
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<td>• Motor Club Assessment: 6mo (-)</td>
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<td>• Nine Hole Peg Test: 6mo (-)</td>
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<td>• Frenchay Arm Test: 6mo (-)</td>
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<tr>
<td>De Diego et al. (2013)</td>
<td>RCT (6)</td>
<td>21</td>
<td>21</td>
<td>E: Conventional training + home training C: Conventional training</td>
<td>• Fugl Meyer Score (-)</td>
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<tr>
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<td>• Motor Activity Log (-)</td>
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<td></td>
<td>• Stroke Impact Scale (-)</td>
</tr>
<tr>
<td>Fluet et al. (2014)</td>
<td>RCT (6)</td>
<td>41</td>
<td>40</td>
<td>E: Hand + finger training C: Finger training</td>
<td>• Wolf Motor Function Test (-)</td>
</tr>
<tr>
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<td>• Jebsen Taylor Hand Test (-)</td>
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<td></td>
<td>• Kinematic measures of shoulder and elbow function: Finger fractionation; Hammer-Task simulation (Time-to-task completion; Reaching trajectory smoothness; End point deviation) (+)</td>
</tr>
<tr>
<td>Repsaite et al. (2015)</td>
<td>RCT (5)</td>
<td>27</td>
<td>27</td>
<td>E: Differential training + standard rehabilitation C: Standard rehabilitation</td>
<td>• Wolf Motor Function Test (+)</td>
</tr>
<tr>
<td>Trombly et al. (1986)</td>
<td>RCT (4)</td>
<td>20</td>
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<td>E1: Resisted Grasp</td>
<td>• Range of Motion (-)</td>
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<td></td>
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<td>E2: Resisted Extension</td>
<td>• Speed of Reversal of Movement (-)</td>
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<td></td>
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<td>C: Ballistic Extension</td>
<td>• Ability to Rapidly Reverse Movement (-)</td>
</tr>
<tr>
<td>Dickstein et al. (1997)</td>
<td>RCT (3)</td>
<td>27</td>
<td></td>
<td>E: Repeated movement therapy C: Conventional therapy</td>
<td>• Barthel Index (-)</td>
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<td>• Fugl Meyer Score (-)</td>
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<td></td>
<td>• Frenchay Tests (-)</td>
</tr>
<tr>
<td>Mazzoleni et al. (2013)</td>
<td>PCT</td>
<td>64</td>
<td>64</td>
<td>E: Shoulder/elbow training + wrist training C: Shoulder/elbow training</td>
<td>• Fugl Meyer (-)</td>
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<tr>
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<td>• Motricity Index (-)</td>
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<td>• Movement velocity (+)</td>
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<td>• Movement distance (-)</td>
</tr>
<tr>
<td>Smedes et al. (2014)</td>
<td>PCT</td>
<td>18</td>
<td>18</td>
<td>E: Manual mobilization therapy + conventional therapy C: Conventional therapy</td>
<td>• Passive wrist extension (+)</td>
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<td>• Active wrist extension (+)</td>
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<td></td>
<td>• Frenchay Arm Test (+)</td>
</tr>
<tr>
<td>Minagawa et al. (2015)</td>
<td>PCT</td>
<td>18</td>
<td>18</td>
<td>E: Hair brushing movement + conventional therapy</td>
<td>• Range of Motion: shoulder abduction (+), external rotation (+)</td>
</tr>
</tbody>
</table>

10. Upper Extremity Interventions  www.ebrsr.com  pg. 20 of 208
Discussion

A variety of treatments were delivered in varying durations and intensities, making general conclusions difficult to draw for additional therapy of the upper limb in general. Additionally, most of the interventions were non-specific in nature.

The majority of RCTs examined found no significant difference between additional therapy and conventional therapy for upper limb motor function (Dickstein et al., 1997; Donaldson et al., 2009; English et al., 2015; Lincoln et al., 1999; Rodgers et al., 2003; Ross et al., 2009). The additional therapies studied included task-specific motor training, enhanced rehabilitation, and functional strength training, among other more broadly defined therapies. Studies by Duncan et al. (2003) and De Diego et al. (2013) found that there was no significant improvement in motor function in participants receiving a therapist-supervised home program, or a home training program, respectively, in comparison to those receiving usual care. Self-regulation was also not found to be superior to conventional rehabilitation on motor function or on measures of independence, except for the FIM motor subsection (Liu & Chan, 2014). Results from a Cochrane review agree with these findings, suggesting no statistically significant result related to the use of home-based therapy programmes on the functional improvement of the upper limb (Coupar, Pollock, Legg, Sackley, & van Vliet, 2012). However, the conclusions derived from this Cochrane review are based on only four poor quality studies, suggesting that future higher-quality RCTs are needed prior to making clinical recommendations.

Kwakkel et al. (1999) found that arm training provided additional improvements in upper limb motor function than conventional therapy, as did Platz et al. (2001), Han et al. (2013), and Repsaite et al. (2015). An RCT by Harris et al. (2009) found that Graded repetitive upper limb supplementary program (GRASP) was superior to education on the Chedoke Arm and Hand Activity Inventory, as well as for grip strength and paretic upper limb use. However, this result should be interpreted with caution because the control group did not receive a conventional active therapy.

Variation between studies may account for some of the differences in results between studies. For example, Han et al. (2013) demonstrated a significant difference in arm motor function between groups receiving only 1 hour of arm training a day and those receiving 2 or 3 hours a day, with no significant difference between those receiving 2 and 3 hours of training a day. This indicates the relevance of duration within interventions for upper limb rehabilitation. Furthermore, Sunderland et al., (1992) and (1994) also demonstrated that participants may differ in outcome after the same intervention based on stroke severity. They found that while participants who had sustained a severe stroke did not improve significantly more from enhanced therapy than those in the conventional therapy group, those with mild stroke, had made significant gains on the Extended Motricity Index and the Nine Hole Peg Test. Therefore, because of the large variation between studies on so many variables, it can be difficult to come to a definite conclusion for all additional therapies.

Conclusions Regarding Additional/Enhanced Therapies

There is level 1a evidence that additional upper limb therapy is not superior to conventional therapy at improving upper extremity motor function or functional independence.
There is level 1b evidence that a therapist-supervised in-home program is not more effective than usual care at improving upper limb motor function.

Additional upper limb therapy does not appear to be superior to conventional therapy for improving upper limb motor function or functional independence.

10.2.5 Strength Training

Studies which evaluated treatments directed at specifically increasing strength in the upper extremity have been compiled below. A much larger pool of studies has been published on strength training in the lower extremity.

RCTs that evaluated strength training and assessed measures of strength, are summarized in Table 10.2.5.1.

Table 10.2.5.1 Summary of RCTs Evaluating Strength Training for Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Da Silva (2015)</td>
<td>RCT (8)</td>
<td>NStart=20 NEnd=20</td>
<td>E: Strength training C: Standard care</td>
<td>• TEMPA (+) • Glumerohumeral flexion strength (+) • Active shoulder Range of Motion (+) • Fugl Meyer Scores (+)</td>
</tr>
<tr>
<td>Hendy &amp; Kidgell (2014)</td>
<td>RCT (7)</td>
<td>NStart=10 NEnd=10</td>
<td>E1: Anodal tD CS + strength training E2: sham tD CS C: Anodal tDCS</td>
<td>• Extensor carpi radialis strength (+)</td>
</tr>
<tr>
<td>Patten et al. (2013)</td>
<td>USA RCT (7) N=19</td>
<td>E: Functional Task Practice and Power Training C: Functional Task Practice</td>
<td>• Wolf Motor Function Test (-) • Ashworth Scale (-) • Functional Independence Measure (+)</td>
<td></td>
</tr>
<tr>
<td>Corti et al. (2012)</td>
<td>RCT (7) N=14</td>
<td>E1: Power Training E2: Functional Task Practice</td>
<td>• Shoulder Flexion and Elbow Extension (+)</td>
<td></td>
</tr>
<tr>
<td>Lin et al. (2015)</td>
<td>RCT (7) NStart=33 NEnd=33</td>
<td>E: Bilateral Isometric Handgrip Force Training with Visual Feedback C: Routine Therapy</td>
<td>• Fugl-Meyer Assessment-Upper Extremity (+) • Wolf Motor Function Test (+) • Motor Assessment Scale (+) • Barthel Index (+)</td>
<td></td>
</tr>
<tr>
<td>Thielman et al. (2013b)</td>
<td>RCT (6) NStart=16 NEnd=16</td>
<td>E: Progressive resistive strength training C: Task-related training</td>
<td>• Activate range of motion for shoulder and elbow (+) • Wolf Motor Function Test at 1 yr (+) • Reaching at 1 yr (+)</td>
<td></td>
</tr>
<tr>
<td>Trombly et al. (1986)</td>
<td>RCT (4) N=20</td>
<td>E1: Resisted Grasp E2: Resisted Extension C: Ballistic Extension</td>
<td>• Finger Extension Range of Motion (-) • Speed of Reversal of Movement (-) • Ability to Rapidly Reverse Movement (-)</td>
<td></td>
</tr>
<tr>
<td>Awad et al. (2015)</td>
<td>RCT (4) NStart=30 NEnd=23</td>
<td>E: Shoulder Strength Training, Trunk Control Training, and Additional Strengthening Exercises. C: Shoulder Strength Training and Trunk Control</td>
<td>• Shoulder Abduction Peak Torque (+) • Shoulder External Rotator Peak Torque (+) • Supraspinatus Peak Force (+) • Upper Trapezius Peak Force (+)</td>
<td></td>
</tr>
</tbody>
</table>
Discussion
Strength training was found to improve motor function and shoulder range of motion of the impaired upper extremity in studies by (Awad et al., 2015; da Silva et al., 2015; C. H. Lin et al., 2015; Thielman, 2013b). Additionally, Weinstein et al. (2004) found that strength training and functional task practice offered similar improvements in motor function when compared to standard care. However, a study by Patten et al. (2013) found that when functional task practice and power training were combined, there was no significant difference on motor function outcomes when combined to functional task practice alone.

Hendy & Kidgell (2014) found a significant increase in extensor carpi radialis strength from strength training, while Corti et al. (2012) found that power training offered greater shoulder flexion and elbow extension than functional task practice. On the other hand, Trombly et al. (1986) found that there was no significant difference in finger range of motion observed after patients received resisted grasp, resisted extension, or ballistic extension.

Harris & Eng (2010) conducted a systematic review and meta-analysis of strength training on upper limb strength, function and ADL performance following stroke. Fourteen studies were identified in total, of which six (306 subjects) evaluated the effect on grip strength. There was a significant effect associated with training (standardized mean difference=0.95, 95% CI 0.05 to 1.85, p=0.04). Two trials assessed other measures of strength with conflicting results.

Conclusions Regarding Strength Training

There is level 1a evidence from a meta-analysis that strength training increases grip strength following stroke.

There is level 1a evidence that strength training improves upper limb motor function and shoulder range of motion.

Strength training likely helps improve grip strength, motor function, and shoulder range of motion following stroke.

10.2.6 Repetitive/Task-Specific Training Techniques
It is well established that task-specific practice is required for motor learning to occur (Schmidt, 1991). According to Classen et al. (1998), focal transcranial magnetic stimulation and functional magnetic resonance imaging have shown that task-specific training, in comparison to traditional stroke rehabilitation, yields long-lasting cortical reorganization specific to the corresponding areas being used. More specifically, Karni et al. (1995), using functional magnetic resonance imaging, and Classen et al. (1998), using transcranial magnetic stimulation, both reported a slowly evolving, long-term, experience-dependent reorganization of the adult primary motor cortex following daily practice of task-specific motor activities. Also of interest is that task-specific sessions (i.e., thumb and hand movements), as short as 15 minutes in duration, are also effective in inducing lasting cortical representational changes.
(Bütefisch, Hummelsheim, Denzler, & Mauritz, 1995; Classen et al., 1998). According to Page (2003), intensity alone does not account for the differences between traditional stroke and task-specific rehabilitation. For example, Galea et al. (2001) reported that stroke patients who underwent a 3-week long program consisting of 45-minute task-specific, upper limb training showed improvements in measures of motor function, dexterity, and increased use of the more affected upper limbs. According to Page (2003), other, task-specific, low-intensity regimens designed to improve use and function of the affected limb have also reported significant improvements (Smith et al., 1999; Whitall et al., 2000; Weinstein et al., 2001).

A summary of controlled trials evaluating repetitive/task-specific training are presented in Table 10.2.6.1.

Table 10.2.6.1 Summary of Controlled Trials Evaluating Repetitive/Task-Specific Techniques for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arya et al., (2012)</td>
<td>MTST Trial RCT (9)</td>
<td>NStart=103, NEnd=102</td>
<td>E: Task-specific training C: Standard training using the Bobath approach</td>
<td>Fugl Meyer Score (+) Action Research Arm Test (+)</td>
</tr>
<tr>
<td>Kim et al., (2015)</td>
<td>RCT (8)</td>
<td>NStart=44, NEnd=40</td>
<td>E: Target reach training with visual biofeedback, routine occupational and physical therapy C: Routine occupational and physical therapy</td>
<td>Fugl-Meyer Upper Extremity (+) Wolf Motor Function Test (+) Reaching speed (+) Range of Motion of the shoulder (+) Reach distance (-)</td>
</tr>
<tr>
<td>Hung et al., (2016)</td>
<td>RCT (8)</td>
<td>NStart=21, NEnd=21</td>
<td>E: Robotic training + task-specific training C: Robotic training + impairment oriented training</td>
<td>Fugl-Meyer Assessment (+) Stroke Impairment Scale (+)</td>
</tr>
<tr>
<td>Graef et al., (2016)</td>
<td>RCT (8)</td>
<td>NStart=28, NEnd=27</td>
<td>E: Task-oriented training C: Non task-oriented training</td>
<td>Upper-Extremity Performance Test (+) Shoulder Strength (-) Grip Strength (-) Shoulder Active Range of Motion (-) Fugl-Meyer Assessment (-) Modified Ashworth Scale (-)</td>
</tr>
<tr>
<td>Shimodzono et al., (2013)</td>
<td>RCT (7)</td>
<td>NStart=52, NEnd=49</td>
<td>E: Repetitive functional exercise C: Conventional rehabilitation</td>
<td>Action Research Arm Test (+) Grasp and pinch (+) Fugl Meyer (+)</td>
</tr>
<tr>
<td>Cauraugh &amp; Kim, (2003)</td>
<td>RCT (6)</td>
<td>N=64</td>
<td>E1: Blocked practice + active stimulation E2: Random practice + active stimulation C: No active stimulation assistance</td>
<td>Box and Block Test (+) Reaction Time (+)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>N Start</td>
<td>N End</td>
<td>Intervention Details</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------</td>
<td>---------</td>
<td>-------</td>
<td>--------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Hubbard et al. (2015)         | RCT (6)| 16      | 16    | E: Task-specific training and standard care  
C: Standard Care                                                                       | • Upper Limb Motor Assessment Scale (-)  
• Modified Rankin Scale (-)                                                    |
| Thielman (2012)               | RCT (6)| 16      | 16    | E1: Task-Related Training  
E2: Resistive Exercise Training  
C: Conventional therapy  
• Motor Activity Log (-)  
• Visual Analogue Scale (-)  
• Ashworth Scale (-)  
• Upper Limb Motor Assessment Scale (-)  
• Modified Rankin Scale (-)  
• Wolf Motor Function Test (-)  
• Fugl Meyer Assessment (-) |
| Kim et al. (2016)             | RCT (6)| 20      | 20    | E: Electromyogram triggered neuromuscular stimulation with task oriented training on paretic arm  
C: Electromyogram triggered neuromuscular stimulation  
• Upper Limb Motor Assessment Scale (+)  
• Modified Rankin Scale (+)  
• Fugl-Meyer Assessment (+)  
• Box and Block Test (+)  
• Jebsen-Taylor Hand Function Test for short sentences and stacking checkers (+)  
• Action Research Arm Test (+)  
• Grip Strength (+) |
| Thielman et al. (2013a)       | RCT (6)| 16      | 16    | E1: Task-Related Training  
E2: Resistive Exercise Training  
C: Conventional therapy  
• Motor Activity Log (-)  
• Visual Analogue Scale (-)  
• Ashworth Scale (-)  
• Upper Limb Motor Assessment Scale (-)  
• Modified Rankin Scale (-)  
• Wolf Motor Function Test (-)  
• Fugl Meyer Assessment (-) |
| Brkic et al. (2016)           | RCT (5)| 24      | 22    | E: Repetitive upper limb functional task practice  
C: Conventional rehabilitation  
• Action Research Arm Test (+)  
• Grip Strength (+) |
| Boyd et al. (2010)            | RCT (5)| 18      |       | E: General arm training  
C: Conventional rehabilitation  
• Change in reaction and movement time (+)                                    |
| Jeon et al. (2016)            | RCT (5)| 12      | 12    | E: Repetitive bilateral and unilateral movements with strength exercises  
C: Conventional rehabilitation  
• Flexion and abduction range of motion (+)  
• Visual analogue scale (+) |
| Lang et al. (2016)            | RCT (5)| 85      | 82    | E1: 3200 repetitions of task-specific upper limb training  
E2: 6400 repetitions of task-specific upper limb training  
E3: 9600 repetitions of task-specific upper limb training  
C: Individualized maximum repetitions  
• Action Research Arm Test (-)  
• Stroke Impact Scale (-)  
• Canadian Occupational Performance Measure (-)  
• Likert Scale evaluating perceived change and its meaningfulness (-)  
• Motor Activity Log: E1/E2 vs. E3/C (+)  
• Wolf Motor Function Test: E1/E2 vs. E3/C (+) |
| Taub et al. (2013)            | RCT (5)| 45      | 40    | E1: Shaping training + transfer package (TP)  
E2: Repetitive task practice + TP  
E3: Repetitive task practice  
C: Shaping training  
• Motor Activity Log: E1/E2 vs. E3/C (+)  
• Wolf Motor Function Test: E1/E2 vs. E3/C (+) |
| Song et al. (2015)            | RCT (5)| 40      | 40    | E1: Task-oriented bilateral arm training  
E2: BATRAC  
• Box and Block Test (+)  
• Jebsen Taylor Hand Function Test (+)  
• Modified Barthel Index (+) |
| Thielman et al. (2004)        | RCT (4)| 12      |       | E: Progressive resistive exercises  
C: Task-related training  
• Kinematic analysis of arm movement (+)  
• Modified Ashworth Scale (-)  
• Rivermead Motor Assessment (-) |
| Mani et al. (2014)            | PCT    | 30      | 30    | E1: Right hemisphere damage (RHD) reaching tasks  
E2: Left hemisphere damage (LHD) reaching tasks  
• Arm performance: contralesional (-), ipsilateral (-)  
• Leftward reaching frequency: E1 vs. E2 (+)  
• Action Research Arm Test (-)  
• Stroke Impact Scale (-)  
• Canadian Occupational Performance Measure (-)  
• Likert Scale evaluating perceived change and its meaningfulness (-)  
• Motor Activity Log: E1/E2 vs. E3/C (+)  
• Wolf Motor Function Test: E1/E2 vs. E3/C (+) |

10. Upper Extremity Interventions
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urbin et al. (2015)</td>
<td>E1: Task-specific training as an inpatient (13 sessions)</td>
<td>• Action Research Arm Test (+; E1)</td>
</tr>
<tr>
<td></td>
<td>E2: Task-specific training as an outpatient (28 sessions)</td>
<td>• Use ratio, magnitude ratio, variation ratio, median paretic upper extremity acceleration magnitude, upper extremity acceleration variability (+; E1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Higher acceleration metric in ratio, magnitude ratio, variation ratio, median paretic upper extremity acceleration magnitude, upper extremity acceleration variability (+; E2)</td>
</tr>
<tr>
<td>Tretriluxana et al. (2015)</td>
<td>E: Observation for 6 min, perform task for 4 min. for 4 sessions</td>
<td>• Movement time (-)</td>
</tr>
<tr>
<td></td>
<td>C: Observation for 1 min, perform task for 1 min. for 24 sessions.</td>
<td>• Reaction Time (-)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

**Discussion**

The majority of studies investigating task-specific training found a significant improvement in upper limb motor function. Of note is a study by Arya et al. (2012), with a large sample size, in which task-specific training was compared to standard training, and was found to be superior on the Fugl Meyer Assessment and the Action Research Arm Test. Similarly, Kim et al. (2015) compared target reach training with visual biofeedback to conventional therapy, while Hung et al. (2016) compared task-specific training with robotic training to impairment-oriented training with robotic training, with both groups finding a significant improvement in the group receiving task-specific training. Shimodozono et al. (2013) likewise found a significant improvement for upper limb motor outcomes in those receiving repetitive function exercise in comparison to conventional therapy, while Kim et al. (2016) found a similar finding when comparing EMG-NMES with task-oriented training to EMG-NMES alone.

Some studies also found no significant difference on upper limb motor function outcomes between groups receiving task-oriented therapy and those receiving other therapies or conventional therapy. For example, Graef et al. (2016) found that those receiving task-oriented training did not have significantly improved grip strength, range of motion, upper limb motor function, and spasticity. The study by Winstein et al. (2016), also known as the ICARE Trial, is a very large, multicenter trial which found that structured, task-oriented upper extremity training did not offer significant improvements in upper limb motor function when compared to those receiving dose-equivalent occupational therapy, or to those receiving monitoring-only occupational therapy. Likewise, Zondervan et al. (2014) found that self-guided, high-repetition home therapy with a mechanical arm exerciser did not provide significantly improved upper limb motor function in comparison to conventional therapy, while Thielman et al. (2012) found a similar result when comparing task-related training to resistive exercise training.

Barreca et al. (2003a) reviewed 2 studies (Bütefisch et al., 1995; Dickstein et al., 1997) which investigated repetitive training for the upper extremity, including repeated practice of elbow, wrist and finger flexion and extension, concluding that there was a positive treatment effect found.

A recent Cochrane review authored by French et al. (2007) evaluated the effect of task-specific training on both upper and lower-extremity function. Trials were included if one of the intervention arms included “an active motor sequence [that] was performed repetitively within a single training session, and where the practice was aimed towards a clear functional goal.” Eight and five RCTs, respectively,
were identified that assessed arm and hand function. Pooled results indicated that task-specific training was not associated with improvement in either hand or arm function. The standardized mean differences were small (0.17 and 0.16) and not statistically significant. A more recent Cochrane review, including 14 trials, also found that there was no significant improvement on measures of hand or arm motor function (French et al., 2010).

Timmermans et al. (2010) conducted a review that examined the effectiveness of task-oriented training following stroke. Fifteen components were identified to characterize task-oriented training. They included exercises that were functional, directed towards a clear goal, repeated frequently, performed in a context-specific environment, and followed by feedback. Sixteen studies representing 528 patients were included. From 3 to 11 training components were reported within the included studies. The components associated with largest effect sizes were "distributed practice" and "feedback". There was no correlation between the number of task-oriented training components used in a study and the treatment effect size. "Random practice" and "use of clear functional goals" were associated with the largest effect sizes at follow-up.

Many of the treatments reviewed were non-specific in nature, not well described and were evaluated on patients at different stages of neurological recovery. Sample sizes were generally small. Furthermore, the interventions varied across studies, severely limiting comparability. Often, multiple outcomes were assessed, some of which demonstrated a benefit, while others did not; typically there was improvement on impairment level outcomes, which did not transfer to functional improvements (disability level). The conclusions that we draw pertain only to the subset of interventions that were assessed, and cannot be generalized to any other specific treatment.

Conclusions Regarding Repetitive Task-Specific Training Techniques

There is level 1a evidence that task-related practice may be superior to conventional training at improving upper extremity motor function.

There is level 1b evidence that task-related training may not be superior to resistive training or bilateral arm training at improving general upper limb motor function; however, it may improve reaching arm movements.

There is level 1b evidence that combining task practice with active stimulation may improve manual dexterity and reaction time.

Due to the variation in the treatment protocols, it is unclear whether repetitive task-specific training in combination with additional treatments improves upper extremity function.

10.2.7 Trunk Restraint

Reaching movements performed with the affected arm in patients are often accompanied by compensatory trunk or shoulder girdle movements, which extend the reach of the arm (Michaelis, Luta, Roby-Brami, & Levin, 2001). Restriction of compensatory trunk movements may encourage recovery of “normal” reaching patterns in the hemiparetic arm when reaching for objects placed within arm’s length (Michaelis & Levin, 2004). Several trials have evaluated the effectiveness of trunk restraint combined with task-specific training to improve the movement quality of reaching tasks.

The results of RCTs evaluating trunk restraint therapy are summarized in Table 10.2.7.1.
Table 10.2.7.1 RCTs Examining Trunk Restraint to Improve Upper Limb Motor Function

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bang et al. (2015)</strong> RCT (9) N&lt;sub&gt;Start&lt;/sub&gt;=18 N&lt;sub&gt;End&lt;/sub&gt;=18</td>
<td>E: CIMT + trunk resistant training C: CIMT</td>
<td>• Action Research Arm Test (+) • Fugl Meyer (+) • Modified Barthel Index (+) • Motor Activity Log: Amount of Use (+), Quality of Movement (+)</td>
</tr>
<tr>
<td><strong>Lima et al. (2014)</strong> RCT (8) N&lt;sub&gt;Start&lt;/sub&gt;=22 N&lt;sub&gt;End&lt;/sub&gt;=15</td>
<td>E: mCIMT + trunk resistant training C: mCIMT</td>
<td>• Motor Activity Log: Amount of Use (-), Quality of Movement (-) • Bilateral Activity Assessment Scale (-) • Wolf Motor Function Test (-) • Global strength (-) • Stroke Specific Quality of Life Scale (-) • Reach and grasp (-)</td>
</tr>
<tr>
<td><strong>Michaelsen et al. (2006)</strong> RCT (7) N&lt;sub&gt;Start&lt;/sub&gt;=30 N&lt;sub&gt;End&lt;/sub&gt;=10</td>
<td>E: Trunk-restraint with object-related reach-to-grasp training C: Non-restraint training</td>
<td>• Upper extremity performance test (+) • Fugl Meyer Arm Section (+) • Box and Block Test (-)</td>
</tr>
<tr>
<td><strong>de Oliveira et al. (2015)</strong> RCT (7) N&lt;sub&gt;Start&lt;/sub&gt;=22 N&lt;sub&gt;End&lt;/sub&gt;=20</td>
<td>E: Trunk resistant training with harness C: Trunk resistant training without harness</td>
<td>• Modified Ashworth Scale (-) • Fugl Meyer Score (-) • Barthel Index (-)</td>
</tr>
<tr>
<td><strong>Wu et al. (2012)</strong> RCT (5) N=57</td>
<td>E1: CIMT + trunk restraint E2: CIMT C: Control</td>
<td>• Kinematics: E1&amp;E2 vs. C (+) • Action Research Arm Test: E1&amp;E2 vs. C (+) • Fugl Meyer: E1&amp;E2 vs. C (+)</td>
</tr>
<tr>
<td><strong>Woodbury et al. (2009)</strong> RCT (5) N=11</td>
<td>E: CIMT + trunk restraint C: CIMT</td>
<td>• Fugl Meyer (-) • Wolf Motor Function Test (-) • Kinematic analyses of reaching (+)</td>
</tr>
<tr>
<td><strong>Wu et al. (2012)</strong> 5 (RCT)</td>
<td>E1: Distributed constraint-induced therapy and trunk restraint E2: Distributed constraint-induced therapy C: Dose-matched control intervention</td>
<td>• Action Research Arm Test: E1/E2 vs C (+) • Frenchay Activities Index: E1/E2 vs C (+) • Hand domain of Stroke Impact Scale: E1/E2 vs C (+) • Motor Activity Log (+)</td>
</tr>
<tr>
<td><strong>Michaelsen &amp; Levin (2004)</strong> RCT (5) N=28</td>
<td>E: Trunk restraint group C: No restraint</td>
<td>• Velocity peak, wrist peak velocity (-) • Movement time and time to peak velocity (-) • Trunk rotation (-) • Shoulder horizontal adduction and shoulder flexion (-) • Trunk displacement (+) • Elbow Extension (+)</td>
</tr>
<tr>
<td><strong>Thielman (2010)</strong> RCT (4) N=16</td>
<td>E: Trunk restraint C: Sensory feedback</td>
<td>• Reaching Performance Scale Near Target (+) • Reaching Performance Scale Far Target (-)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

**Discussion**
One recent study by Bang et al. (2015) suggested that combining constraint-induced movement therapy (CIMT) with trunk restraint training improved upper limb motor function when compared to CIMT alone; however, these results have not been replicated by other studies (De Oliveira Cacho et al., 2015; Lima et al., 2014; Woodbury et al., 2009; Wu et al., 2012). When trunk restraint therapy was combined with object-related reach-to-grasp training, results have demonstrated an improvement in general upper limb function but not in manual dexterity when compared to non-restraint training (Michaelsen et al., 2006).

In a recent systematic review and meta-analysis, Wee et al. (2014) evaluated the effect of trunk restraint therapy on upper extremity recovery in patients with chronic stroke. The review included six RCTs, involving a total of 187 participants. The meta-analysis was conducted on several upper limb functional outcomes including the FMA, shoulder flexion, elbow extension, Motor Activity Log-Amount of Use, Motor Activity Log-Quality of Movement, trunk displacement, and reaching trajectory smoothness and straightness. The overall results indicated that the majority of the measures showed no preference of trunk displacement over the control condition, with only the FMA and shoulder flexion demonstrating significant effects. It is also pertinent to note that the outcomes evaluated in the review were measured in three studies on average. Shoulder flexion and elbow extension were evaluated in four studies each, while reaching trajectory straightness was evaluated in two studies. Although all studies included in the review scored ≥6 on the Physiotherapy Evidence Database (PEDro) tool, signifying high methodological quality, the authors indicated that there is still insufficient evidence to demonstrate a beneficial effect of trunk restraint therapy on upper extremity motor function. Future studies investigating the effects of this intervention during the acute stage of stroke are encouraged.

**Conclusions Regarding Trunk Restraint**

*There is conflicting level 1a evidence regarding the efficacy of trunk restraint therapy on upper extremity function when combined with constraint induced movement therapy or delivered alone.*

Trunk restraint may improve some aspects of upper limb motor function but not others (i.e. elbow extension, reaching trajectory, trunk displacement).

### 10.2.8 Sensorimotor Training and Somatosensory Stimulation

Somatosensory deficits are common following stroke. Connell et al. (2008) reported that among 70 patients with first-ever stroke, 7-53% had impaired tactile sensation, 31-89% impaired stereognosis, and 34-64% impaired proprioception. Sensorimotor impairment is associated with slower recovery following stroke; therefore, therapies to increase sensory stimulation may help to improve motor performance. Stimulation can be applied using a variety of methods including transcutaneous electrical nerve stimulation (TENS), vibration therapy, peripheral nerve/afferent stimulation, thermal stimulation, or transcutaneous electrical acupoint stimulation (TEAS)/electroacupuncture.

**Transcutaneous Electrical Nerve Stimulation (TENS)**

The application of electrical stimulation at a sensory level may help to enhance plasticity of the brain, which in turn may help with motor recovery (Sonde, Gip, Fernaeus, Nilsson, & Viitanen, 1998). Robbins et al. (2006) described the current intensity of TENS to be beneath motor threshold, although capable of generating a “pins-and-needles sensation”. Similar to acupuncture, TENS is one method through which to achieve increased afferent stimulation.
A Cochrane review Pomeroy et al. (2006) examined the use of all forms of electrostimulation (ES) in the recovery of functional ability following stroke. This review assessed the efficacy of functional electrical stimulation (both as a form of neuromuscular retraining and as a form of neuromuscular electrical stimulation (TENS), EMG and electroacupuncture. The primary outcome included nine measures of functional motor ability and two ADL measures. The review included four planned treatment contrasts: 1) ES vs. no treatment; 2) ES vs. placebo stimulation; 3) ES vs. conventional therapy and 4) One type of ES vs. an alternative type of ES. With respect to the assessment of treatments specific to the upper extremity and neuromuscular electrical stimulation, five outcomes were associated with a statistically significant treatment effect. With one exception, all of the pooled analyses were based on the results from only one study. The results from pooled analyses with positive results are presented in Table 10.2.8.1. The authors concluded that there was insufficient evidence to guide practice on the efficacy of ES.

Table 10.2.8.1 Pooled Analysis from 2006 Cochrane Review Assessing Efficacy of ES as a Therapy for the Upper Extremity

<table>
<thead>
<tr>
<th>Treatment Contrast</th>
<th>Outcome Assessed</th>
<th>Standardized Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ES vs. No treatment</td>
<td>Motor reaction time</td>
<td>1.18 (0.00, 2.37)</td>
</tr>
<tr>
<td></td>
<td>Isometric torque</td>
<td>1.02 (0.46, 1.59)</td>
</tr>
<tr>
<td></td>
<td>Box &amp; Block test</td>
<td>1.28 (0.00, 2.56) *</td>
</tr>
<tr>
<td></td>
<td>Upper Extremity Drawing test</td>
<td>-1.40 (-2.25, -0.56) (favours no treatment)</td>
</tr>
<tr>
<td>ES vs. Placebo</td>
<td>Jebsen Hand Function test feeding</td>
<td>1.36 (0.24, 2.48)</td>
</tr>
<tr>
<td>ES vs. Conventional Therapy</td>
<td></td>
<td>No outcomes were statistically significant</td>
</tr>
</tbody>
</table>

* All 3 studies included in the pooled analysis were authored by the same person (Cauraugh)

Laufer & Gabyzon (2011) conducted a systematic review of the effectiveness of TENS for motor recovery, including the findings from 15 studies. Seven of these studies examined treatments focused on the upper extremity, while two included both the upper and lower extremities. The majority of studies recruited participants in the chronic stage of stroke. The outcomes assessed in these studies included movement kinematics during reaching, pinch force, the Jebsen-Taylor Hand Function test, the ARAT, the Barthel Index, and the Modified Motor Assessment Scale. The authors stated while there was much variability in the stimulation protocols and the timing and selection of outcome measures to enable definitive conclusions, there was still evidence that TENS treatment, when combined with rehabilitation therapies, may help to improve motor recovery.

**Vibration Therapy**

Vibration therapy is investigated for its potential therapeutic effects on balance, muscle strength after stroke, although the protocol has not been established (Liao, Ng, Jones, Chung, & Pang, 2015).

**Peripheral Nerve Stimulation/ Afferent Stimulation**

Repetitive peripheral magnetic stimulation (rpMS) for upper limb rehabilitation, like functional neuromuscular stimulation, generates repetitive contraction-relaxation cycles to enhance proprioceptive input to the affected arm (Krewer, Hartl, MÄ¼ller, & Koenig, 2014). Repetitive rpMS is also believed to penetrate to deeper regions of muscles and be more tolerable than functional
neuromuscular stimulation. It has also been suggested that PNS stimulates the somatosensory cortex and elicits cortical reorganisation of the primary motor cortex, thereby modifying motor function (Conforto, Kaelin-Lang, & Cohen, 2002; Wu, Seo, & Cohen, 2006).

Based on a review of studies investigating peripheral nerve stimulation after stroke, outcomes related to upper limb motor function improved in those receiving the intervention in comparison to a control (Obiglio et al., 2016). The review included 5 RCTs and a total of 224 patients.

**Thermal Stimulation**

Thermal stimulation can be applied in both rehabilitation clinics and home-care-based settings, and may work through neurofacilitation techniques (Tai et al., 2014). It may be combined with teaching compensatory strategies, augmented exercise therapy, and task-oriented programs, in a way that is thought to enhance its effect.

**Transcutaneous Electrical Acupoint Stimulation (TEAS) / Electroacupuncture**

TEAS and electroacupuncture use similar mechanisms of action, by which acupoints are stimulated by electrical impulses that are given through needles (Zhao et al., 2015). Previous studies on animal and human models have determined that EA may block pain through activating bioactive chemicals which in turn desensitize peripheral nociceptors and reduce proinflammatory cytokines (Zhao et al., 2015).

The results of RCTs evaluating sensorimotor stimulation treatments are summarized in Table 10.2.8.1.

**Table 10.2.8.1 Summary of Results from RCTs Evaluating Sensorimotor Training or Stimulation for the Upper Extremity**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TENS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Page et al.</td>
<td>RCT (7)</td>
<td>E1: 30 minutes of electrical stimulation therapy with repetitive task specific practice</td>
<td>Fugl-Meyer Assessment: E3 vs E2 (+); E3 vs E1 (+); E2 vs E1 (-)</td>
</tr>
<tr>
<td></td>
<td>N=32</td>
<td>E2: 60 minutes of electrical stimulation therapy with repetitive task specific practice</td>
<td>Arm Motor Ability Test: E3 vs E2 (+); E3 vs E1 (+); E2 vs E1 (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E3: 120 minutes of electrical stimulation therapy with repetitive task specific practice</td>
<td>Action Research Arm Test: E3 vs E2 (+); E3 vs E1 (+); E2 vs E1 (-)</td>
</tr>
<tr>
<td>Celnik et al.</td>
<td>RCT (6)</td>
<td>E1: Single session of peripheral nerve stimulation</td>
<td>Jebsen-Taylor Hand Function Test (1hr) (+)</td>
</tr>
<tr>
<td></td>
<td>N=9</td>
<td>E2: No stimulation</td>
<td>Jebsen-Taylor Hand Function Test (24hr) (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C: Asynchronous nerve stimulation</td>
<td></td>
</tr>
<tr>
<td>Tekeoglu et al.</td>
<td>RCT (6)</td>
<td>E: Rehabilitation + TENS</td>
<td>Barthel Index (+)</td>
</tr>
<tr>
<td></td>
<td>N=60</td>
<td>C: Rehabilitation</td>
<td></td>
</tr>
<tr>
<td>Kim et al.</td>
<td>RCT (7)</td>
<td>E: TENS + task related training</td>
<td>Fugl Meyer Score (+)</td>
</tr>
<tr>
<td></td>
<td>NStart=30</td>
<td>C: Placebo + Task related training</td>
<td>Manual Function Test (+)</td>
</tr>
<tr>
<td></td>
<td>NEnd=30</td>
<td></td>
<td>Box and Block Test (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Modified Ashworth Scale (-)</td>
</tr>
<tr>
<td>Sonde et al.</td>
<td>RCT (5)</td>
<td>E: TENS + physiotherapy</td>
<td>Fugl Meyer (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C: Physiotherapy</td>
<td>Pain (-)</td>
</tr>
</tbody>
</table>

2016. The review included 5 RCTs and a total of 224 patients.
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bütefisch et al.</td>
<td>Enhanced specific therapy + TENS (C: Enhanced non-specific therapy)</td>
<td>Grip strength (-)</td>
</tr>
<tr>
<td>RCT (3)</td>
<td></td>
<td>Peak force of isometric hand extension (-)</td>
</tr>
<tr>
<td>N=27</td>
<td></td>
<td>Peak acceleration of isometric hand extension (-)</td>
</tr>
</tbody>
</table>

### Vibration Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stein et al.</td>
<td>Enhanced specific therapy (E: Stochastic resonance stimulation + electrical stimulation)</td>
<td>Fugl Meyer (-)</td>
</tr>
<tr>
<td>RCT (10)</td>
<td></td>
<td>Motor Activity Log (-)</td>
</tr>
<tr>
<td>N=30</td>
<td></td>
<td>Action Research Arm Test (-)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tavernese et al.</td>
<td>Enhanced specific therapy (E: Segmental muscle vibration + standard therapy) C: Standard therapy</td>
<td>Velocity of movement (+)</td>
</tr>
<tr>
<td>RCT (8)</td>
<td></td>
<td>Angular velocity at shoulder (+)</td>
</tr>
<tr>
<td>NStart=44 NEnd=44</td>
<td></td>
<td>Movement duration (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normalized jerk (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Elbow angle, shoulder angle, shoulder abduction (-)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paoloni et al.</td>
<td>Enhanced specific therapy (E: Segmental muscle vibration + conventional therapy) C: Conventional therapy</td>
<td>Muscle onset time (+)</td>
</tr>
<tr>
<td>RCT (8)</td>
<td></td>
<td>Co-contraction index (+)</td>
</tr>
<tr>
<td>NStart=22 NEnd=22</td>
<td></td>
<td>Muscle modulation: anterior deltoid (+), biceps brachii (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximal voluntary contraction muscle activation (+)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caliandro et al.</td>
<td>Enhanced specific therapy (E: Focal muscle vibration) C: Sham</td>
<td>Wolf Motor Function Test (+)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costantino et al.</td>
<td>Enhanced specific therapy (E: 300 Hz vibrations on the upper limbs) C: Sham vibrations</td>
<td>Hand Grip Strength (+)</td>
</tr>
<tr>
<td>RCT (7)</td>
<td></td>
<td>Modified Ashworth Scale (+)</td>
</tr>
<tr>
<td>NStart=32 NEnd=32</td>
<td></td>
<td>Disabilities of the Arm, Shoulder and Hand Score (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Functional Independence Measure (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fugl-Meyer Assessment (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Jebsen Taylor Hand Function Test (+)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT (6)</td>
<td></td>
<td>Grip Strength: E1 vs C (+); E2 vs C (+); E1 vs E2 (+)</td>
</tr>
<tr>
<td>NStart=45 NEnd=45</td>
<td></td>
<td>Wolf Motor Function Test: E1 vs. E2/C (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Modified Ashworth Scale: E1 vs. E2/C (+)</td>
</tr>
</tbody>
</table>

### Peripheral Nerve Stimulation/Afferent Stimulation

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krewer et al.</td>
<td>Repetitive peripheral magnetic stimulation C: Sham stimulation</td>
<td>Modified Tardieu Scale: Post 1st session: Elbow flexors (-), Elbow extensors (-)</td>
</tr>
<tr>
<td>RCT (9)</td>
<td></td>
<td>Wrist flexors (+), Wrist extensors (-); Post 2nd session (-); Post-intervention (-)</td>
</tr>
<tr>
<td>NStart=63 NEnd=44</td>
<td></td>
<td>2wk post-intervention: Elbow flexors (-), Elbow extensors (+), Wrist flexors (-),</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wrist extensors (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fugl Meyer Assessment (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Barthel Index (-)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Description</th>
<th>Measured Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikuno et al.</td>
<td>Repetitive peripheral sensory nerve stimulation + task-specific therapy C: Task-specific therapy</td>
<td>Wolf Motor Function Test (-)</td>
</tr>
<tr>
<td>RCT (8)</td>
<td></td>
<td>Wolf Motor Function Test: Mean Time (+)</td>
</tr>
<tr>
<td>N=22</td>
<td></td>
<td>Box and Block Test (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pinch Strength (-)</td>
</tr>
<tr>
<td>Study</td>
<td>Intervention Details</td>
<td>Outcomes</td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Grip Strength (•)</strong></td>
<td>• Grip Strength (•)</td>
<td></td>
</tr>
</tbody>
</table>
| dos Santos-Fontes et al. (2013) | E: Peripheral nerve stimulation  
 C: Sham nerve stimulation                        | • Jebsen Taylor Test (+)                                                |
| **Pinch Strength (•)**       | • Pinch Strength (•)                                                                 |                                                                          |
| Klaiput et al. (2009)        | E: Peripheral Sensory Stimulation                                                         | • Modified Ashworth Scale (-)  
 • Box and Block Test (+)  
 • FIM (-)  
 • Action Research Arm Test (+) |
| Lin et al. (2014)            | E: Mirror therapy + Mesh glove  
 C: Mirror therapy                               | • Modified Ashworth Scale (-)  
 • Box and Block Test (+)  
 • FIM (-)  
 • Action Research Arm Test (+) |
| Fleming et al. (2015)        | E: Active Somatosensory Stimulation  
 C: Sham Somatosensory Stimulation            | • Action Research Arm Test (+)  
 • Fugl Meyer Assessment (-)  
 • Motor Activity Log (-) |
| Hunter et al. (2011)         | E: Mobilization and Tactile Stimulation (3 dose levels)  
 C: Conventional therapy                   | • Motricity Index (-)  
 • Action Research Arm Test (-) |
| Cambier et al. (2003)        | E: Intermittent pneumatic compression  
 C: Sham short-wave therapy                   | • Nottingham Sensory Assessment (+)  
 • Fugl Meyer (+)  
 • Ashworth Scale (-)  
 • Visual Analog Scale (-) |
| Lee et al. (2015)            | E1: Mirror Therapy with Mesh Glove Afferent Stimulation  
 E2: Mirror Therapy  
 C: Mirror Therapy with Sham Stimulation | • Extensor Digitorum Muscle Tone: E1 vs E2/C (+)  
 • Muscle stiffness on the flexor carpi radialis: E1 vs C (+)  
 • Box and Block Test: E1/C vs E2 (+)  
 • Functional Independence Measure: E1/C vs E2 (+)  
 • Fugl-Meyer Assessment (-)  
 • Revised Nottingham Sensory Assessment (-) |
| McDonnell et al. (2007)      | E: Task-specific training with afferent stimulation  
 C: Task-specific training without afferent stimulation | • Fugl Meyer Score (-)  
 • Action Research Arm Test (-)  
 • Dexterity (+) |
| Feys et al. (1998)           | E: Sensorimotor stimulation  
 C: Control                                    | • Fugl Meyer: 6wk (-), 6mo (+), 12mo (+)  
 • Action Research Arm Test (-)  
 • Barthel Index (-) |
| Wu et al. (2006)             | E: Single session of peripheral nerve (somatosensory) stimulation  
 C: No stimulation                           | • Jebsen-Taylor Hand Function Test (+)                                     |
| Conforto et al. (2002)       | E: Single session of medial nerve (somatosensory) stimulation  
 C: Sham stimulation                          | • Pinch muscle strength (+)                                                  |
| Jongbloed et al. (1989)      | E: Sensorimotor integrative approach  
 C: Functional approach                        | • Barthel Index (-)  
 • Sensorimotor Integration Test: 8 subsets (-) |

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N Start</th>
<th>N End</th>
<th>Type of Intervention</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tai et al. (2014)</td>
<td>RCT (8)</td>
<td>16</td>
<td>16</td>
<td>P: Painful thermal stimulation, I: Innocuous thermal stimulation</td>
<td>Cortical map size (+), Motor evoked potential (+), Motor threshold (-)</td>
</tr>
<tr>
<td>Chen et al. (2005)</td>
<td>RCT (7)</td>
<td>46</td>
<td>29</td>
<td>T: Thermal stimulation + standard therapy, C: Standard therapy</td>
<td>Brunnstrom (+), Modified Ashworth Scale (-), Grasping (-), Sensation (+)</td>
</tr>
<tr>
<td>Wu et al. (2010)</td>
<td>RCT (6)</td>
<td>23</td>
<td></td>
<td>T: Thermal stimulation, C: No stimulation</td>
<td>UE-STREAM (+), Action Research Arm Test (+)</td>
</tr>
<tr>
<td>Chen et al. (2005)</td>
<td>RCT (7)</td>
<td>46</td>
<td>29</td>
<td>E: Thermal stimulation + standard therapy, C: Standard therapy</td>
<td>Brunnstrom (+), Modified Ashworth Scale (-), Grasping (-), Sensation (+)</td>
</tr>
<tr>
<td>Wu et al. (2010)</td>
<td>RCT (6)</td>
<td>23</td>
<td></td>
<td>E: Thermal stimulation, C: No stimulation</td>
<td>UE-STREAM (+), Action Research Arm Test (+)</td>
</tr>
<tr>
<td>Lim et al. (2015)</td>
<td>RCT (6)</td>
<td>29</td>
<td>27</td>
<td>E: Hypothermia Intervention and sensory training, C: Sensory training</td>
<td>Fugl-Meyer Assessment (+), Nottingham Sensory Assessment proprioception of affected upper extremity and two-point discrimination (+), Blinded Functional Test (+)</td>
</tr>
<tr>
<td>Zhao et al. (2015)</td>
<td>RCT (9)</td>
<td>60</td>
<td>51</td>
<td>E1: Transcutaneous electrical acupoint stimulation (TEAS) (100Hz), E2: Transcutaneous electrical acupoint stimulation (TEAS) (2Hz), C: Sham stimulation</td>
<td>MAS (wrist): Simulation groups vs. control at 2, 3, and 4wk, and 1mo (+), MAS (wrist): E1 vs E2 at 2wk (+), MAS (wrist): E1 vs. E2 at 3 and 4wk and at 1mo (-), MAS (wrist): E2 vs Cat 4wk (+), Disability Assessment Scale (-), Global Assessment Scale (-)</td>
</tr>
<tr>
<td>Hsieh et al. (2007)</td>
<td>RCT (8)</td>
<td>63</td>
<td></td>
<td>E: Electroacupuncture, C: No acupuncture</td>
<td>FIM (-), Fugl-Meyer (+)</td>
</tr>
<tr>
<td>Hsing et al. (2012)</td>
<td>RCT (7)</td>
<td>62</td>
<td></td>
<td>E: Scalp electro-acupuncture, C: sham acupuncture</td>
<td>BI (-), Rankin score (-)</td>
</tr>
<tr>
<td>Wen et al. (2014)</td>
<td>RCT (7)</td>
<td>300</td>
<td>276</td>
<td>E: Electroacupuncture + moxibustion, C: Basic therapy</td>
<td>Fugl-Meyer Assessment (-)</td>
</tr>
<tr>
<td>Li et al. (2012)</td>
<td>RCT (6)</td>
<td>120</td>
<td></td>
<td>E: Electroacupuncture + massage, C: Rehabilitation therapy</td>
<td>Numeric pain rating scale (+), Fugl-Meyer (-), Modified Rankin Scale (+)</td>
</tr>
<tr>
<td>Wang et al. (2014)</td>
<td>RCT (6)</td>
<td>235</td>
<td></td>
<td>E: Electroacupuncture, C: No stimulation with no needle</td>
<td>R1 and R2 component of elbow joint (+)</td>
</tr>
</tbody>
</table>
### Discussion

Page et al. (2012) conducted a study in which varying dosages of transcutaneous electrical stimulation were administered with repetitive task specific practice. The researchers found that those receiving 30 minutes of electrical stimulation did not improve on upper limb motor function when compared to those receiving 60 minutes of electrical stimulation. However, there was a significant difference between those receiving 30 minutes and those receiving 120 minutes of transcutaneous electrical stimulation, as well as between those receiving 60 minutes and those receiving 120 minutes of transcutaneous electrical stimulation. Outcomes measured motor function, and included the Fugl-Meyer Assessment, Arm Motor Ability Test, and the Action Research Arm Test. This suggests that duration of transcutaneous electrical stimulation may play an important role in the effectiveness of the intervention. Transcutaneous electrical nerve stimulation (TENS) was shown to be more effective than a control for improving upper limb motor function (Celnik et al., 2007; Kim, In, & Cho, 2013b; Sonde et al., 1998). There are mixed results on whether TENS improves independence in patients post stroke with a study by Tekeoglu et al. (1998) indicating that it does, while another study by Sonde et al. (1998) indicating that it does not. A systematic review by de Kroon et al. (2002) evaluated six RCTs from which only 2 reported a motor function outcome, and with only one reporting a positive effect. Furthermore, four of the six studies found a positive increase in motor control after the intervention, with researchers discussing that this is the only significant effect of TENS for upper limb recovery that they found.

The effectiveness of vibration therapy for improving upper limb motor function has been demonstrated in studies by Caliandro et al. (2012); Costantino et al. (2017); and Jung-Sun et al. (2016). However, a study with high methodological quality by Stein et al. (2010) found no significant difference in motor function in those receiving stochastic resonance stimulation with subthreshold electrical stimulation and vibration when compared to sham stimulation.

Peripheral nerve/afferent stimulation more often produced a significant difference on the Fugl-Meyer Assessment, Jebsen-Taylor Hand Function Test, Wolf Motor Function Test, or the Action Research Arm Test than a sham therapy in patients after stroke (Cambier et al., 2003; dos Santos-Fontes et al., 2013; Wu et al., 2006). However, when peripheral nerve/afferent stimulation was compared to a conventional therapy, it was more likely to produce a negative result on the above measures of function (Feys et al., 1998; Hunter et al., 2011; Ikuno et al., 2012; Y.-y. Lee et al., 2015; K. C. Lin, P. C. Huang, et al., 2014).
On the other hand, scores based on the Box and Block test, a motor function test that is more focused on dexterity, more often improved in patients receiving mirror with mesh glove therapy in comparison to mirror therapy alone (Y.-y. Lee et al., 2015; K. Lin, P. Huang, Y. Chen, C. Wu, & W. Huang, 2014; K. C. Lin, Y. T. Chen, et al., 2014).

Four studies examining thermal stimulation were found (Chen et al., 2005; Lima et al., 2015; Tai et al., 2014; Wu et al., 2010) from which two examined upper limb motor function outcome (Lima et al., 2015; Wu et al., 2010). Wu et al. (2010) found a significant improvement in upper limb motor function in those receiving thermal stimulation in comparison to those not receiving it, while Lima et al. (2015) found a significant improvement in those undergoing hypothermia and sensory training in comparison to those only receiving sensory training.

Electroacupuncture was found to be no more effective for improving upper limb motor function than conventional therapy based on the results of three studies with high methodological quality and large sample sizes (Li et al., 2012; Wen et al., 2014; Y. Zhang et al., 2017). Two studies with smaller sample sizes found an improvement in upper limb motor function between receiving electroacupuncture and no acupuncture (R. L. Hsieh et al., 2007) or typical acupuncture (Yao & Ouyang, 2014). However, the results of these two studies are less credible because Hsieh et al. (2007) did not have an active or sham control group, while Yao et al. (2014) used both relaxed needling with electrocupuncture as the intervention, while the control was typical acupuncture rather than relaxed needling.

A review of sensory-motor training by Steultjens et al. (2003) included three RCTs (Feys et al., 1998) (Jongbloed et al., 1989; Kwakkel et al., 1999), one case control trial (Turton & Fraser, 1990), and one noncontrolled trial (Whitall, Waller, Silver, & Macko, 2000). The authors concluded that sensory-motor training was not effective for improving ADLs, extended ADLs, social participation, or arm and hand function.

In a more recent review, including the results of 14 RCTs (Schabrun & Hillier, 2009), the authors distinguished between passive forms of sensory retraining through electrical stimulation and active forms, primarily through specific exercises. The included trials assessed the outcomes of function, sensation and proprioception in both the upper and lower extremity. However, only 2 of the included trials assessed sensation in the upper extremity, which reported ambiguous results.

A recent Cochrane review included the results from 13 studies (467 participants) examining a variety of treatments for sensory impairment following stroke and concluded that there was insufficient high-quality evidence available to recommend the use of any of them (Doyle, Bennett, Fasoli, & McKenna, 2010). Treatments with preliminary evidence of benefit included mirror therapy, thermal stimulation and intermittent pneumatic compression.

**Conclusions Regarding Sensorimotor Training/Somatosensory Stimulation**

*There is level 1a evidence that transcutaneous electrical nerve stimulation (TENS) improves upper limb motor function.*

*There is level 1a evidence that focal or whole-body vibration therapy improves upper limb motor function.*

*There is level 1a evidence that peripheral nerve/afferent stimulation does not significantly improve overall upper limb motor function.*
There is level 1a evidence that mesh glove therapy improves motor function and dexterity based on the Box and Block test.

There is level 1b evidence that thermal stimulation is effective for upper limb motor function.

There is level 1a evidence that electroacupuncture is not more effective than an active control for improving upper limb motor function.

Transcutaneous electrical nerve stimulation, vibration therapy, mesh glove, and thermal stimulation may improve upper limb motor function.

Peripheral nerve stimulation and electroacupuncture may not improve upper limb motor function.

10.2.9 Mental Practice/ Motor Imagery
The use of mental practice or motor imagery as a means to enhance performance following stroke was adapted from the field of sports psychology where the technique has been shown to improve athletic performance, when used as an adjunct to standard training methods. The technique, as the name suggests, involves rehearsing a specific task or series of tasks, mentally. A series of small trials have adapted and evaluated the effects of mental practice as a treatment following stroke. The ability of the treatment to improve motor function or ADL performance is the outcome most frequently assessed in these studies. The most plausible mechanism to explain the success of the technique is that stored motor plans for executing movements can be accessed and reinforced during mental practice (Page, Levine, Sisto, & Johnston, 2001). Mental practice can be used to supplement conventional therapy and can be used at any stage of recovery.

Zimmermann-Schlatter et al. (2008) also assessed the efficacy of motor imagery in recovery post stroke. The authors included the results from only 4 RCTs (Liu, Chan, Lee, & Hui-Chan, 2004; Page & Levine, 2006; Page, Levine, & Leonard, 2007; Page et al., 2001) in which the duration and frequency of treatment lasted from 10 minutes to one-hour per day, with 3 to 5 sessions per week for 3 to 6 weeks. Mean time of stroke onset ranged from several days to several years. Three of these studies reported improvements in the mean ARAT and FMA scores. Two of these studies also found higher mean change scores than the minimally clinically relevant difference in the ARAT and FMA scores. These authors concluded that although there was evidence of benefit of treatment, larger and more rigorous studies are required to confirm these findings.

Nilsen et al. (2010) conducted a systematic review on the use of mental practice as a treatment for motor recovery, including the results from 15 studies, 4 of which were classified as Level 1 (i.e., RCTs). Although the authors concluded that there was evidence that mental practice was effective, especially when combined with upper-extremity therapy, they also discussed the problems in summarizing the results of heterogeneous trials. Studies varied with respect to treatment protocols, patient characteristics, eligibility criteria, dosing, methods used to achieve mental practice (audiotapes, written instruction, pictures) the chronicity of stroke, and outcomes assessed. The authors cautioned that additional research must be conducted before specific recommendations regarding treatment can be made.
A Cochrane review on the subject (Barclay-Goddard, Stevenson, Poluha, & Thalman, 2011), restricted to RCTs (n=6) concluded that there was limited evidence that mental practice in addition to other rehabilitation therapies was effective compared with the same therapies without mental practice. There were significant treatment effects for the outcomes associated with both impairment and disability.

A meta-analysis (Cha, Yoo, Jung, Park, & Park, 2012) included the results from 5 RCTs and assessed the additional benefit of mental practice combined with functional task training. The outcomes assessed in the individual studies included the FMA, ARAT and Barthel index. The estimated treatment effect size when the studies were pooled was 0.51 (95% CI 0.27 to 0.750, indicating a moderate effect.

However, a meta-analysis by Machado et al. (2015) found that compared to the control, mental practice was not more effective at improving upper limb motor function when used as an adjunct therapy, based on the results of 7 RCTs.

The results of RCTs evaluating mental practice are summarized in Table 10.2.9.1.

**Table 10.2.9.1 Summary of Controlled Trials Evaluating Mental Practice/ Motor Imagery Therapy for the Upper Extremity**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
</table>
| Mihara et al. (2013) | RCT (9) NStart=20 NEnd=20 | E: Mental practice  
C: Sham intervention | • Fugl Meyer Score (+)  
• Action Research Arm test (-) |
| Ang et al. (2014) | RCT (8) NStart=22 NEnd=21 | E1: Motor imagery + brain computer interface + haptic knob  
E2: Brain computer interface  
E3: Haptic knob | • Fugl Meyer Score (-) |
| Boventd'Eerdt et al. (2010) | RCT (8) N=50 | E: Conventional therapy + Mental practice  
C: Conventional therapy | • Goal Attainment Scale (-)  
• Barthel Index (-)  
• Rivermead Mobility (-)  
• Nottingham Extended ADL (-)  
• Action Research Arm Test (-) |
| Oostra et al. (2013) | RCT (8) NStart=20 NEnd=20 | E: Mental practice + physical training  
C: Physical training | • Action Research Arm Test (+) |
| Ietswaart et al. (2011) | RCT (7) N=121 | E1: Motor imagery  
E2: Attention placebo  
C: Usual care | • Action Research Arm Test (-) |
| Park et al. (2016) | RCT (7) NStart=30 NEnd=30 | E: Nintendo Wii + mental practice  
C: Nintendo Wii | • Fugl-Meyer Assessment (-)  
• Motor Activity Log (-) |
| Park et al. (2015) | RCT (7) NStart=26 NEnd=26 | E: Mental practice + mCIT  
C: mCIT | • Fugl Meyer Score (+)  
• Action Research Arm Test (+)  
• Modified Barthel Index (+) |
<p>| Liu et al. (2014) | RCT (7) | E: Motor imagery + mental practice of affected hand | • Action Research Arm test (+) |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N Start</th>
<th>N End</th>
<th>Intervention Details</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| You et al. (2013)                         | RCT (7) | 18      | 16    | E: Mental activity training + EMG                                                     | Range of Motion (-)  
Fugl Meyer Score (+)  
Modified Ashworth Scale (-)  
Modified Barthel Index (-)  
Motor Activity Log: Amount of Use (-), Quality of Movement (-) |
|                                           |        |         |       | C: Functional electrical stimulation                                                 |                                                                          |
| Oh et al. (2016)                          | RCT (7) | 10      | 10    | E: Mental Practice and Conventional Therapy alone followed by Conventional Therapy alone followed by Mental Practice and Conventional Therapy | Fugl-Meyer Assessment of the Upper Extremity (-)  
Motor Activity Log (-) |
|                                           |        |         |       | C: Conventional Therapy alone followed by Mental Practice and Conventional Therapy |
| Page et al. (2005a)                       | RCT (6) | 11      |       | E: Mental practice                                                                   | Action Research Arm Test (+)  
Motor Activity Log: Amount of Use (+), Quality of Movement (+) |
|                                           |        |         |       | C: Relaxation techniques                                                             |                                                                          |
| Page et al. (2007)                        | RCT (6) | 32      |       | E: Mental practice                                                                   | Fugl Meyer Score (+)  
Action Research Arm test (+) |
|                                           |        |         |       | C: Sham intervention                                                                |                                                                          |
| Page et al. (2011)                        | RCT (6) | 29      |       | E: Audiotaped mental practice                                                         | Fugl Meyer Score (-)  
Action Research Arm Test (-) |
|                                           |        |         |       | C: Audiotaped sham intervention                                                      |                                                                          |
| Park et al. (2015)                        | RCT (6) | 29      | 29    | E: Mental practice                                                                   | Fugl Meyer Score (+)  
Action Research Arm Test (+)  
Modified Bartheil Index (+) |
|                                           |        |         |       | C: Physical therapy                                                                 |                                                                          |
| Page et al. (2001)                        | RCT (5) | 13      |       | E: Occupational therapy + imagery training                                           | Fugl Meyer Score (+)  
Action Research Arm Test (+) |
|                                           |        |         |       | C: Occupational therapy                                                              |                                                                          |
| Liu et al. (2009)                         | 5 (RCT)| 35      |       | E: Mental Imagery                                                                   | Improvement in Trained Tasks (+) |
|                                           |        |         |       | C: Conventional Functional Rehabilitation                                             |                                                                          |
| Riccio et al. (2010)                      | RCT (5) | 36      |       | E: Mental practice then conventional rehab then mental practice                      | Motricity Index: crossover point (+), post therapy (-)  
Arm Function Test: crossover point (+), post therapy (-) |
|                                           |        |         |       | C: Conventional rehab then mental practice                                           |                                                                          |
| Lee et al. (2012)                         | RCT (5) | 26      |       | E: Mental practice + standard care                                                    | Fugl Meyer Score (+)  
Brunnstrom stages (+)  
Manual Function Test (+) |
|                                           |        |         |       | C: Standard care                                                                     |                                                                          |
| Page et al. (2000)                        | RCT (4) | 16      |       | E: Occupational therapy + Imagery training                                           | Fugl Meyer Scores (+) |
|                                           |        |         |       | C: Occupational therapy                                                              |                                                                          |
| Liu et al. (2004)                         | RCT (4) | 46      |       | E: Mental Imagery                                                                   | Fugl Meyer Score (-)  
Colour Trials Test (-) |
|                                           |        |         |       | C: Functional training                                                               |                                                                          |
| Page et al. (2009)                        | RCT (4) | 10      |       | E: Mental practice + mCIT                                                            | Action Research Arm Test: post and follow-up (+)  
Fugl Meyer Score: post and follow-up (+) |
|                                           |        |         |       | C: mCIT                                                                              |                                                                          |
| Müller et al. (2007)                      |        |         |       | E1: Mental practice                                                                  | Jebsen Hand Function Test: E1/E2 vs. C (+) |

10. Upper Extremity Interventions
RCT (4)  
N=17  
E2: Motor practice  
C: Conventional therapy  
• Pinch grip: E1/E2 vs. C (+)

Dijkerman et al. (2004)  
PCT  
N=20  
E1: Mental task practice  
E2: Visual imagery task practice  
C: No mental imagery practice  
• Barthel Index (-)  
• Hospital Anxiety and Depression Scores (-)  
• Recovery of Locus Control (-)  
• Performance of Practiced Reaching (+)

Rajesh et al. (2015)  
PCT  
N_{Start}=30  
N_{End}=30  
E: Motor Imagery + conventional therapy  
C: Conventional therapy  
• Motor Activity Log (+)  
• Stroke Specific Quality of Life (+)

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

Discussion

Overall, the studies that have been compiled investigated the effectiveness of a variety of mental practice/motor imagery training techniques on upper limb motor function in individuals with stroke. Most of the studies of higher methodological quality that were included demonstrated that mental practice improved upper limb motor function on at least one measure (Liu et al., 2014; Mihara et al., 2013; Oostra et al., 2013; Page & Levine, 2006; Page et al., 2007; S.J. Page et al., 2005a; Park, Lee, Cho, Kim, & Yang, 2015; Y. Park et al., 2015; You & Lee, 2013). Some of the other higher methodological quality studies also showed no significant improvement in upper limb motor function (Ang et al., 2014; Bovend'Eerdt et al., 2010; Ietswaart et al., 2011; Page et al., 2011; Park & Park, 2016). From these five studies, two investigated motor imagery rather than mental practice (Ang et al., 2014; Ietswaart et al., 2011), one paired mental practice with the Nintendo Wii (Park & Park, 2016), and one audiotaped the mental practice and the sham practice (Page et al., 2011). Therefore, there may be a difference in the type of intervention that was provided in the studies that found a significant difference between groups as opposed to those that did not. Measures of independence and daily living indicated an even split, with some finding an effect, and others not.

It is also noteworthy to mention that it is unclear whether some of the same participants took part in multiple studies conducted by the same group (Page, 2000; Page et al., 2011; Page et al., 2009; Page et al., 2007; S.J. Page et al., 2005a; Page et al., 2001). To improve the quality, studies with larger samples are required in the future for larger statistical power. Many of these trials were conducted in the chronic phase, so it is recommended that studies include patients in the acute phase post stroke in the future.

Kho et al. (2014) conducted a recent meta-analysis on the effects of mental imagery on motor recovery of the upper extremity following a stroke. A total of six studies were included in the analysis, of which only five were RCTs and one was a controlled clinical trial. The pooled effects from three studies regarding the FMA showed no significant effect favouring the intervention. Conversely, when evaluating the ARAT measured in four studies, the findings revealed a significant effect in favour of mental imagery (Kho et al., 2014). The authors suggested that a possible explanation for the lack of effect observed on the FMA may be due to a ceiling effect in performance, given that a large proportion of participants had mild motor impairment.

Conclusions Regarding Mental Practice

There is level 1a evidence that mental practice therapy is effective for improving upper extremity motor function; however, the evidence for its effect on activities of daily living is limited and conflicting.
There is level 1a evidence that motor imagery is not effective for improving upper extremity motor function.

Mental practice may improve upper limb motor function after stroke, while motor imagery likely does not.

10.2.10 Splinting

Splints may be applied to achieve various objectives, including reduction in spasticity, reduction in pain, prevention of contracture, and prevention of edema (Lannin & Herbert, 2003).

The effectiveness of the use of splints to improve upper extremity function is reviewed in this section. The use of splints to prevent the development of contracture, or reduce spasticity following stroke is reviewed in section 10.5.1.

In a systematic review of hand splinting for adults with stroke, Lannin and Herbert (2003) included the results from 19 studies, of which only 4 were RCTs. The authors concluded that there was insufficient evidence to either support or refute the effectiveness of hand splinting for a variety of outcomes for adults following stroke.

Tyson and Kent (2011) conducted a systematic review on the effect of upper limb orthotics following stroke, which included the results from 4 RCTs representing 126 subjects. The treatment effects associated with measures of disability, impairment, range of motion, pain, and spasticity were small and not statistically significant.

The results of RCTs evaluating splinting interventions for upper extremity function are summarized in Table 10.2.10.1.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lannin et al. (2003) RCT (8) N=28</td>
<td>E: Hand splint C: No hand splint</td>
<td>• Contracture formation (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bartolo et al. (2014) RCT (8) NStart=28 NEnd=28</td>
<td>E: Arm orthosis C: Conventional physiotherapy</td>
<td>• Range of Motion: abduction and adduction (+), flexion and extension (+) • Normalized jerk (+) • Fugl Meyer Score (-) • Modified Ashworth Scale (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lannin et al. (2007) RCT (7) N=63</td>
<td>E1: Extension splint E2: Neutral splint C: No splint</td>
<td>• Wrist contracture (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim et al. (2015) RCT (7) NStart=30 NEnd=30</td>
<td>E: Taping C: No taping</td>
<td>• Manual Function Test (+) • Modified Motor Assessment Scale (+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barry et al. (2012) RCT (7) N=19</td>
<td>E: Dynamic hand orthosis C: Manual assisted therapy</td>
<td>• Grip strength (-) • Action Research Arm Test (-) • Box and Block Test (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>N Start/End</td>
<td>Intervention Details</td>
<td>Outcome Measures</td>
</tr>
<tr>
<td>---------------</td>
<td>--------</td>
<td>-------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>-----------------------------------------</td>
</tr>
</tbody>
</table>
| Page et al. (2013) | RCT (6) | N Start=16/End=16 | E: Myomo brace  
C: Repetitive task practice | Stroke Impact Scale (-)  
Fugl Meyer Scale (-)  
Canadian Occupational Performance Measure (-)  
Stroke Impact Scale (-) |
| Poole et al. (1990) | RCT (5) | N=19 | E: Splint  
C: No splint | Fugl Meyer (-) |
| Choi et al. (2016) | RCT (5) | N Start=30/End=30 | E: Hand Splints and a General Rehabilitation Program  
C: General Rehabilitation Program | Visual Analogue Scale (+)  
Volume of Hand (+)  
Modified Ashworth Scale (-) |
| Lannin et al. (2016) | RCT (5) | N Start=9/End=6 | TPS=acute  
E: Task-specific training + training with the Saebo-Flex device  
C: Task-specific training | Motor Assessment Scale (-)  
Box and Block Test (-)  
Grip Strength (-) |
| Choi et al. (2016) | RCT (4) | N Start=52/End=52 | E: Dorsal Resting Hand Splint  
C: Volar Resting Hand Splint | Modified Ashworth Scale (+)  
Active Range of Motion (+) |

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

**Discussion**

Ten studies were reviewed to determine whether various interventions related to splinting can improve upper limb motor function. Various splinting interventions were included such as a hand splint, arm orthosis, taping, Myomo brace, and the Saebo-Flex device. Of the studies that reported motor function outcomes, all indicated no benefit of splinting for upper limb motor function when compared to conventional therapy (Barry et al., 2012; Bartolo et al., 2014; Lannin et al., 2016; Page, Persch, & Murray, 2013; Poole et al., 1990).

**Conclusions Regarding Splinting**

*There is level 1a that hand splinting/taping/orthoses do not improve upper extremity motor function.*

**Splinting, taping, and orthoses likely do not improve upper limb motor function.**

**10.2.11 Constraint-Induced Movement Therapy (CIMT)**

CIMT refers to a set of rehabilitation techniques designed to reduce functional deficits in the more affected upper extremity of stroke survivors. The two key features of CIMT are restraint of the unaffected hand/term and increased practice/use of the affected hand/arm (Fritz, Light, Patterson, Behrman, & Davis, 2005). Since stroke survivors may experience “learned non-use” of the affected upper extremity within a short period of time (Taub, 1980), CIMT is designed to overcome learned non-use by promoting neuroplasticity and use-dependent cortical reorganization (Taub, Uswatte, & Pidikiti, 1999). While the biological mechanism(s) responsible for the benefit are unknown and the contribution from intense practice is difficult to disassociate from the effect of constraining the unaffected limb, this
form of treatment shows promise, especially for survivors with moderate upper limb disability following stroke.

Several reviews have been published on the effectiveness of CIMT (Barreca et al., 2003a; Hakkennes & Keating, 2005; Taub & Morris, 2001) and while the results have been generally positive, uncertainty of its effectiveness remain due to the small number of trials published, the small sample sizes of the studies, heterogeneity of patient characteristics, duration and intensity of treatment, and outcomes assessed.

A meta-analysis conducted by Van Peppen et al. (2004) concluded that CIMT was associated with improvements in dexterity, as measured by the Arm Motor Activity Test or the ARAT, but not in terms of ADL performance, as measured by the FIM or Barthel Index scores. Hakkennes and Keating (2005) included the results from 14 RCTs and concluded that there was a benefit associated with treatment, although larger well-designed studies are still required. Several treatment contrasts were examined including traditional CIMT versus alternative therapy or control, modified CIMT versus alternative therapy or control and traditional CIMT versus modified CIMT, although pooled estimates of the treatment sizes for the subgroups were not provided.

Taub et al. (2003) noted that constraint-induced movement therapy has limitations as in the improvement seen does not restore the stroke patients’ movement to their motor status prior to the stroke. The same authors note that constraint-induced movement therapy “produces a variable outcome that depends on the severity of initial impairment. If patients with residual motor function are categorized on the basis of their active range of motion, the higher functioning individuals tend to improve more than persons who are more disabled” (Taub et al., 1999). For patients with the lowest motor functioning, constraint-induced therapy does improve movement at the shoulder and elbows. Because these people have little or no ability to move the fingers, there is no adequate motor basis for carrying out training of hand function. Consequently, because most daily activities that are carried out by the upper extremity are performed by the hand, there is relatively little translation of the therapy induced movement in proximal joint function into an increase in the actual amount of use of the more affected extremity in the real life situation. Thus, constraint-induced therapy is clearly not a complete answer to motor deficits after stroke. The work so far does show that motor function in a large percentage of patients with chronic stroke is substantially modifiable,” (Taub, Uswatte, & Morris, 2003).

van der Lee (2001) suggests that the positive results attributed to CIMT may simply reflect a greater intensity of training of the affected arm and questions the concept of non-use implying that it may not be a distinct entity, but rather the result of sensory disorders or hemineglect.

According to Dromerick et al. (2000), constraint of the unaffected arm with the use of a mitten (6 hours per day for 14 days), and ‘forced use’ of the affected arm soon after stroke (approximately six days), is feasible. However, trials reporting small but significant reductions in arm impairment, especially for patients with sensory disorders and hemineglect (Ploughman & Corbett, 2004; van der Lee et al., 1999), have also reported a high number of deviations from the randomized treatment schedule, due to patients’ noncompliance. This led to trials investigating the effectiveness of modified or shorter periods of constraint-induced therapy treatment.

There is promising evidence that the drawbacks to stroke patient participation in CIMT (i.e., required practice intensity and duration of restraint) may be overcome through modifications to the basic procedures. These include a less intense, modified therapy schedule, termed mCIMT, that combines structured functional practice with the affected limb, with restricted use of the less affected limb (Page, Sisto, Levine, & McGrath, 2004), as well as forced use therapy, which employs constraint without
intensive training of the affected limb (Ploughman & Corbett, 2004). Page et al. (2005b; 2002; 2004) provide one example of the distinction between CIMT and mCIMT: CIMT is defined by the i) restriction of a patient’s less affected upper-limb throughout 90% of waking hours during a 2-week period and ii) participation in an intensive upper-extremity therapy program for 6 hours per day, using the affected limb during the same 2-week period. In contrast, mCIMT involves restriction of the unaffected limb for periods of 5 hours per day, 5 days per week for 2 weeks combined with structured, ½ hour therapy sessions, 3 days per week. However, other criteria for defining mCIMT have also been used, which overlap with CIMT, blurring the distinction. Lin et al. (2007) cite mCIMT as 2 hours of therapy per day for 10-15 consecutive weekdays, with restraint for 6 hours per day. There also exist trials, presented in the following tables, in which the intervention was provided for periods of up to 10 weeks.

The optimal timing of treatment remains uncertain. While there is evidence that patients treated in the acute phase of stroke may benefit preferentially (Taub & Morris, 2001), there is also evidence that it may, in fact, be harmful (Dromerick et al., 2009). Grotta et al. (2004) suggest that the greatest benefit is likely to be conferred during the chronic stages of stroke and that the treatment has shown to be harmful in animal studies of “forced use” immediately post stroke.

The results from the largest and most rigorously conducted trial - The Extremity Constraint Induced Therapy Evaluation (EXCITE), may provide the strongest evidence of a benefit of CIMT treatment, to date. The study recruited 222 subjects with moderate disability 3 to 9 months following stroke, over 3 years from 7 institutions in the US. Treatment was provided for up to 6 hours a day, 5 days a week for 2 weeks. Patients were reassessed up to 24 months following treatment. At 12 months, compared with the control group who received usual care, subjects in the treatment group had significantly higher scores on sections of the WMFT and the Motor Activity Log. At 24 months these gains were maintained. While these results are encouraging, the number of patients for whom this treatment may be suitable, remains uncertain (Cramer, 2007). In the EXCITE trial, only 6.3% of patients screened were eligible. While larger estimates of 20-25% have been suggested, it remains uncertain if subjects with greater disability would benefit from treatment.

A Cochrane review (Siritori, Corbetta, Moja, & Gatti, 2009) examined the benefit of all forms of CIMT including studies that used the traditional protocol as described by Taub, in addition to trials of modified CIMT and forced use. The review included the results from 19 trials involving 619 subjects. The primary outcome was disability, which was measured as arm motor function. The authors reported that there was a significant improvement in arm motor function, assessed immediately following the intervention, but not at 3-6 months post-intervention. A subgroup analysis compared the benefit of CIMT in terms of time since stroke onset (0-3 months and >9 months). No studies were included that measured disability 3-9 months following stroke. The associated effect sizes were not statistically significant for either subgroup. The authors caution that the findings cannot be considered robust due to the small sample sizes and poor methodological quality of the primary studies.

The same group of authors (Corbetta, Siritori, Moja, & Gatti, 2010) updated their Cochrane review and included the results from 4 recently published trials. Disability was the primary outcome. Among the 8 studies (n=276) that included an upper extremity assessment of function, or an ADL instrument, there was no significant treatment effect associated with CIMT. There was a moderate treatment effect associated with arm motor function. However, this review did not include sub analysis based on chronicity of stroke or type of CIMT treatment (i.e. forced use vs. traditional CIMT vs. modified CIMT).

Shi et al. (2011) conducted a review examining modified CIMT compared with traditional rehabilitation strategies. The results from 13 RCTs (278 patients) were included. The mean differences in scores
favoured patients in the CIMT group on the following outcome measures: FMA (7.8), ARAT (14.2) FIM (7) and the Motor Activity Log (amount of use: 0.78), suggesting that the treatment can be used to reduce post stroke disability. The authors noted that none of the included RCTs included information on compliance with the study protocol. Furthermore, the study did not differentiate between different stroke phases as the analysis combined patients from acute to chronic stroke stages.

Nijland et al. (2011) conducted a systematic review of CIMT, limited to trials that evaluated the effectiveness of treatment initiated within the first 2 weeks of stroke. The review included the results from 5 RCTs (106 subjects). There was evidence of a benefit of treatment assessed using the ARAT, FMA (arm section) and the Motor Activity Log. Although there were only a small number of studies that examined the contrast, the authors suggested that low-intensity (<3 hours of therapy/day) CIMT was superior to high-intensity (>3 hours of therapy/day) CIMT.

Peurala et al. (2012) examined the impact of CIMT and mCIMT on activity and participation measures, as defined by the ICF. The review included the results from 30 trials. The authors identified 4 broad categories of treatment intensity: 60-72 and 20-56 hours over 2 weeks, 30 hours over 3 weeks and 15-30 hours over 10 weeks. Significant improvements were associated with Motor Activity Log scores for all intensity categories; however this was not the case with the other. Outcomes examined include: FIM, WMFT scores, ARAT and the SIS. ARAT scores were significantly improved at both treatment intensity categories (20-56 hrs x 2 weeks & 15-30 hrs x 10 weeks). FIM scores were significantly increased in only 1 of 3 treatment intensity categories (15-30 hours x 10 weeks) and there were no significant improvements in SIS scores, regardless of treatment intensity.

To enable better examination of the included studies, they were classified according to type of treatment (CIMT or mCIMT) as well as chronicity of stroke (subacute (<6 months), chronic (>6 months)). We used the authors' own declaration of the type of therapy that was provided (i.e. mCIMT or CIMT).

A review by Etoom et al. (2016) found that after analyzing 36 trials, CIMT produced a significant effect when compared to a control intervention, although there was a high level of heterogeneity. The authors suggested that the significant effect found may have been skewed by publication bias. However, studies in this review that investigated the effectiveness of CIMT during the first 6 months after stroke overall found a nonsignificant effect (Etoom et al., 2016). The results are summarized in tables 10.2.11.1 to 10.2.11.4.

A summary of the results from RCTs that evaluated CIMT during the subacute stage post stroke is presented in Table 10.2.11.1.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Interventions</th>
<th>CIMT Intensity/Duration</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrane et al. (2015)</td>
<td>RCT (7)</td>
<td>E: CIMT</td>
<td>3hr/d x 10d</td>
<td>Wolf Motor Function Test (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C: Usual Care</td>
<td></td>
<td>Stroke Impact Scale (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fugl-Meyer Assessment (-)</td>
</tr>
<tr>
<td>Yoon et al. (2014)</td>
<td>RCT (7)</td>
<td>E1: CIMT, Mirror Therapy (MT), and Conventional Therapy (CT)</td>
<td>6h/d x 5d/wk x 2wk</td>
<td>Brunstrom Recovery Stage (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E2: CIMT and Conventional Therapy (CT)</td>
<td></td>
<td>Wolf Motor Function Test (+)</td>
</tr>
<tr>
<td>Trial</td>
<td>C &amp; E</td>
<td>Intervention Details</td>
<td>Study Design</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Dromerick et al. (2000)</td>
<td>C: Conventional Therapy (CT)</td>
<td>E: CIMT C: Traditional therapy</td>
<td>RCT (6)</td>
<td>N=20</td>
</tr>
<tr>
<td>Ro et al. (2006)</td>
<td>E: CIMT C: Traditional rehabilitation</td>
<td>3hr/d x 6d/wk x 2wk</td>
<td>RCT (6)</td>
<td>N=8</td>
</tr>
<tr>
<td>VECTORS Dromerick et al. (2009)</td>
<td>E1: High-intensity CIMT E2: Standard CIMT C: ADL and UE bilateral training Exercises</td>
<td>E1: 3hr/d x 5/wk x 2wk E2: 2hr/d x 5/wk x 2wk</td>
<td>RCT (6)</td>
<td>N=52</td>
</tr>
<tr>
<td>Boake et al. (2007)</td>
<td>E: CIMT C: Traditional rehabilitation</td>
<td>3hr/d x 6d/wk x 2wk</td>
<td>RCT (5)</td>
<td>N=23</td>
</tr>
<tr>
<td>Page et al. (2005b)</td>
<td>E: CIMT C: Regular rehabilitation</td>
<td>0.5h/d x 3d/wk x 10wk</td>
<td>RCT (5)</td>
<td>N=10</td>
</tr>
<tr>
<td>Ploughman &amp; Corbett (2004)</td>
<td>E: Forced Use Therapy (Constraint without Shaping) C: Conventional Therapy</td>
<td>1h/d initially, increasing to 6h/d by 2wk</td>
<td>RCT (5)</td>
<td>N=23</td>
</tr>
<tr>
<td>Song et al. (2016)</td>
<td>E: Scalp cluster acupuncture and Constraint Induced Movement Therapy C: Body acupuncture and traditional rehabilitation therapy</td>
<td>5-6 h/d x 6 d/wk x 2 wk</td>
<td>RCT (5)</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=30 N&lt;sub&gt;End&lt;/sub&gt;=30</td>
</tr>
<tr>
<td>Shah et al. (2016a)</td>
<td>E: CIMT C: Motor Relearning Program</td>
<td>80% of working hours</td>
<td>RCT (5)</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=45 N&lt;sub&gt;End&lt;/sub&gt;=40</td>
</tr>
<tr>
<td>Seok et al. (2016)</td>
<td>E1: CIMT with Visual Biofeedback E2: Visual Biofeedback C: Conventional Occupational Therapy</td>
<td>1 h/d x 2 wk</td>
<td>RCT (5)</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=32 N&lt;sub&gt;End&lt;/sub&gt;=30</td>
</tr>
<tr>
<td>Batool et al. (2015)</td>
<td>E: CIMT C: Motor Relearning Programme</td>
<td>2 h/d x 6 d/wk x 3wk</td>
<td>RCT (5)</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=42 N&lt;sub&gt;End&lt;/sub&gt;=42</td>
</tr>
<tr>
<td>Azab et al. (2009)</td>
<td>E: CIMT</td>
<td>6 h/d x 4 wk</td>
<td>• Barthel Index (+)</td>
<td></td>
</tr>
</tbody>
</table>
Both Dromerick et al. (2000) and Ro et al. (2006) had high methodological quality and reported significant improvements in upper extremity motor function measured by the Action Research Arm Test and the Fugl Meyer Assessment. Furthermore, a study by Yoon et al. (2014) found that CIMT with mirror therapy was superior to conventional therapy. However, one higher quality study by Thran et al. (2015) and several other studies of lower quality did not support these conclusions (Boake et al., 2007; S. J. Page, P. Levine, & A. C. Leonard, 2005; Seok et al., 2016; Shah, Kumar, & Muragod, 2016b) as they found no significant difference in motor function of the affected limb between CIMT and a control group.

In a more recent study (Dromerick et al., 2009) including 2 CIMT groups (standard and high intensity), participants in the higher-intensity group fared, on average, worse than those in either the control group or the standard CIMT group, demonstrating an inverse dose-response curve. The authors proposed possible explanations to explain their results, including implementation of intervention too early following stroke, overtraining, and a blocked rather than distributed practice schedule.

A summary of the results from RCTs that evaluated CIMT in the chronic stages post stroke is presented in Table 10.2.11.2.

Table 10.2.11.2 Summary of RCTs Evaluating CIMT in the Chronic (>6 months) Phase Following Stroke

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>CIMT Intensity/Duration</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
</table>
| Wolf et al. (2006) | RCT (8) | E: CIMT + shaping procedure | 6hr/d x 5x/wk x 2wk | • Wolf Motor Function Test (+)
• Motor Activity Log: Amount of Use (+), Quality of Movement (+)
• Functional ability measures (-)
• Quality/frequency of performance of 30 daily activities (-) |
| Wolf et al. (2008) | EXCITE | C: Usual care | | |
| Dahl et al. (2008) | RCT (8) | E: CIMT | 6hr/d x 5x/wk x 2wk | • Wolf Motor Function Test: post (+), 6mo (-)
• Motor Activity Log (-)
• FIM (-)
• SIS (-) |
| N=30 | C: Community-based rehabilitation | | |
| Wolf et al. (2010) USA 8 (RCT) | E1: CIMT early (3-9 months post stroke) | 90% of waking time for 2 weeks | • Wolf Motor Function Test (+), at 24 mo (-)
• Motor Activity Log (+), at 24 mo (-)
• Stroke Impact Scale Hand and Activities Domains Score (+), at 24 mo (-) |
| E2: CIMT delayed (15 to 21 months post stroke) | | | |
| Sawaki et al. (2008) | RCT (8) | E: Early CIMT | 90% of day for 2 weeks | • Grip strength (+)
• Wolf Motor Function Test (-) |
| N=30 | C: Delayed CIMT | | |
| Underwood et al. (2006) | RCT (8) | E: CIMT + shaping procedure | 6hr/d x 5x/wk x 2wk | • Pain scale of Fugl Meyer (-)
• Wolf Motor Function Test (-) |
<p>| N=41 | C: Usual care | | |
| Richards et al. (2006) | E1: Traditional CIMT (CIMT-6) + donepezil | E1: 6hr/d in clinic x 5d/wk x 2wk | • Wolf Motor Function Test: E1 vs C1 (-); E2 vs C2 (-) |</p>
<table>
<thead>
<tr>
<th>Study Reference</th>
<th>Study Type</th>
<th>N Start</th>
<th>N End</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Intervention Details</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT (7) N=39</td>
<td></td>
<td></td>
<td></td>
<td>C1:</td>
<td>E2:</td>
<td>C1: Traditional CIMT (CIMT-6) + placebo E2: Shortened CIMT (CIMT-1) + repetitive transcranial magnetic stimulation (rTMS) C1: Shortened CIMT (CIMT-1) + sham rTMS</td>
<td>Motor Activity Log: Amount of Use E1 vs C1 (+); E2 vs C2 (-)</td>
</tr>
<tr>
<td>Brogårdh &amp; Bengt (2006) RCT (7) N=16</td>
<td>RCT</td>
<td></td>
<td></td>
<td>E: CIMT</td>
<td>C:</td>
<td>E: CIMT and using mitt at home for another 3 months every other day C: CIMT</td>
<td>Modified Motor Assessment Scale (-) Sollerman Hand Function Test (-) Motor Activity Log (-)</td>
</tr>
<tr>
<td>Wu et al. (2007) RCT (6) N=47</td>
<td>RCT</td>
<td></td>
<td></td>
<td>E:</td>
<td>C:</td>
<td>E: CIMT C: Regular interdisciplinary rehab</td>
<td>Motor Activity Log (+) Fugl Meyer Score (-)</td>
</tr>
<tr>
<td>Khan et al. (2011) RCT (6) N=44</td>
<td>RCT</td>
<td></td>
<td></td>
<td>E1:</td>
<td>E2:</td>
<td>E1: CIMT E2: Therapeutic Climbing C: Conventional Neurological Therapy</td>
<td>Wolf Motor Function Test: Post-Intervention: E1 vs E2 (+); E1 vs C (-); E2 vs C (-); 6 months: E1 vs C (-) Motor Activity Log (-)</td>
</tr>
<tr>
<td>Taub et al. (1993) RCT (6) N=9</td>
<td>RCT</td>
<td></td>
<td></td>
<td>E:</td>
<td>C:</td>
<td>E: Unaffected upper extremity restrained in a sling + practice using impaired upper extremity C: Procedures designed to focus attention use of impaired upper extremity</td>
<td>Emory Test: post (+), 2yr (+) Arm Motor Activity Rest Test: post (+), 2yr (+) Motor Activity Log: increase in ability to use affected upper extremity (+)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Treatment</td>
<td>Control</td>
<td>Interventions</td>
<td>Duration</td>
<td>Outcome Measures</td>
<td></td>
</tr>
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<tr>
<td>Huseyinsinoglu et al. (2012)</td>
<td>RCT (6)</td>
<td>E: CIMT</td>
<td>C: Bobath</td>
<td>3hr/d x 10 weekdays</td>
<td>• Motor Activity Log: Amount of Use (+), Quality of Movement (+) • Wolf Motor Function Test (-) • FIM (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wittenberg et al. (2003)</td>
<td>RCT (5)</td>
<td>E: Intense CIMT</td>
<td>C: Less intense CIMT</td>
<td>E: 6hr/d x 10d C: 3hr/d x 10d</td>
<td>• Motor Activity Log (+) • Wolf Motor Function Test (-) • Assessment of Motor and Process Skills (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu et al. (2011) Taiwan</td>
<td>RCT (5)</td>
<td>E1: Distributed CIMT E2: Bilateral Arm Training C: Routine Therapy</td>
<td></td>
<td>2hr/d x 5d/wk x 3wk</td>
<td>• Unilateral and Bilateral Smoothness while Reaching: E1/E2 vs C (+) • Unilateral and Bilateral Force Movement Initiation while Reaching: E2 vs E1/C (+) • Motor Activity Log: E1 vs E2/C (+) • Wolf Motor Function Test: E1 vs E2/C (+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin et al. (2007)</td>
<td>RCT (5)</td>
<td>E: CIT C: Traditional therapy (neurodevelopmental)</td>
<td></td>
<td>2hr/d x 5d/wk x 3wk</td>
<td>• Fugl Meyer (+) • FIM (+) • Motor Activity Log (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Takebayashi et al. (2013)</td>
<td>RCT (5)</td>
<td>E: CIMT + transfer package C: CIMT</td>
<td></td>
<td>4.5hr for 2wk</td>
<td>• Fugl Meyer Score: post (-), follow-up (+) • Motor Activity Log: Amount of Use: post (+), follow-up (+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Souza et al. (2015)</td>
<td>RCT (5)</td>
<td>E1: CIMT high intensity E2: CIMT low intensity</td>
<td></td>
<td>E1: 3hr x 3-4x/wk for 10 sessions over 22d E2: 1hr x 3-4x/wk for 10 sessions over 22d</td>
<td>• Fugl Meyer Assessment (-) • Motor Activity Log (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin et al. (2008)</td>
<td>RCT (5)</td>
<td>E: CIMT C: Traditional Intervention</td>
<td></td>
<td>2h/d x 5d/wk x 3wk</td>
<td>• Fugl Meyer Assessment (+) • Functional Independence Measure (+) • Motor Activity Log (-) • Nottingham Extended Activities of Daily Living Scale (-), mobility subsection (+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sterr et al. (2002)</td>
<td>RCT (4)</td>
<td>E1: Longer CIMT + ‘shaping procedure’ E2: Shorter CIMT + ‘shaping procedure’</td>
<td></td>
<td>E1: 6hr/d for a target of 90% of waking time E2: 3hr/d x 2wk</td>
<td>• Motor Activity Log (+) • Wolf Motor Function Test (-) • Quality of Movement (+) • Amount of Use (+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taub et al. (2006)</td>
<td>PCT</td>
<td>E: CIMT C: Placebo, General Fitness Program</td>
<td></td>
<td>6h/d x 10d, restraint for 90% of waking time</td>
<td>• Motor Activity Log (+)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Overall, the majority of studies examined showed a positive effect for CIMT in the chronic phase of stroke for upper limb motor function. These studies included: Wolf et al. (2006), Wolf et al. (2008), Dahl et al. (2008), van der Lee et al. (1999), Suputtitada et al. (2004), Taub et al. (1993), Wu et al. (2011), Lin et al. (2007), Lin et al. (2009), Lin et al. (2010), Lin et al. (2008). Studies which found no significant impact on upper limb motor function included Underwood et al. (2006); Khan et al. (2011); Huseyinsinolu et al. (2012). Studies investigating duration or intensity of CIMT included those by Brogard & Bengt (2006), Wittenberg et al. (2003), Souza et al. (2015), and Sterr et al. (2002). Outcomes of these studies indicated that there is either no difference between varying intensities or durations of CIMT between groups on
upper limb motor outcomes, or mixed results. Other studies have investigated early versus delayed CIMT including Wolf et al. (2010), Sawaki et al. (2008), and Alberts et al. (2004), and results were mixed with some positive and negative upper limb motor outcomes.

Combination therapy of CIMT with pharmacological agents was studied by Nadeau et al. (2014), to determine the benefit of cycloserine on the paretic upper extremity compared to placebo therapy. The study also investigated the effects of intervention intensity by delivering CIMT at a frequency of 6 hours per day or 2 hours per day. Results revealed no significant difference between the groups receiving cycloserine and those receiving placebo regarding their effect on upper limb motor function as measured by the FMA, WMFT and MAL (Nadeau et al., 2014). A similar study evaluated the effects of donepezil and repetitive transcranial magnetic stimulation (rTMS) compared to placebo and sham stimulation (Richards et al., 2006). Both groups receiving either the drug or the placebo performed CIMT for 6 hours per day, while those receiving rTMS or sham stimulation performed CIMT for 1 hour per day. There was a significant improvement in the MAL favouring the group receiving CIMT for 6 hours per day compared to the rTMS group performing less frequent CIMT. However, after 2 weeks of therapy, motor skill gains for both groups were equivalent, and at 6 months the gains made were not maintained by either group (Richards et al., 2006). In contrast, Abo et al. (2014) found that when rTMS was compared to CIMT, the results were in favour of rTMS as demonstrated by significantly greater improvements on the FMA, and the Functional Assessment Score, but not on the WMFT.

A recent systematic review and meta-analysis by McIntyre et al. (2012) evaluated the effect of CIMT on impaired upper extremity motor function in patients with stroke in the chronic phase. A total of 16 studies were included in the analysis, ranging in methodological quality from 4 (fair) to 8 (excellent) as measured by the PEDro. The time post-stroke also ranged from 6.7 months to 10 years. The meta-analysis revealed a significant effect favouring CIMT regarding both the Amount of Use and the Quality of Movement subscales of the MAL (McIntyre et al., 2012). Similarly, the same effects were found on the FMA and on the ARAT, however the WMFT and the FIM were not found to favour CIMT over the control (McIntyre et al., 2012).

A summary of the results from RCTs that evaluated mCIMT in the subacute (<6 months) stage post stroke is presented in Table 10.2.11.3.

### Table 10.2.11.3 Summary of RCTs Evaluating Modified CIMT in the Subacute (<6 months) Phase Following Stroke

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>CIMT Intensity/Duration</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
</table>
| **Myint et al. (2008)** | RCT (7) | N=43 | E: mCIMT C: Traditional rehabilitation | 4 hrs/day x 10 days | • Action Research Arm Test (+)  
• Motor Activity Log (+) |
| **Treger et al. (2012)** | RCT (7) | N=28 | E: mCIMT C: Traditional rehabilitation | 4 hrs/day x 2 days/wks | • Functional Independence Measure (-)  
• Manual Function Test (-) |
| **Kwakkel et al. (2016)** | RCT (7) | N.Seek=159 N.End=159 | E1: Electromyographic Neuromuscular Stimulation on finger extensors  
E2: Modified Contrain Induced Movement Therapy | 3h/d x 5d/wk x 3wk | • Action Research Arm Test: E1 vs C1 (-); E2 vs C2 (+)  
• Fugl-Meyer Assessment: E1 vs C1 (-); E2 vs C2 (-)  
• Wolf Motor Function Test: E1 |
C1: Unfavourable prognosis based on voluntary finger extension. Received usual care.  
C2: Favourable prognosis based on voluntary finger extension. Received usual care.  

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention 1</th>
<th>Intervention 2</th>
<th>Comparator 1 vs C1</th>
<th>Comparator 2 vs C2</th>
<th>Outcome Measures</th>
</tr>
</thead>
</table>
| El-Helow et al. (2014) | E: Modified Constraint Induced Movement Therapy | C: Conventional Rehabilitation               | E1 vs C1 (-); E2 vs C2 (-) | Motricity Index: E1 vs C1 (-); E2 vs C2 (-) | Fugl-Meyer Assessment (+)  
|                        |                                             |                                             |                    | Erasmus modified Nottingham Sensory Assessment: E1 vs C1 (-); E2 vs C2 (-) | Action Research Arm Test (+) |
|                        |                                             |                                             |                    | Nine-Hole Peg Test: E1 vs C1 (-); E2 vs C2 (-) | Motor Activity Log: Quality of Movement: E1 vs C1 (-); E2 vs C2 (-)  
|                        |                                             |                                             |                    | Frenchay Arm Test: E1 vs C1 (-); E2 vs C2 (-) | Motor Activity Log: Amount of Use: E1 vs C1 (-); E2 vs C2 (-)  
|                        |                                             |                                             |                    |                                                   | Stroke Impact Scale: Hand E1 vs C1 (-); E2 vs C2 (+) |
| Liu et al. (2016)     | E1: Modified Constraint Induced Movement Therapy | E2: Self-Regulated Modified Constraint Induced Movement Therapy | E2 vs E1 (+); E2 vs C (+) | Fugl-Meyer Assessment: E2 vs E1 (+); E2 vs C (+) | Action Research Arm Test: E2 vs E1 (+); E2 vs C (+)  
|                        |                                             |                                             |                    | Independent Activities of Daily Living: E2 vs E1 (+); E2 vs C (+) | Motor Activity Log: E2 vs E1 (+); E2 vs C (+)  
|                        |                                             |                                             |                    |                                                   | Self-Pereived Quality of Arm Use: 1 month, E2 vs E1 (+); E2 vs C (+) |
| Hammer & Lindmark     | E: Restraining sling and Standard Rehabilitation | C: Standard Rehabilitation                    |                    | Fugl-Meyer (-) | Motor Assessment Scale (-)  
| Hammer & Lindmark     |                                             |                                             |                    | Action Research Arm Test (-) | Motor Assessment Scale (-)  
|                        |                                             |                                             |                    | 16-Hole Peg Test (-) | Motor Assessment Scale (-)  
|                        |                                             |                                             |                    | Grip strength ratio (-) | Motor Assessment Scale (-)  
|                        |                                             |                                             |                    | Modified Ashworth Scale (-) | Motor Assessment Scale (-)  
| Brogårđh et al. (2009)| E: Shortened CIMT (mitt use) | C: No mitt use                            |                    |                     | Motor Assessment Scale (-)  
|                        |                                             |                                             |                    | Sollerman Hand Function Tst (-) | 2-Point Discrimination Test (-)  
|                        |                                             |                                             |                    | 2-Point Discrimination Test (-) | Motor Activity Log Test (-) |

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

Several studies found an improvement in Action Research Arm Test scores in those receiving mCIMT in the early phase after stroke compared to those receiving conventional therapy (El-Helow et al., 2014; Kwakkel et al., 2016; K. P. Liu et al., 2016; Myint et al., 2008). However, many studies also found no
significant improvement in those receiving mCIMT when compared to conventional therapy on other motor function based outcomes that focus more on improvements of impairment (Brogardh et al., 2009; Hammer & Lindmark, 2009; Kwakkel et al., 2016; Treger et al., 2012).

This suggests that mCIMT optimizes already preserved function through adaptation strategies, but that it doesn’t improve neurological impairment in the early stage after stroke.

A summary of the results from RCTs that evaluated mCIMT in the chronic (>6 months) stages post stroke is presented in Table 10.2.11.4.

Table 10.2.11.4 Summary of RCTs Evaluating Modified CIMT in the Chronic (>6 months) Phase Following Stroke

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>CIMT Intensity/Duration</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
</table>
| Smania et al. (2012) | RCT (8) | N=66 | E: mCIMT C: Dose-match task-specific therapy | 2hr/d x 5d/wk x 2wk | • Wolf Motor Function Test (+)  
• Motor Activity Log (+) |
| Lin et al. (2007) | RCT (7) | N=32 | E: mCIMT C: Traditional rehab | 6hr/d x 5hr/d x 3wk. | • Motor Activity Log (+)  
• FIM (+) |
| Hsieh et al. (2016) | RCT (7) | NStart=34 NEnd=34 | E: Modified Constraint-Induced Therapy C: Regular Therapy | 20 sessions x 105min/d x 5 d/wk x 4 wk | • Wolf Motor Function Test  
• Functional Ability Score (+)  
• Wolf Motor Function Test Times (-)  
• Nottingham Extended Activities of Daily Living (+)  
• Functional Independence Measure (-) |
| Barzel et al. (2015) | RCT (6) | NStart=156 NEnd=156 | E: Home CIMT C: Standard Therapy | 5h/wk x 4wk | • Motor Activity Log Quality of Movement (+)  
• Motor Activity Log Amount of Arm Usage (+)  
• Wolf Motor Function Test (-)  
• Nine Hole Peg Test (-)  
• Stroke Impact Scale (-)  
• Barthel Index (-)  
• Instrumental Activities of Daily Living (-) |
| Wu et al. (2007) | RCT (6) | N=30 | E: mCIMT C: Regular occupational therapy | 2hr/d x 5d/wk x 3wk | • Motor Activity Log (+)  
• FIM (+) |
| Page et al. (2004) | RCT (6) | N=17 | E1: mCIMT E2: Traditional Rehabilitation C: No Therapy | 30 min/d x 3d/wk x 10 wk | • Fugl-Meyer Assessment (+)  
• Action Research Arm Test (+) |
| Page et al. (2004) | RCT (6) | N=17 | E1: mCIMT + physical and occupational therapy E2: Traditional rehab C: No therapy | 5hr/d x 5d/wk x 10wk | • Fugl Meyer: mCIMT at post (+)  
• Action Research Arm Test: mCIMT at post (+) |
<p>| Page et al. (2002) | RCT (6) | N=17 | E1: mCIMT + physical and | 5hr/d x 5d/wk x 10wk | • Fugl Meyer Score: mCIMT at |</p>
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<td>RCT</td>
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<td>E1: mCIMT group therapy E2: mCIMT individual therapy</td>
<td>3 h/d x 10 d</td>
<td>• Action Research Arm Test: mCIMT at post (+)</td>
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<td>• Action Research Arm Test (+)</td>
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<td>• Functional Independence Measure Motor (+)</td>
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<td>• Functional Independence Measure Total (+)</td>
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<tr>
<td>Page et al. (2008)</td>
<td>RCT</td>
<td>35</td>
<td>E1: mCIT + physical and occupational therapy E2: Traditional rehab C: No therapy</td>
<td>5 h/d x 5 d/6 wk x 10 wk</td>
<td>• Fugl Meyer Assessment (-)</td>
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<td>• Action Research Arm Test (+)</td>
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<tr>
<td>Yadav et al. (2016)</td>
<td>RCT</td>
<td>65/60</td>
<td>E: mCIT and conventional rehabilitation C: Conventional rehabilitation</td>
<td>3 h/d x 3 d/wk x 4 wk</td>
<td>• Fugl-Meyer Assessment: 1mo (+); 3mo (+)</td>
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<td>• Amount of Use: 1mo (+); 3mo (+)</td>
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<td>• Quality of Use: 1mo (+); 3mo (-)</td>
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<td>Wu et al. (2007)</td>
<td>RCT</td>
<td>26</td>
<td>E: mCIT + a restraining mitt on the unaffected hand C: Traditional therapy</td>
<td>2 h/d x 5 d/wk x 3 wk</td>
<td>• Fugl Meyer Assessment (+)</td>
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<td>• FIM (+)</td>
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<td>• Motor Activity Log (+)</td>
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<td>• Stroke Impact Scale (+)</td>
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<tr>
<td>Hayner et al. (2010)</td>
<td>RCT</td>
<td>12</td>
<td>E: mCIMT C: Bilateral training</td>
<td>6 h/d x 10 d</td>
<td>• Wolf Motor Function Test (-)</td>
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<td>• COPM (-)</td>
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<td>Wang et al. (2011)</td>
<td>RCT</td>
<td>30</td>
<td>E1: mCIMT E2: Intensive conventional therapy C: Conventional therapy</td>
<td>3 h/d x 5 d/wk x 4 wk</td>
<td>• Wolf Motor Function Test: mCIMT (+)</td>
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<td>Shaping Only</td>
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<td>• Wolf Motor Function Test (-)</td>
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</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Compared to conventional therapy, mCIMT in the chronic stage after stroke has demonstrated its effectiveness on upper limb motor function outcomes based on the results of studies by Smania et al. (2012), Hsieh et al. (2016), Page et al. (2004), Page et al. (2004), Page et al. (2002), Doussoulin et al. (2017), Page et al. (2008), Yadav et al. (2016), Wu et al. (2007), and Wang et al. (2011). Barzel et al. (2015), Wu et al. (2007), and Lin et al. (2007) found that mCIMT provided improvements on the Motor Activity Log, which is a self-reported measurement of arm function, when compared to conventional therapy. One RCT found that mCIMT was not superior to bilateral training for upper limb motor function (Hayner et al., 2010). This is one of few studies examining mCIMT with the inclusion of a control group receiving the same duration, frequency and intensity of therapy as the treatment group. The authors suggested that the intensity, rather than the type of therapy, explained the gains made in both groups which resulted in a lack of significant difference between the groups on the outcomes measured. The addition of a third group consisting of conventional therapy at a lower intensity may have helped to elucidate the effect of treatment.

**Conclusions Regarding Constraint-Induced Movement Therapy**
There is level 1b and level 2 evidence that there is no benefit of CIMT in the early stage of stroke for improving upper limb motor function or dexterity.

There is level 1a evidence that CIMT in the chronic phase of stroke may help improve upper extremity motor function. The evidence regarding the ideal frequency of CIMT is currently unclear.

There is level 1a evidence that mCIMT in the early phase of stroke may improve adaptation strategies as it optimizes already preserved function. However, mCIMT does not improve neurological impairment in the early stage of stroke.

There is level 1a evidence that mCIMT in the chronic phase of stroke may improve upper limb function relative to conventional therapy.

Constraint-induced movement therapy (CIMT) may be ineffective in the acute stage of stroke, but likely effective in the chronic phase for improving upper extremity motor function.

Modified constraint-induced movement therapy (mCIMT) may improve adaption to preserved function, but not neurological impairment in the early stage of stroke. However, mCIMT may improve upper limb motor function in the chronic phase.

10.2.12 Mirror Therapy
Mirror therapy is a technique that uses visual feedback about motor performance to improve rehabilitation outcomes. Ramachandran et al. (1995) first used this method to understand the effect of vision on phantom sensation in arm amputees. This method has since been adapted from its original use (as a method to “re-train the brain”) as a means to enhance upper-limb function following stroke and to reduce pain (Sathian, Greenspan, & Wolf, 2000). In mirror therapy, patients place a mirror beside the unaffected limb, blocking their view of the affected limb and creating an illusion of two limbs which are functioning normally. It is believed that by viewing the reflection of the unaffected arm in the mirror, this may act as substitute for the decreased or absent peripheral and proprioceptive input to the affected arm.

The effectiveness of mirror therapy was evaluated recently in a Cochrane review (Thieme, Mehrholz, Pohl, Behrens, & Dohle, 2012). The results from 14 RCTs (567 subjects) were included. A modest benefit of treatment was reported in terms of motor function, but the treatment effect was difficult to isolate due to the variability of control conditions. Improvement in performance of ADLs (SMD=0.33, 95% CI 0.05 to 0.60, p=0.02), pain (SMD=-1.1, 95% CI -2.10 to -0.09, p=0.03) and neglect (SMD=1.22, 95% CI 0.24 to 2.19, p=0.01) were also noted.

A summary of the results from RCTs evaluating mirror therapy is presented in Table 10.2.12.1.

Table 10.2.12.1 Summary of Controlled Trials Evaluating Mirror Therapy for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arya et al. (2015)</td>
<td>RCT (8)</td>
<td>E: Task-based mirror therapy; C: Standard Rehabilitation</td>
<td>• Fugl-Meyer Assessment of the Upper Extremity (+): wrist and hand (+); arm (-)</td>
</tr>
<tr>
<td>Study Authors</td>
<td>Year</td>
<td>Design</td>
<td>N Start/N End</td>
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</tbody>
</table>
| Yavuzer et al.        | 2008       | RCT(7) | 40            | E: Mirror Therapy and conventional stroke rehabilitation  
                             C: Sham Therapy and conventional stroke rehabilitation                        | Brunnstrom Stages for the Hand and Upper Extremity (⁺)  
                             • Functional Independence Measure for Self Care (⁺)  
                             • Modified Ashworth Scale (-)                      |
| Timmerman et al.      | 2013       | RCT(7) | 42            | E: Mirror Therapy + conventional therapy  
                             C: Sham Therapy + conventional therapy               | Frenchay Arm Test (⁻)  
                             • Wolf Motor Function Test (⁻)                      |
| Yoon et al.           | 2014       | RCT(7) | 26            | E1: CIMT + Mirror therapy  
                             E2: CIMT  
                             C: Control therapy                                    | Box and Block Test: E1 vs E2 (⁺)  
                             • Nine Hole Peg Test: E1 vs E2 (⁺)  
                             • Grip strength: E1 vs E2 (⁺)                      |
| Ji et al.             | 2014       | RCT(7) | 35            | E1: Mirror Therapy + rTMS  
                             E2: Mirror Therapy  
                             C: Sham Therapy                                       | Fugl Meyer Score: E1 vs. E2 (+), E2 vs. C (+)  
                             • Box and Block Test: E1 vs. E2 (+), E2 vs. C (+) |
| Invernizzi et al.     | 2013       | RCT(7) | 26            | E: Mirror therapy  
                             C: Conventional therapy                                | • Action Research Arm Test (+)  
                             • Motoric Index (+)  
                             • Fugl Meyer Scores (+)                              |
| Altschuler et al.     | 1999       | RCT(7) | 40            | E: Mirror therapy  
                             C: Sham therapy                                       | Brunnstrom stages (+)  
                             • Fugl Meyer self-care Score (+)  
                             • Modified Ashworth Scale (-)                      |
| Dohle et al.          | 2009       | RCT(7) | 36            | E: Mirror Therapy  
                             C: Control therapy                                      | Fugl Meyer Score (-)                                                        |
| Michielsen et al.     | 2011       | RCT(7) | 40            | E: Mirror therapy  
                             C: Control therapy                                      | • Action Research Arm Test (-)  
                             • ABILHAND (-)  
                             • Grip force (-)  
                             • Tardieu Scale (-)  
                             • Fugl Meyer Scores (+)                              |
| Kojima et al.         | 2014       | RCT(7) | 13            | E: Neuromuscular stimulation + mirror therapy then PT + OT  
                             C: PT + OT then neuromuscular stimulation + mirror therapy | Fugl Meyer Assessment: Phase 1 (+); Phase 2 (-)  
                             • Maximum active range of wrist extension:  
                             Phase 1 (-); Phase 2 (+)  
                             • Hand Ratio (-)  
                             • Box and Block Test (-)  
                             • Wolf Motor Function Test (-)  
                             • Motor Activity Log (-)                           |
| Samuelkamaleshkumar et al. | 2014   | RCT(7) | 20            | E: Mirror therapy + bilateral arm training  
                             C: Control group                                        | Fugl Meyer score (+)  
                             • Brunnstrom stage (+)  
                             • Box and Block Test (+)  
                             • Modified Ashworth Scale (-)                      |
| Selles et al.         | 2014       | RCT(7) | 103           | E1: Mirror + bimanual training  
                             E2: Bimanual training  
                             E3: Mirror therapy for unaffected hand  
                             E4: Bimanual training for unaffected hand  
                             C: No mirror therapy for unaffected hand              | Peak velocity: Bimanual no mirror vs. affected (+), bimanual mirror vs. affected (+)  
                             • Fugl Meyer Score: E1/E2 vs. C (+)                  |
| Lin et al.            | 2014       | RCT(7) | 20            | E1: Mirror therapy + mesh glove  
                             C: Control group                                        | Fugl Meyer Score: E1/E2 vs. C (+)                  |
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<th>Study</th>
<th>Design</th>
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<th>N End</th>
<th>Intervention E2</th>
<th>Intervention C</th>
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<td>Control Therapy</td>
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<td>Maximum shoulder abduction: E1/E2 vs. C (+)</td>
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<td>Normalized shoulder flexion: E2 vs. C (+)</td>
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<td>Colomer et al. (2016)</td>
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<td>Nottingham Sensory Assessment Tactile Subscale (+)</td>
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<td>E: Mirror therapy + tDCS</td>
<td>Box and Block Test (+)</td>
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<td>Grip strength (+)</td>
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<th>N_{End}</th>
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<th>C: Conventional rehabilitation</th>
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<th>N_{Start}</th>
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<td>Modified Barthel Index (+)</td>
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<th>E1: NMES + mirror therapy</th>
<th>E2: NMES</th>
<th>E3: Mirror therapy</th>
<th>Fugl Meyer Score: E1 vs E2/E3 (+)</th>
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<tr>
<td>60</td>
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<th>C: Conventional therapy</th>
<th>Fugl Meyer Assessment (+)</th>
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<th>C: Action observation</th>
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<thead>
<tr>
<th>N_{Start}</th>
<th>N_{End}</th>
<th>E: Mirror Therapy</th>
<th>C: Conventional Therapy</th>
<th>Action Research Arm Test (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>25</td>
<td></td>
<td></td>
<td>Fugl-Meyer Assessment (+)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N_{Start}</th>
<th>N_{End}</th>
<th>E: Mirror Therapy and neurodevelopmental treatment</th>
<th>C: Neurodevelopmental treatment</th>
<th>Fugl-Meyer Assessment (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>8</td>
<td></td>
<td></td>
<td>Motricity Index (-)</td>
</tr>
</tbody>
</table>

Discussion

Overall, a positive effect of mirror therapy on upper extremity motor function has been found. Studies by Ji et al. (2014), Invernizzi et al. (2013), Altschuler et al. (1999), Park et al. (2015), Wu et al. (2013), Pervane Vural et al. (2016), Gurbuz et al. (2016), Lim et al. (2016), and Yun et al. (2011) demonstrated that mirror therapy is superior to conventional, control, or sham therapies for improving upper limb motor function. In addition, a study by Arya et al. (2015) found that task-based mirror therapy was superior to standard therapy based on functional outcomes of the arm and hand. Yoon et al. (2014) found that mirror therapy with CIMT was superior to CIMT on various motor function tests, and Samuelkamaleshkumar et al. (2014) found that mirror therapy with bilateral arm training were superior to a control group. Studies by Michielsen et al. (2011), Lin et al. (2014), and Kim et al. (2015) found some positive and some negative motor function outcomes. Studies by Dohle et al. (2009), Colomer et al. (2016), and Thieme et al. (2012) found that there was no difference between mirror therapy and sham on motor function outcomes. A study by Timmerman et al. (2013) also found no significant difference on
the Wolf Motor Function Test when comparing mirror therapy and conventional therapy to the Bobath method.

On the studies that found a significant difference between mirror-based therapy and a control group, they more often found an improvement on the wrist and hand Fugl-Meyer subscales rather than on the shoulder, elbow, forearm, and coordination subscales.

**Conclusions Regarding Mirror Therapy**

*There is level 1a evidence that mirror therapy improves upper limb motor function following stroke, especially for the wrist and hand.*

*There is level 1b evidence that Mirror therapy in combination with conventional therapy is not superior to the Bobath method for upper limb motor function.*

*There is conflicting level 1a evidence regarding the effect of mirror therapy on spasticity.*

**Mirror therapy is likely effective for improving upper limb motor function.**

**10.2.13 Feedback Therapy**

As with athletic performance, feedback can be used as a means to improve motor learning following stroke. There are two types of feedback, intrinsic and extrinsic. Intrinsic feedback refers to the use of a person’s own sensory-perceptual information to enhance their performance during a given task. It may take the form of touch, sound, pressure, and/or proprioception. Extrinsic feedback can augment the effect of intrinsic and refers to feedback provided from the environment. Extrinsic feedback can be both verbal and non-verbal. Comments from a therapist would be an example of extrinsic verbal feedback. Extrinsic feedback can be further classified as either knowledge of results (KR) or knowledge of performance (KP). KR is often given at the end of a task and is feedback related to the outcome of the performance of that task. A patient’s performance time on a particular task is an example of KR. KP is information about the movement characteristics that led to the performance outcome. For example, the position of the hand when a patient is reaching towards a glass of water.

Subramanian et al. (2010) conducted a systematic review which included the results from 9 studies. Results show evidence that external feedback, particularly KP, in the forms of verbal, virtual environments, videotape, robotics, audition, or vision, improved motor learning of the more affected upper limb.

A summary of the results of RCTs evaluating feedback therapy are presented in Table 10.2.13.1.

**Table 10.2.13.1 Summary of Controlled Trials Evaluating Feedback Therapy for the Upper Extremity**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piron et al., (2010)</td>
<td>RCT (8) N=50</td>
<td>E: Feedback in virtual environment C: Bobath therapy</td>
<td>• Fugl Meyer Score (+)</td>
</tr>
<tr>
<td>Yang et al., (2016)</td>
<td>RCT (8) N_{Start}=60</td>
<td>E1: Repetitive Transcranial Magnetic stimulation with sensory cueing E2: Repetitive Transcranial Magnetic</td>
<td>• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Modified Barthel Index (-)</td>
</tr>
<tr>
<td>Study</td>
<td>Intervention</td>
<td>Outcome Measures</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Abdollahi et al. (2014)</td>
<td>E: Hepatic and visual error augmentation C: No error augmentation</td>
<td>• Fugl Meyer Score: Phase 1 (+); Phase 2 (-)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Wolf Motor Function Test (+)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Wolf Motor Function Test (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Motor Assessment Scale (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Barthel Index (+)</td>
<td></td>
</tr>
<tr>
<td>Bang (2016)</td>
<td>E: Auditory feedback with constraint induced movement therapy (CIMT) C: Constraint induced movement therapy (CIMT)</td>
<td>• Action Research Arm Test (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fugl-Meyer Assessment for the upper limb (+)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Modified Barthel Index (+)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Motor Action Log Amount of Use (+)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Motor Action Log Quality of Movement (-)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Modified Ashworth Scale (-)</td>
<td></td>
</tr>
<tr>
<td>Durham et al. (2014)</td>
<td>E1: External focus (EF) feedback E2: Internal focus (IF) feedback</td>
<td>• Reach to grasp task: Peak velocity (+); Peak deceleration (-); Peak aperture (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Push object task: Peak velocity; Peak deceleration (+); Peak aperture; Movement duration (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Raise object task (-)</td>
<td></td>
</tr>
<tr>
<td>Mukherjee et al. (2013)</td>
<td>E: Visual feedback for reaching tasks C: No feedback for reaching tasks</td>
<td>• Approximate entropy (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Movement variability (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Movement time (-)</td>
<td></td>
</tr>
<tr>
<td>Ballester et al. (2016)</td>
<td>E: Reinforcement-induced movement therapy + feedback movement amplification C: Reinforcement-induced movement therapy</td>
<td>• Fugl-Meyer Assessment (+)</td>
<td></td>
</tr>
<tr>
<td>Cirstea &amp; Levin (2007)</td>
<td>E1: 20% Knowledge of Results about Movemet Precision E2: Faded Knowledge of Performance about arm joint movements C: Nondisabled control practiced same task as E1.</td>
<td>• Range of Shoulder Movements: E2 vs E1 (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Improved Elbow and Shoulder Temporal Interjoint Co-ordination: E2 vs E1 (+)</td>
<td></td>
</tr>
<tr>
<td>Cirstea et al. (2006)</td>
<td>E1: Knowledge of Results and reaching task E2: Knowledge of Performance with reaching task C: Control with nonreaching task</td>
<td>• Fugl-Meyer Assessment (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Performance Test for the Elderly (TEMPA) (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Precision in movement: E1 vs C (+); E2 vs E1 (-); E2 vs C (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Movement time and variability: E2 vs C (+); E1 vs E2 (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Composite Spasticity Index for Elbow (-)</td>
<td></td>
</tr>
<tr>
<td>Cruz et al. (2014)</td>
<td>E: Rehab device then vibratory feedback C: Vibratory feedback then rehab device</td>
<td>• Range of Motion (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Correct movements (-)</td>
<td></td>
</tr>
<tr>
<td>van Vugt et al. (2016)</td>
<td>E: Jittered auditory feedback with</td>
<td>• The Nine Hole Pegboard Test (-)</td>
<td></td>
</tr>
</tbody>
</table>
RCT (5)  
N_{Start}=43  
N_{End}=34  
random delays post-treatment and piano treatment  
C: Normal auditory feedback and piano treatment  
• Finger Tapping (-)  
• Finger Tapping Speed (-)

Gilmore & Spaulding (2007)  
RCT (5)  
N=10  
E: Verbal and Visual Feedback  
C: Verbal Feedback  
• Klein-Bell Activities of Daily Living Scale (-)  
• Canadian Occupational Performance Measure (-)

Kim et al. (2014)  
PCT  
N_{Start}=16  
N_{End}=16  
E: Auditory rhythmic stimulation  
C: No rhythmic auditory stimulation  
• Range of Motion: elbow extension (+)  
• Muscle activation (+)

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

Discussion
Several methods of feedback therapy have been used for upper extremity rehabilitation for individuals with stroke. Most studies investigated the effectiveness of external feedback, using methods such as visual stimuli, performance based reports, and auditory stimuli. Overall more studies indicated some benefit to feedback therapy than not.

Three studies investigated the use of auditory feedback for upper limb motor function, specifically Bang et al. (2016), van Vugt et al. (2016), and Kim et al. (2014). Bang et al. (2016) found a significant benefit to auditory feedback with CIMT to CIMT alone for upper limb motor function and spasticity. Likewise, Kim et al. (2014) also found a positive effect in terms of range of motion for auditory rhythmic stimulation compared to a control not receiving auditory stimulation. However, van Vugt et al. (2016) found that there was no significant difference between groups receiving jittered auditory feedback with random delays post-treatment and piano treatment compared to those only receiving piano treatment on the Nine-Hole Peg Test, a measure of upper limb function and dexterity.

Two studies investigated the use of visual feedback, both finding a significant improvement in upper limb motor function based on the Fugl-Meyer Assessment and Wolf Motor Function Test (Abdollahi et al., 2014; C. H. Lin et al., 2015). Abdollahi et al. (2014) compared hepatic and visual error augmentation to a control while Lin et al. (2015) compared bilateral isometric handgrip force training with visual feedback to routine therapy.

Four studies investigated studies which used knowledge of results (KR) or knowledge of performance (KP) (Ballester et al., 2016; Cirstea et al., 2006; Cirstea & Levin, 2007; Piron et al., 2010). Piron et al. (2010) compared knowledge of results and performance-based feedback in a virtual environment to Bobath therapy and found that feedback was significantly superior based on upper limb motor function scores. Ballester et al. (2016) compared feedback movement amplification with reinforcement-induced movement therapy to reinforcement-induced movement therapy and found a similar result. Cristea & Levin (2007) compared knowledge of results to knowledge of performance, and found that knowledge of performance was superior for improving range of motion of the shoulder. On the other hand, a study by Cristea et al. (2006) with similar interventions found no significant difference between groups for upper limb motor function.

Lastly, a study by Yang et al. (2016) investigated repetitive transcranial magnetic stimulation with sensory cueing through vibrations in comparison to repetitive transcranial magnetic stimulation alone. There was no significant difference on upper limb motor function outcomes between groups.
Conclusions Regarding Feedback Therapy

There is level 1a evidence that feedback is effective for improving upper limb motor function, and that it is ineffective for improving spasticity.

Feedback may improve upper limb motor function post stroke.

10.2.14 Action Observation
Action observation is a form of therapy whereby a motor task is performed by an individual while watching a mirror image of another individual perform the same task. The therapy is designed to increase cortical excitability in the primary motor cortex by activating central representations of actions through the mirror neuron system ((E. Kim & K. Kim, 2015a). Although action observation has been evaluated mainly in healthy volunteers, a number of studies have evaluated its benefit in motor relearning following stroke.

A summary of the results of RCTs evaluating action observation are presented in Table 10.2.14.1.

Table 10.2.14.1 Summary of RCTs Evaluating Action Observation for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Franceschini et al. (2012) RCT (8) N=102</td>
<td>E: Video footage C: Static images</td>
<td>• Box and Block Test (+) • Frenchay Arm Test (-) • Modified Ashworth Scale (-) • FIM (-)</td>
</tr>
<tr>
<td>Cowles et al. (2013) RCT (7) N=29</td>
<td>E: Action observation C: Conventional therapy</td>
<td>• Motricity Index (-) • Action Research Arm Test: conventional (+)</td>
</tr>
<tr>
<td>Sale et al. (2014) RCT (7) NStart=67 NEnd=67</td>
<td>E: Action observation C: Standard rehabilitation</td>
<td>• Box and Block Test (+) • FIM (+)</td>
</tr>
<tr>
<td>Kim et al. (2016) RCT (7) NStart=34 NEnd=30</td>
<td>E: Action observation training with CBI and functional electrical stimulation C: Conventional training</td>
<td>• Fugl-Meyer Assessment of Upper Extremity - Shoulder (+) • Fugl-Meyer Assessment of Upper Extremity - Wrist (+) • Motor Activity Log – Activity of Use (+) • Motor Activity Log – Quality of Movement (+) • Modified Barthel Index (+) • Wrist Flexion (+)</td>
</tr>
<tr>
<td>Kim and Kim (2015a) RCT (6) NStart=12 NEnd=12</td>
<td>E: Action observation + occupational therapy C: Placebo observation + occupational therapy</td>
<td>• Wolf Motor Function Test (-)</td>
</tr>
<tr>
<td>Lee et al. (2013) RCT (6) NStart=33 NEnd=33</td>
<td>E1: Action observation E2: Action practice E3: Action observation + action practice C: No treatment</td>
<td>• Number of drinking motions: Post-intervention: E1 vs. C (+), E2 vs. C (+), E3 vs. C (+), E1 vs. E2 (-), E1 vs. E3 (+), E2 vs. E3 (-); 1wk post-intervention: E1 vs. C (+), E2 vs. C (+), E3 vs. C (+), E1 vs. E2 (-), E1 vs. E3 (-), E2 vs. E3 (-)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Treatment</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------</td>
<td>-----------</td>
</tr>
<tr>
<td>Celnik et al. (2007)</td>
<td>RCT (5)</td>
<td>E1: Physical therapy + congruent action observation&lt;br&gt;E2: Physical therapy + incongruent action observation&lt;br&gt;C: Physical therapy</td>
</tr>
<tr>
<td>Zhu et al. (2015)</td>
<td>RCT (5)</td>
<td>E: Upper Limb Action Observation Therapy&lt;br&gt;C: Conventional Rehabilitation Therapy</td>
</tr>
<tr>
<td>Ertelt et al. (2007)</td>
<td>RCT (5)</td>
<td>E: Action observation therapy&lt;br&gt;C: Traditional therapy</td>
</tr>
<tr>
<td>Kuk et al. (2016)</td>
<td>RCT (5)</td>
<td>E: Video clip of a motor task followed by execution of the same motor task&lt;br&gt;C: Pictures of landscapes followed by execution of the motor task</td>
</tr>
<tr>
<td>Kim et al. (2015b)</td>
<td>RCT (4)</td>
<td>E: Purposeful Action Observation&lt;br&gt;C: Purposeful Action without Action Observation</td>
</tr>
<tr>
<td>Sun et al. (2016)</td>
<td>PCT</td>
<td>E: Motor Imagery Practice guided by daily synchronous action observation&lt;br&gt;C: Motor Imagery Practice guided by daily asynchronous action observation</td>
</tr>
</tbody>
</table>

*Indicates non-statistically significant differences between treatment groups<br>+ Indicates statistically significant differences between treatment groups

**Discussion**
Of the studies included to assess action observation, only one RCT was adequately powered (Franceschini et al., 2012). The study compared the effects of watching video footage of physical upper limb movements to those when patients observed static images of the same movements. The findings showed a significant difference between the groups on manual dexterity as measured by the Box and Block Test (BBT) and motor function through the Fugl Meyer Assessment, but not on the Frenchay Arm Test, another measure of motor function. Studies by Sale et al. (2014), Lee et al. (2013), Zhu et al. (2015), Ertelt et al. (2007), and Kuk et al. (2016) also supported the idea that action observation may improve upper limb motor function outcomes. However, most of these studies have low methodological quality and are severely underpowered, as mentioned above. Furthermore, studies by Cowles et al. (2013) and Kim & Kim (2015b) found that there was no significant difference between action observation and a control group.

A study by Kim et al. (2016) examining action observation in combination with computer-brain interface-based functional electrical stimulation found a significant improvement on upper limb motor functions in this group when compared to a conventional training group.

**Conclusions Regarding Action Observation**
There is conflicting level 1a evidence regarding the effect of action observation on upper motor function.
There is level 1b evidence that action observation with brain–computer interface-based functional electrical stimulation is effective for improving upper limb motor function.

Evidence for the use of action observation is conflicting, although the combination of action observation with brain–computer interface-based functional electrical stimulation may be effective for upper limb motor rehabilitation.

10.2.15 Music Therapy

Music therapy is a promising rehabilitation technique for improving function of the hemiparetic arm following stroke. It involves many components of conventional upper limb rehabilitation interventions including repetitive task practice, finger individualization, as well as tactile and auditory feedback (van Wijck et al., 2012). The rehabilitation program can also be shaped by increasing the tempo of the songs or incorporating more difficult musical pieces based on individual performance. Additionally, music therapy may be more emotionally involving than traditional upper limb interventions which could lead to increased engagement of the patient (Van Vugt, Ritter, Rollnik, & Altenmüller, 2014).

RCTs evaluating the use of music therapy for upper extremity rehabilitation following stroke are summarized in Table 10.2.15.1.

Table 10.2.15.1 Summary of RCTs Evaluating Music Therapy for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
</table>
| **Thielbar et al.** (2014) | RCT (6)  
N\text{\textsubscript{Start}}=14  
N\text{\textsubscript{End}}=14 | E: Virtual keyboard music playing  
C: High intensity, task oriented occupational therapy | • ARAT (-)  
• Fugl Meyer Assessment: Upper extremity (+); Hand (-)  
• Jebsen Taylor Hand Function Test (+)  
• Grip strength (-)  
• Lateral pinch strength (-)  
• 3-point pinch strength (-) |
| **Altenmüller et al.** (2009) | RCT (5)  
N\text{\textsubscript{Start}}=62  
N\text{\textsubscript{End}}=62 | E: MIDI piano and electronic drum training + conventional therapy  
C: Conventional therapy only | • Box and Block Test (+)  
• 9 Hole Pegboard Test (+)  
• Action Research Arm Test (+)  
• Arm Paresis Score (+)  
• Finger/Hand tapping (+) |
| **Tong et al.** (2015) | RCT (5)  
N\text{\textsubscript{Start}}=33  
N\text{\textsubscript{End}}=30 | E: Audible Musical Instrumental Training  
C: Mute Musical Instrumental Training | • Fugl-Meyer Assessment (-)  
• Wolf Motor Function Test (+) |
| **Van Vugt et al.** (2014) | RCT (4)  
N\text{\textsubscript{Start}}=36  
N\text{\textsubscript{End}}=28 | E: Playing piano together  
C: Playing piano sequentially | • Un-paced finger tapping scores: middle finger (-), index finger (-)  
• Paced finger tapping score: index to thumb (-)  
• Nine Hole Peg Test (-) |
| **Scholz et al.** (2016) | RCT (4)  
N\text{\textsubscript{Start}}=25  
N\text{\textsubscript{End}}=25 | E: Musical Sonification Therapy  
C: Sham Movement Training | • Fugl-Meyer Assessment (-)  
• Action Research Arm Test (-)  
• Nine Hold Peg Test (-)  
• Stroke Impact Scale (-) |
<table>
<thead>
<tr>
<th>Jun et al. (2013)</th>
<th>E: Music movement therapy</th>
<th>- Range of motion (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT (4)</td>
<td>C: Routine intervention</td>
<td>- Muscle strength (-)</td>
</tr>
<tr>
<td>NStart=40</td>
<td></td>
<td>- Modified Barthel Index (-)</td>
</tr>
<tr>
<td>NEnd=30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion

Overall, there is conflicting evidence for the effectiveness of music therapy for motor function and dexterity. This may be because of the large variation in intervention type and the low power of some of these studies. Thielbar et al. (2014) compared virtual playing of keyboard music to high intensity, task oriented occupational therapy, and found that the music group performed significantly better than the control group on some motor function outcomes, but not on others. The authors proposed that while the occupational therapy group practised a wider variety of motor skills, the music playing group repeated the same movement task which resulted in greater refinement of a specific motor skill. This improved hand motor control and was also found to generalize to the manipulation of real world objects measured by the Jebsen Taylor Hand Function Test. Despite this, no between group differences were found for measures of hand strength. Tong et al. (2015) also found mixed motor function outcomes when comparing audible musical instrumental training to mute musical instrumental training. Altenmuller et al. (2009) found a positive effect of musical instrument digital interface (MIDI) piano and electronic drum set in terms of upper limb motor function and dexterity in comparison to conventional training.

Jun et al. (2013) found that music movement therapy was superior to routine therapy only in terms of improving range of motion. The main activities of the music movement therapy included singing along to a song and playing basic percussion instruments (tambourines, maracas) with the less affected arm. Although greater improvement was found for the music group for range of motion, no between group differences were found for functional ability and muscle strength. These results indicate that music therapy not involving repetitive movements of the affected arm may not be effective for improving motor function. Furthermore, it is important to note that a major limiting factor to music therapy as an upper limb rehabilitation intervention is the severity of hemiparesis. In order to benefit from this treatment, individuals must have a certain level of control over the affected arm in addition to being able to individualize finger movements, particularly if a piano is used (Morris & Van Wijck, 2012). In addition, Van Vugt et al. (2014) found no difference in upper limb dexterity between playing piano together or sequentially, and Scholz et al. (2016) found no significant difference in upper limb motor function between musical sonification therapy and sham movement training.

Conclusions Regarding Music Therapy

There is level 1a and level 1b evidence that music therapy can improve some aspects of upper extremity motor function but not muscle strength when compared to conventional rehabilitation.

Music therapy may improve upper limb motor function but not muscle strength.

10.2.16 Telerehabilitation

It is known that distance to a rehabilitation centre can impede patients from receiving the care they need once they are discharged from the hospital. Therefore, providing rehabilitation services remotely via a kiosk or by telephone can limit the challenge of location and transportation especially for patients isolated from these services. This form of service provision has been termed “telerehabilitation”. It is an
intervention that can be delivered for a longer duration and at a reduced cost when compared to therapies provided in the inpatient rehabilitation setting (Benvenuti et al., 2014).

The studies investigating telerehabilitation for rehabilitation of the upper limb following stroke are presented in Table 10.2.16.1.

**Table 10.2.16.1 Summary of Controlled Trials Evaluating Telerehabilitation for the Upper Extremity**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
</table>
| **Wolf et al. (2015)** | RCT (7) | E: Telerehabilitation with home exercise program + robotic assistance training  
C: Telerehabilitation with home exercise program only | • Fugl Meyer Assessment (-)  
• Action Research Arm Test (-)  
• Wolf Motor Function Test: Performance time: Total (+), Fine (+), Gross (-); Functional ability (-); Mean number of tasks: Total (+), Fine (+), Gross (-) |
| | NStart=99  
NEnd=92 |  |  |
| **Emmerson et al. (2017)** | RCT (7) | E: Home exercise program using an electronic tablet with automated reminders  
C: Paper-based home exercise program | • Wolf Motor Function Test (-)  
• Grip Strength (-)  
• Functional Score (-) |
| | NStart=62  
NEnd=58 |  |  |
| **Majeed et al. (2015)** | RCT (6) | E: Bilateral Self-telerehabilitation program and Error augmentation through a robotically-applied force  
C: Bilateral Self-telerehabilitation program | • Fugl-Meyer Assessment (-) |
| | NStart=28  
NEnd=28 |  |  |
| **Benvenuti et al. (2014)** | PCT | E: Kiosk telerehab  
C: No kiosk availability | • Motricity Index (+)  
• Nine Hole Peg Test (+)  
• Wolf Motor Function Test (+)  
• Nottingham Extended Activities of Daily Living (+)  
• Barthel Index (+)  
• Stroke Impact Scale (+) |
| | NStart=256  
NEnd=188 |  |  |

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

**Discussion**

In a multicenter RCT conducted by Wolf et al. (2015), therapists made use of weekly phone calls or e-mails to administer telerehabilitation to groups receiving only home exercise practice or home exercise practice with robotic assistance. None of the upper limb motor function outcomes assessed indicated a difference between the two groups. Emmerson et al. (2017) also found a similar result when comparing a home exercise program using an electronic tablet with automated reminders to a paper-based home exercise program. Majeed et al. (2015) compared bilateral self-telerehabilitation program and error augmentation through a robotically-applied force to a bilateral self-telerehabilitation program, also finding no difference between groups in upper limb motor function.

One large prospective controlled trial (PCT) made use of community based kiosks to administer the telerehabilitation intervention (Benvenuti et al., 2014). The kiosks were designed to be easily accessible and allowed patients to perform upper extremity exercises with supervision and feedback delivered through videoconferencing. Benvenuti et al. (2014) found telerehabilitation to improve upper extremity motor outcomes to a significantly greater degree than conventional outpatient rehabilitation. Patients
receiving telerehabilitation were found to exercise more when compared to patients receiving conventional rehabilitation, suggesting that the telerehabilitation program provided extra motivation.

A systematic review by Johansson & Wild (2010) found four studies that examined the effectiveness of telerehabilitation-related interventions for upper limb motor function. The results were mixed, and the methodological quality of the studies found was low. The authors concluded that telerehabilitation may be effective for improving physical health of patients who have sustained a stroke, although additional evidence is needed.

**Conclusions Regarding Telerehabilitation**

*There is level 1a evidence that telerehabilitation interventions are not effective for improving upper limb motor function.*

*Home-based telerehabilitation interventions are likely not effective for improving upper limb motor function.*

### 10.2.17 Exercise Therapy

Physical therapy is one of the key disciplines in interdisciplinary stroke rehabilitation (Veerbeek et al., 2014). Engaging in exercise programs could improve fitness, reduce sedentary behaviour, and may be beneficial for reducing post-stroke symptoms.

The results of two RCT evaluating exercise therapy for upper extremity rehabilitation is presented in Table 10.2.17.1.

**Table 10.2.17.1 Summary of RCT(s) Evaluating Exercise Therapy for the Upper Extremity**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
</table>
| **English et al. (2015)** | RCT (8) | E1: Circuit class (3hr/d morning and afternoon)  
E2: Seven day therapy (7d/wk)  
C: Usual care (5d/wk) | • Wolf Motor Function Test (-)  
• FIM (-) |
| **Wang et al. (2016)** | RCT (5) | E: Low intensity aerobic training and a rehabilitation training program  
C: Rehabilitation training program | • Barthel Index (+)  
• Functional Ambulation Category (+)  
• Frenchay Activities Index (+)  
• Fugl-Meyer Assessment (+) |

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

**Discussion**

English et al. (2015) allocated patients to receive different intensities of conventional physical therapy or intensive circuit class training. Both of the group exercise programs were shown to significantly improve upper limb motor function; however, no significant differences between the two groups were found regarding FIM and Wolf Motor Function Test scores.

Wang et al. (2016) compared low intensity aerobic training to a rehabilitation training program and found a significant improvement in upper limb motor function in those receiving the aerobic training.
The lack of difference found between different therapies reported in English et al. (2015) was inconsistent with the results of a recent meta-analysis conducted by Veerbeek et al. (2014) which found that more therapy time leads to better recovery of stroke symptoms. English et al. (2015) suggest that this discrepancy may be due to their broad inclusion and exclusion criteria.

Although group programs can be provided with a lower ratio of staff to patients and may be more feasible than individual therapy, individual therapy allows therapists to more easily shape the intervention to the needs of the patient (English & Veerbeek, 2015). Further research is required to determine the benefit of different therapy intensities.

**Conclusions Regarding Exercise Therapy**

*There is conflicting evidence regarding the effectiveness of additional exercise therapy for improving upper limb motor function.*

Additional research is needed to evaluate the effectiveness of additional exercise therapy for upper limb motor function.

### 10.3 Robotic Devices for Movement Therapy

Robotic devices can be used to assist the patient in a number of circumstances. First of all, the robot can aid with passive range of motion to help maintain range and flexibility, to temporarily reduce hypertonia or resistance to passive movement. The robot can also assist when the patient has active movements, but cannot complete a movement independently. Robotics may be most appropriate for patients with dense hemiplegia, although robotics can be used with higher-level patients who wish to increase strength by providing resistance during the movement. According to Lum et al. (2002) “even though unassisted movement may be the most effective technique in patients with mild to moderate impairments, active- assisted movement (with robotic devices) may be beneficial in more severely impaired patients...especially during the acute and subacute phases when patients are experiencing spontaneous recovery,”. Krebs et al. (2002) noted that robotic devices rely on the repetition of specific movements to improve functional outcomes.

A systematic review of robot-aided therapy on recovery of the hemiparetic arm on recovery was conducted (Prange, Jannink, Groothuis-Oudshoorn, Hermens, & Ijzerman, 2006). The authors included the results from 8 studies evaluating the MIT-Manus, MIME and ARM Guide and concluded that robotic devices improved short and long term motor function of the paretic shoulder and elbow beyond that which could be achieved through therapy alone.

A Cochrane review (Mehroholz, Hadrich, Platz, Kugler, & Pohl, 2012) included the results from 19 trials (328 subjects) evaluating electromechanical and robot-assisted arm training devices. Compared with routine therapy, usually conventional physical therapy, the authors reported significantly greater improvement in activities of daily living (SMD=0.43; 95% CI 0.11 to 0.75, p <0.009) and arm function (SMD=0.45; 95% CI 0.20 to 0.69, p<0.001), but not arm strength (SMD=0.48; 95% CI -0.04 to 0.04, p=0.82).

A table of various robotic devices used in stroke rehabilitation is outlined below (see Table 10.3.1).

**Table 10.3.1 Robotic devices used for upper limb rehabilitation post-stroke**
<table>
<thead>
<tr>
<th>Robotic Devices</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>InMotion robot (Massachusetts Institute of Technology/MIT-Manus)</td>
<td>MIT-Manus was one of the first robotic devices to be developed. It features a 2-degree-of-freedom robot manipulator that assists in shoulder and elbow movement by guiding the patient’s hand in a horizontal plane, while visual, auditory and tactile feedback is provided during goal-directed movements. A commercially available unit (InMotion²) of this device is also available.</td>
</tr>
<tr>
<td>Mirror-Image Motion Enabler Robots (MIME)</td>
<td>MIME is a 6 degree of freedom robotic device developed “to provide therapy that combines bimanual movements with unilateral passive, active-assisted and resisted movements of the hemiparetic upper extremity,” (Burgar et al. 2011). The unit applies force to the more affected forearm during goal-directed movements.</td>
</tr>
<tr>
<td>ARMin</td>
<td>This exoskeleton robot has 7 degrees of freedom and also provides intensive and task-specific training to target improvements in motor function.</td>
</tr>
<tr>
<td>Assisted Rehabilitation and Measurement (ARM) Guide</td>
<td>This unit uses a motor and chain drive to move the user’s hand along a linear rail, which assists reaching in a straight-line trajectory.</td>
</tr>
<tr>
<td>Bi-Manu-Track</td>
<td>This arm-training device enables bilateral and passive and active practice of forearm and wrist movement.</td>
</tr>
<tr>
<td>Neuro-Rehabilitation-Robot (NeReBot)</td>
<td>The NeReBot device was developed in Italy designed to produce sensorimotor stimulation. The 3 degrees of freedom device can perform spatial movements of the shoulder and elbow, is portable and can be used when the patient is either prone or sitting.</td>
</tr>
<tr>
<td>Robot-mediated therapy system (GENTLE/s)</td>
<td>This device is a three-degree of freedom haptic interface arm with a wrist attachment mechanism, two embedded computers, a monitor and speakers and an overhead arm support system. The affected arm is de-weighted through a free moving elbow splint attached to the overhead frame. The subject is connected to the device by a wrist splint. Exercises such as hand-to-mouth and reaching movements can then be practised, while feedback is provided.</td>
</tr>
<tr>
<td>Amadeo</td>
<td>This device assists in hand rehabilitation, having an end-effector design. It helps with finger movements to allow for synchronization.</td>
</tr>
<tr>
<td>MusicGlove</td>
<td>The glove is used with a game that promotes specific pinching movements to match musical notes displayed on a screen.</td>
</tr>
</tbody>
</table>

Results of the studies evaluating the efficiency of these devices at improving upper limb motor function are presented in table 10.3.2. The time post-stroke (TPS) has been extracted from all selected studies and divided in three stages of stroke recovery: acute (<3 months), subacute (3-6 months), and chronic (>6 months).

### Table 10.3.2 Summary of Results From Studies Evaluating Sensorimotor Training: Robotic Devices

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MIT-Manus / InMotion</strong></td>
<td></td>
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</tr>
</tbody>
</table>
- Wolf Motor Function Test: E1 vs. C (-), E1 vs. E2 (-)  
- Stroke Impact Scale: E1 vs. C (+), E1 vs. E2 (-)  
- Modified Ashworth Scale: E1 vs. C (-), E1 vs. E2 (-) |
<p>| <em>Ang et al.</em> (2014) | RCT (7) N_{Start}=26 N_{End}=25 TPS=chronic | E: Brain Computer Interface Coupled with MIT-Manus shoulder-elbow robotic feedback C: Training with the MIT-Manus | - Fugl-Meyer Assessment (-) |
| <em>Volpe et al.</em> (1999) | | E: Robot | Motor Status score: shoulder/elbow at d/c (+), |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volpe et al. (2000)</td>
<td>RCT</td>
<td>N=20</td>
<td>Sham</td>
<td>and at 3yr follow-up (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TPS=acute</td>
<td></td>
<td>Motor Status score: wrist/hand at d/c (-), and at 3yr follow-up (-)</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td>Motor Power score: shoulder and elbow at d/c (+)</td>
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<td></td>
<td>Fugl Meyer: shoulder/elbow at d/c (-), and at 3yr follow-up (-)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Fugl Meyer: wrist/hand at d/c (-), and at 3yr follow-up (-)</td>
</tr>
<tr>
<td>Rabadi et al. (2008)</td>
<td>RCT</td>
<td>N=30</td>
<td>Robot</td>
<td>Fugl Meyer Score (-)</td>
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<tr>
<td></td>
<td></td>
<td>TPS=acute</td>
<td></td>
<td></td>
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<tr>
<td>Volpe et al. (2008)</td>
<td>RCT</td>
<td>N=21</td>
<td>Robot</td>
<td>Fugl Meyer Score (-)</td>
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<td></td>
<td></td>
<td>TPS=chronic</td>
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<tr>
<td>Conroy et al. (2011)</td>
<td>RCT</td>
<td>N=62</td>
<td>Robot</td>
<td>Fugl Meyer score (-)</td>
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<td></td>
<td></td>
<td>TPS=acute</td>
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<tr>
<td>Sale et al. (2014)</td>
<td>RCT</td>
<td>N=56</td>
<td>Robot</td>
<td>Fugl Meyer Score (+)</td>
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<td></td>
<td></td>
<td>TPS=acute</td>
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<tr>
<td>Fasoli et al. (2004)</td>
<td>RCT</td>
<td>N=56</td>
<td>Robot</td>
<td>Fugl Meyer Score (+)</td>
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<td></td>
<td></td>
<td>TPS=acute</td>
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<tr>
<td>McCabe et al. (2015)</td>
<td>RCT</td>
<td>N=39</td>
<td>Robot</td>
<td>Fugl Meyer Score (+)</td>
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<td></td>
<td></td>
<td>TPS=chronic</td>
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<tr>
<td>Abdullah et al. (2011)</td>
<td>RCT</td>
<td>N=20</td>
<td>Robot</td>
<td>Fugl Meyer Score (+)</td>
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<tr>
<td></td>
<td></td>
<td>TPS=acute</td>
<td></td>
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<tr>
<td>Stein et al. (2004)</td>
<td>RCT</td>
<td>N=49</td>
<td>Robot</td>
<td>Fugl Meyer Score (+)</td>
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<td></td>
<td></td>
<td>TPS=chronic</td>
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<tr>
<td>Volpe et al. (2000)</td>
<td>RCT</td>
<td>N=21</td>
<td>Robot</td>
<td>Fugl Meyer Score (-)</td>
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<td>TPS=chronic</td>
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<tr>
<td>Volpe et al. (2008)</td>
<td>RCT</td>
<td>N=21</td>
<td>Robot</td>
<td>Fugl Meyer Score (-)</td>
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<td>TPS=chronic</td>
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<tr>
<td>Rabadi et al. (2008)</td>
<td>RCT</td>
<td>N=30</td>
<td>Robot</td>
<td>Fugl Meyer Score (-)</td>
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<td></td>
<td></td>
<td>TPS=acute</td>
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<tr>
<td>Study</td>
<td>Design</td>
<td>N Start</td>
<td>N End</td>
<td>TPS</td>
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<tr>
<td>Lum et al. (2002)</td>
<td>RCT</td>
<td>27</td>
<td></td>
<td>chronic</td>
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<tr>
<td>Burgar et al. (2000)</td>
<td>RCT</td>
<td>21</td>
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<td>chronic</td>
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<tr>
<td>Burgar et al. (2011)</td>
<td>RCT</td>
<td>54</td>
<td></td>
<td>acute</td>
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<tr>
<td>Lum et al. (2006)</td>
<td>RCT</td>
<td>30</td>
<td></td>
<td>subacute</td>
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<tr>
<td>Arm Guide</td>
<td>RCT</td>
<td>19</td>
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</tr>
<tr>
<td>Hesse et al. (2005)</td>
<td>RCT</td>
<td>44</td>
<td></td>
<td>subacute</td>
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</tr>
<tr>
<td>Hesse et al. (2008)</td>
<td>RCT</td>
<td>54</td>
<td></td>
<td>subacute</td>
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<tr>
<td>Hesse et al. (2014)</td>
<td>RCT</td>
<td>50</td>
<td></td>
<td>acute</td>
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<tr>
<td>Hsieh et al. (2011)</td>
<td>RCT</td>
<td>18</td>
<td></td>
<td>acute</td>
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<td></td>
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</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>TPS</td>
<td>TPS Level</td>
<td>Intervention Details</td>
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<tr>
<td>Liao et al. (2012)</td>
<td>RCT (7)</td>
<td>chronic</td>
<td>N=20</td>
<td>E: Robotic therapy&lt;br&gt; C: Dose-matched conventional therapy</td>
</tr>
<tr>
<td>Hsieh et al. (2012)</td>
<td>RCT (7)</td>
<td>chronic</td>
<td>N=54</td>
<td>E1: High intensity robotic therapy&lt;br&gt; E2: Low intensity robotic therapy&lt;br&gt; C: Conventional therapy</td>
</tr>
<tr>
<td>Fan et al. (2016)</td>
<td>RCT (4)</td>
<td>chronic</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=6</td>
<td>E: Robot-assisted bilateral arm therapy&lt;br&gt; C: Dose-matched control therapy</td>
</tr>
<tr>
<td>NeReBot</td>
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</tr>
<tr>
<td>Masiero et al. (2014)</td>
<td>RCT (7)</td>
<td>chronic</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=34</td>
<td>E: Robotic therapy&lt;br&gt; C: Standard therapy</td>
</tr>
<tr>
<td>Masiero et al. (2006)</td>
<td>RCT (5)</td>
<td>chronic</td>
<td>N=35</td>
<td>E: Additional sensorimotor robotic training&lt;br&gt; C: Exposure to robotic device with no training</td>
</tr>
<tr>
<td>Masiero et al. (2007)</td>
<td>RCT (5)</td>
<td>chronic</td>
<td>N=20</td>
<td>E: Robotic Training&lt;br&gt; C: Exposure to robotic device</td>
</tr>
<tr>
<td>Masiero et al. (2011)</td>
<td>RCT (5)</td>
<td>chronic</td>
<td>N=21</td>
<td>E: Robotic arm therapy&lt;br&gt; C: Conventional therapy</td>
</tr>
<tr>
<td>Continuous Passive Motion (CPM)</td>
<td></td>
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</tr>
<tr>
<td>Hu et al. (2009)</td>
<td>RCT (5)</td>
<td>chronic</td>
<td>N=27</td>
<td>E: EMG-driven robot&lt;br&gt; C: Passive motion device</td>
</tr>
</tbody>
</table>
### Upper Extremity Interventions

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RCT (4)</strong>&lt;br&gt;N=32&lt;br&gt;TPS=acute</td>
<td></td>
<td></td>
<td>C: Control</td>
<td>• Motor Status score: elbow/shoulder (-)&lt;br&gt;• Modified Ashworth Scale (-)</td>
</tr>
<tr>
<td><strong>GENTLE/s</strong></td>
<td></td>
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<tr>
<td><strong>Timmermans et al. (2014)</strong>&lt;br&gt;RCT (8)&lt;br&gt;N&lt;sub&gt;Start&lt;/sub&gt;=22&lt;br&gt;N&lt;sub&gt;End&lt;/sub&gt;=22&lt;br&gt;TPS=chronic</td>
<td></td>
<td></td>
<td>E: Robotic arm training&lt;br&gt;C: Task oriented arm training</td>
<td>• Fugl Meyer Score: arm and hand (-)&lt;br&gt;• Action Research Arm test: arm and hand (-)&lt;br&gt;• Motor Activity Log: arm and hand (-)</td>
</tr>
<tr>
<td><strong>Lemmens et al. (2014)</strong>&lt;br&gt;RCT (7)&lt;br&gt;N&lt;sub&gt;Start&lt;/sub&gt;=16&lt;br&gt;N&lt;sub&gt;End&lt;/sub&gt;=16&lt;br&gt;TPS=chronic</td>
<td></td>
<td></td>
<td>E: Robotic therapy&lt;br&gt;C: No robotic therapy</td>
<td>• Fugl Meyer Score: motor (-)&lt;br&gt;• Action Research Arm Test (-)&lt;br&gt;• Motor Activity Log (-)</td>
</tr>
<tr>
<td><strong>Coote et al. (2008)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N=20</td>
<td></td>
<td></td>
<td>E: Robot-mediated therapy&lt;br&gt;C: Sling suspension phase</td>
<td>• Rate of recovery during robot-mediated therapy phase basd on Fugl-Meyer scores (+)</td>
</tr>
<tr>
<td><strong>Amadeo</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>Sale et al. (2014)</strong>&lt;br&gt;RCT (7)&lt;br&gt;N&lt;sub&gt;Start&lt;/sub&gt;=20&lt;br&gt;N&lt;sub&gt;End&lt;/sub&gt;=20&lt;br&gt;TPS=acute</td>
<td></td>
<td></td>
<td>E: Amadeo robotic therapy + physiotherapy&lt;br&gt;C: Occupational therapy</td>
<td>• Box and Block Test (+)&lt;br&gt;• Fugl-Meyer Assessment (+)</td>
</tr>
<tr>
<td><strong>Hwang et al. (2012)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N=17&lt;br&gt;TPS=chronic</td>
<td></td>
<td></td>
<td>E: Active robot training&lt;br&gt;C: Early passive therapy</td>
<td>• Jebsen-Taylor Hand Function (-)&lt;br&gt;• Fugl Meyer Score (-)&lt;br&gt;• Ashworth Scale (-)&lt;br&gt;• Nine Hole Peg Test (-)&lt;br&gt;• Stroke Impact Scale (-)</td>
</tr>
<tr>
<td><strong>MusicGlove</strong></td>
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<tr>
<td><strong>Friedman et al. (2014)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N&lt;sub&gt;Start&lt;/sub&gt;=12&lt;br&gt;N&lt;sub&gt;End&lt;/sub&gt;=12&lt;br&gt;TPS=chronic</td>
<td></td>
<td></td>
<td>E1: IsoTrainer&lt;br&gt;E2: Music glove training&lt;br&gt;C: Control</td>
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<td>E: Home-based training with a MusicGlove&lt;br&gt;C: Conventional tabletop exercise</td>
<td>• Motor Activity Log – Quality of Movement (+)&lt;br&gt;• Motor Activity Log – Amount of Use (+)&lt;br&gt;• Box and Block Test (-)&lt;br&gt;• 9-Hole Peg Test (-)&lt;br&gt;• Action Research Arm Test (-)</td>
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<td><strong>Shin et al. (2016)</strong>&lt;br&gt;RCT (8)&lt;br&gt;N&lt;sub&gt;Start&lt;/sub&gt;=46&lt;br&gt;N&lt;sub&gt;End&lt;/sub&gt;=46</td>
<td></td>
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<td>E: SmartGlove virtual reality task training&lt;br&gt;C: Conventional therapy</td>
<td>• Fugl-Meyer Assessment (+)&lt;br&gt;• Jebesen Taylor Hand Function Test (+)&lt;br&gt;• Stroke Impact Scale (+)&lt;br&gt;• Purdue Pegboard Test (-)</td>
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<td>N (Start/End)</td>
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<td>Susanto et al. (2015)</td>
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<td>RCT (6)</td>
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<td>Lee et al. (2016)</td>
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<td>Bustamante Valles et al. (2016)</td>
<td>RCT (3)</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=27, N&lt;sub&gt;End&lt;/sub&gt;=20</td>
<td>Chronic</td>
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<td>Fukuda et al. (2016)</td>
<td>PCT</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=23, N&lt;sub&gt;End&lt;/sub&gt;=23</td>
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</tr>
<tr>
<td>Fluet et al. (2015)</td>
<td>PCT</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=21, N&lt;sub&gt;End&lt;/sub&gt;=21</td>
<td>Chronic</td>
<td>E: Robotic and virtually simulated training &lt;br&gt; C: Repetitive task practice</td>
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</tbody>
</table>

* Indicates non-statistically significant differences between treatment groups

+ Indicates statistically significant differences between treatment groups

**Discussion**

Robotic therapies show promise for helping to provide safe and intensive rehabilitation to patients who have mild to severe motor impairment. Robotic devices can be used to provide rehabilitation that is of high-intensity, repetitive and task-specific in a manner that is similar to physical therapy. A number of different devices have thus far been evaluated: MIT-Manus, MIME, ARMin, Bi-Manu-Track, NeReBot, CPM, GENTLE/s, Amadeo, ARM Guide, and hand and arm exoskeletons.
MIT-Manus
Of all the 13 identified RCT’s, 7 were conducted in the chronic phase and all of them found that there was no significant difference on upper limb motor outcomes between an intervention involving MIT-Manus/InMotion therapies in comparison to a control (Ang et al., 2014; Conroy et al., 2011; Lo et al., 2010; McCabe et al., 2015; Stein et al., 2004; Volpe et al., 2000; Volpe et al., 2008). The other six RCT’s were conducted in the acute phase, of which 4 found that there was no significant difference on upper limb motor outcomes between an intervention involving MIT-Manus/InMotion therapies in comparison to a control. Two of the studies done in the acute phase did find a significant difference between robot aided therapy with reaching tasks in comparison to reaching tasks (Sale et al., 2014) and robot assisted movement training in comparison with robot exposure (Fasoli et al., 2004) on the Fugl-Meyer Assessment. Overall, this suggests that Manus/InMotion therapies are not more effective than a control for improving upper limb motor function.

MIME
Only 4 RCTs included in this review evaluated the MIME device of which 2 were conducted in the chronic phase of stroke, 1 included patients in the acute phase of stroke, and 1 included patients in the subacute phase of stroke. Lum et al. (2002) showed that chronic stroke patients benefited from training with the MIME, as scores showed greater improvements in strength, reach, and upper limb motor function when compared to conventional therapy. Conversely, Burgar et al. (2000) did not find a beneficial effect of using the MIME over conventional therapy at improving upper limb motor function in chronic stroke survivors. The literature is currently limited to draw strong conclusions regarding the efficacy of the MIME on upper limb motor function in the acute and subacute stroke populations since only one study was found during each stroke phase and the power of these studies as well as the methodological quality was low (Burgar et al., 2011; Lum et al., 2006). However, Burgar et al. (2011) found no significant difference in upper limb motor function between those in the acute phase receiving high intensity robot therapy, low intensity robotic therapy, and those receiving conventional therapy, although an improvement in spasticity was found. Lum et al. (2006) found that for patients in the subacute phase, robot-unilateral therapy, robot-bilateral therapy, and robot-combined therapy were superior to conventional therapy for upper limb motor function.

ARMin
Only two RCTs using the ARMin were found, both evaluating the effect of the device compared to conventional therapy in chronic stroke individuals (Brokaw et al., 2014; Klamroth-Marganska et al., 2014). The studies demonstrated mixed findings regarding the effectiveness of the device in improving motor function of the upper limbs and manual dexterity. More RCTs are needed to determine whether the ARMin is superior to conventional therapy at improving upper limb motor function in chronic and acute stroke individuals.

ARM Guide
One RCT was found that assessed active-assistive reaching exercise using a robotic device in comparison to task-matched conventional reaching (Kahn et al., 2006). The results of this trial indicated no significant benefit of the intervention for upper limb motor function. However, the power and methodological quality of the trial were low indicating that additional studies are needed to provide a clear picture regarding the effectiveness of ARM Guide therapy.

Bi-Manu-Track
A total of 8 RCTs investigated the effect of the Bi-Manu-Track on upper limb motor function in stroke individuals. One RCT was acute (Hesse et al., 2014), two were subacute (Hesse et al., 2008; Hesse et al.,
Upper Extremity Interventions

The trial conducted in the acute phase by Hesse et al. (2014) did not find any significant difference between group robot therapy with individual arm therapy in comparison to individual arm therapy on upper limb motor function outcomes.

The trials conducted in the subacute phase had conflicting results, with Hesse et al. (2005) finding a positive effect, and Hesse et al. (2008) finding no significant difference between computerized arm trainer and electrical stimulation for upper limb motor function.

Hsieh et al. (2014) and Liao et al. (2012) found that robotic therapy improved upper limb motor function more than conventional therapy. Hsieh et al. (2011) and Hsieh et al. (2012) found similar results, and they also found that higher intensity robotic therapy was superior to lower intensity robotic therapy.

NeReBot

Of the studies found, one RCT was conducted during the chronic phase (Masiero, Armani, et al., 2014), and the other 3 were conducted during the acute phase (Masiero et al., 2011; Masiero et al., 2006; Masiero et al., 2007).

Two acute stroke studies found that robotic training compared to exposure to the robotic device (without training on the device) improved motor function of the upper extremity but not that of the wrist (Masiero et al., 2006; Masiero et al., 2007). One study also found that there was no significant difference between use of the robotic device and conventional therapy on measures of motor function, spasticity, and independence (Masiero et al., 2011).

Regarding chronic stroke individuals, one study found no significant difference between robotic therapy and conventional therapy on motor function (Masiero, Poli, et al., 2014).

CPM

Continuous passive motion devices were found to evoke significantly greater changes in shoulder and elbow motor function and spasticity (elbow and wrist) in patient with chronic stroke (Hu et al., 2009), but not in acute stroke patients (Volpe et al., 2004).

GENTLE/s

Two studies analyzing the effectiveness of GENTLE/s devices in the chronic stroke population found that there was a lack of superiority of the robotic device over standard arm therapy regarding upper limb motor function and manual dexterity (Lemmens et al., 2014; Timmermans et al., 2014). A third study, also in the chronic phase, found that rate of recovery improved based on motor function outcomes in comparison to a control (Coote et al., 2008).

Amadeo

One study evaluating chronic stroke individuals showed no significant difference between patients using the Amadeo for active robot training and those performing passive therapy on functional motor outcomes and spasticity (Hwang et al., 2012). However, another study with participants during the acute phase after stroke found a significant improvement in upper limb motor function and dexterity following Amadeo robotic therapy with physiotherapy in comparison to occupational therapy (Sale et al., 2014).

ARM Guide
The ARM Guide was not found to be effective at improving upper limb motor function based on one study (Kahn et al., 2006).

**Music Glove**

One study in the chronic phase found that while Music Glove training was not superior to control on some measures of upper limb motor function, other measures of motor function which also account for dexterity indicated that Music Glove training was superior to conventional therapy (Friedman et al., 2014). However, another study by Zondervan et al. (2016) found that a home-based training program with MusicGlove was not superior to conventional exercise on any of the above mentioned outcomes.

**Other Devices**

A variety of additional robotic devices were studied, including the SmartGlove, Hand Mentor, PneuWREX, exoskeleton device, ArmeoBoom, and the Neuro-X among others. The phase post stroke of these studies varied, as did the results. Further trials are required to come to any conclusions regarding the effectiveness of these robotic devices.

**Summary**

Summarizing the results from the above studies can be challenging as a variety of devices were assessed using patients in the acute, sub-acute and chronic stages of stroke. The population groups also differed in other ways in addition to time of recruitment. The majority of these studies were also not adequately powered as many were pilot trials and functioned to evaluate the preliminary efficiency of a particular device with respect to its effect primarily on upper limb motor function. While many of these trials had low sample sizes, some had large samples, creating additional differences to be taken into account when synthesizing the evidence. The studies also examined interventions at varying intensities and durations and compared them to varying control groups. Furthermore, studies assessed had differing outcomes, making it difficult to weigh all studies equally. Overall, these differences between studies increases the variability of the results and this may explain why the evidence is conflicting.

Robot-assisted therapy was evaluated in a systematic review and meta-analysis by Norouzi-Gheidari et al. (2012) where the results of 12 studies were pooled for analysis. Outcomes such as the Fugl-Meyer, FIM, Motor Power scale, and the Motor Status scale were extracted and the effect sizes estimated. The methodological quality ranged from 2 to 7 on the PEDro scale. From the 12 studies, six evaluated the effects of the MIT-Manus, two evaluated the MIME, and the remaining 4 evaluated a different robotic device each (i.e. REHAROB, T-WREX, ARM Guide, and the NeReBot). When the robotic therapy was delivered in addition to the conventional therapy, the effect significantly favoured the robotic therapy when the Fugl-Meyer was considered. However, further analysis revealed that this effect may have been driven by the fact that the majority of the studies were evaluated in an acute-subacute population and all of which were positive for the robotic device, and only one study evaluated a chronic stroke population showing no significant effect of the intervention. When the robotic device was delivered in place of the conventional therapy, no significant overall effect regarding the Fugl-Meyer was found, regardless of the stroke phase. Whether the robotic therapy was delivered in addition to conventional therapy or instead of it, no significant effect was found regarding the FIM. Conversely, a significant effect favouring the robotic therapy was determined when the intervention supplemented conventional therapy as measured by the Motor Power Scale, but not when the intervention substituted conventional therapy. A similar effect resulted when the studies were pooled for the Motor Status Scale, favouring rehabilitation with a robotic device in addition to conventional therapy. This study therefore suggests that robotic devices may be more beneficial for rehabilitation when they are additional to conventional therapy. Furthermore, not all stroke patients may benefit from using a robotic device for upper limb rehabilitation and therefore stroke phase is to be considered prior to providing the intervention.
A recent systematic review identified 34 RCTs of low to very low quality which evaluated nineteen different electromechanical assisted devices for their efficacy at improving upper limb motor function (Mehrholz, Pohl, Platz, Kugler, & Elsner, 2015). Results demonstrate that robotic devices targeting arm and hand movement allowed for improvements in activities of daily living and recovery of impaired function and muscle strength (Mehrholz et al., 2015).

**Conclusions Regarding Robotics in the Rehabilitation for Movement Therapy**

*There is level 1a and 2 evidence in the acute phase and level 1a evidence in the chronic phase that MIT-Manus/InMotion therapies are no more effective than a control for improving upper limb motor function in the chronic phase.*

*There is level 2 evidence that Mirror-Image Motion Enabler Robots (MIME) are effective in the acute phase, level 2 evidence that (MIME) are not effective in the subacute phase, and level 1a conflicting evidence for the effectiveness in the chronic phase for improving upper limb motor function.*

*There is conflicting level 1b and 2 evidence for the use of ARMin during the chronic phase for improving upper limb motor function.*

*There is level 2 evidence that ARM Guide is not effective for improving upper limb motor function.*

*There is level 2 evidence during the acute phase that Bi-Manu-Track is not effective, level 1a conflicting evidence for the subacute phase, and level 1a evidence during the chronic phase that Bi-Manu-Track is effective for improving upper limb motor function.*

*There is conflicting level 2 evidence for the use of NeReBot during the acute phase, and level 1b evidence that NeReBot is not effective during the chronic phase for improving upper limb motor function.*

*There is level 2 evidence that Continuous Passive Motion (CPM) is not effective during the acute phase, and there is level 2 evidence that CPM is effective during the chronic phase for improving upper limb motor function.*

*There is level 1a evidence that the use of GENTLE during the chronic phase is not effective for improving upper limb motor function.*

*There is level 1b evidence that the use of Amadeo during the acute phase is effective, while there is level 1b evidence that the use of Amadeo during the chronic phase is not effective for improving upper limb motor function.*

*There is conflicting level 1a evidence regarding the effectiveness of MusicGlove during the chronic phase.*

*There is conflicting evidence as to whether the use of robotic devices is effective for improving upper limb motor function.*
10.4 Virtual Reality and Computer Brain Interface Technology

Virtual reality (VR), also known as virtual environment, is a technology that allows individuals to experience and interact with three-dimensional environments. The most common forms of virtual environments simulators are head-mounted displays (immersion) or with conventional computer monitors or projector screens (nonimmersion) (Sisto, Forrest, & Glendinning, 2002). According to Merians et al. (2002), a computerized virtual environment has opened the doors to an “...exercise environment where the intensity of practice and positive feedback can be consistently and systematically manipulated and enhanced to create the most appropriate, individualized motor learning approach. Adding computerized VR to computerized motor learning activities provides a three-dimensional spatial correspondence between the amount of movement in the real world and the amount of movement seen on the computer screen. This exact representation allows for visual feedback and guidance for the patient.”

10.4.1 Virtual Reality (VR)

Henderson et al. (2007) conducted a systematic review that included 6 studies evaluating immersive and nonimmersive VR technology for rehabilitation of the upper extremity. The authors concluded that immersive VR may be more effective at improving upper limb function compared to no therapy, while the results from studies examining nonimmersive VR are conflicting.

A Cochrane review, which included results from 19 RCTs (565 subjects) and of which 8 examined upper-limb training, reported a moderate treatment effect for arm function (SMD=0.53, 95% CI 0.25 to 0.81) (Laver, George, Thomas, Deutsch, & Crotty, 2011). Only two of the studies used readily available commercial devices (Playstation EyeToy and Nintendo Wii), while the remainder used customised VR programs.

In a recent systematic review, Laver et al. (2015) sought to determine the efficacy of virtual reality on upper limb motor function. In total, 37 trials were included in the analysis, consisting of 1019 participants. The results revealed that there were no significant effects of virtual reality on grip strength or global motor function. The authors also noted that the participants were relatively young and in the chronic phase of stroke (>1 year), therefore the effect of virtual reality during the acute phase of stroke could not be determined.

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<tr>
<td>McNulty et al. (2015) RCT (7) NStart=41 NEnd=40</td>
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<tr>
<td>Study</td>
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<tr>
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<td>E1: Virtual reality</td>
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<td>E2: Occupational therapy</td>
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<td>E3: Placebo board game</td>
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<td><strong>Lee et al. (2014)</strong></td>
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<td>• Modified Barthel Index (-)</td>
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<td><strong>Standen et al. (2016)</strong></td>
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<td><strong>Kong et al. (2016)</strong></td>
<td>E: Nintendo Wii virtual reality training</td>
<td>• Fugl-Meyer Assessment (-)</td>
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<td>C: Conventional therapy</td>
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<td><strong>Lee et al. (2016)</strong></td>
<td>E: Virtual reality-based rehabilitation</td>
<td>• Fugl-Meyer Assessment (+)</td>
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<td>C: Group-based rehabilitation</td>
<td>• Manual Function Test (+)</td>
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<td>• Box and Block Test (-)</td>
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<td></td>
<td>• Modified Barthel Index (-)</td>
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<tr>
<td><strong>Lee et al. (2016)</strong></td>
<td>E: Virtual reality-based bilateral training</td>
<td>• Jebsen Taylor Hand Function Test (+)</td>
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<td>C: Bilateral training</td>
<td>• Box and Block Test (+)</td>
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<td>• Strength (+)</td>
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<td><strong>Yavuzer et al. (2008)</strong></td>
<td>E: Playstation EyeToy games</td>
<td>• Brunnstrom score (-)</td>
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<td>C: Conventional therapy</td>
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<tr>
<td><strong>Lee &amp; Chun (2014)</strong></td>
<td>E1: tDCS</td>
<td>• Manual Function Test (+)</td>
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<td></td>
<td>E2: Virtual reality training</td>
<td>• Fugl Meyer Score (+)</td>
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<td></td>
<td>E3: tDCS + virtual reality</td>
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<tr>
<td><strong>Kiper et al. (2014)</strong></td>
<td>E: Reinforced feedback in virtual environment</td>
<td>• Fugl Meyer Score (+)</td>
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<td></td>
<td>C: Traditional rehabilitation</td>
<td>• FIM (+)</td>
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<td>• Kinematic characteristics (velocity): time (+), peak (+), speed (-)</td>
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<tr>
<td><strong>Thielbar et al. (2014)</strong></td>
<td>E: Virtual reality glove</td>
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<td></td>
<td>C: Occupational therapy</td>
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<tr>
<td><strong>Lee et al. (2013)</strong></td>
<td>E: Virtual reality games</td>
<td>• Manual Muscle Test (-)</td>
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<td></td>
<td>C: Control conventional therapy</td>
<td>• Modified Ashworth Scale (-)</td>
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<td>• FIM (-)</td>
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<tr>
<td><strong>Fluet et al. (2015)</strong></td>
<td>E: Virtual reality training</td>
<td>• Fugl Meyer Score (-)</td>
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<td>C: Repetitive task training</td>
<td>• Wolf Motor Function Test (-)</td>
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<td>Study</td>
<td>Intervention Details</td>
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<td></td>
<td></td>
<td>Short Form Health Survey: role limitation (+)</td>
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<td></td>
<td>RCT (6)</td>
<td>NStart=35 NEnd=32</td>
</tr>
<tr>
<td></td>
<td>E: Virtual reality rehabilitation program + conventional occupational therapy C: Conventional occupation therapy alone</td>
<td>Fugl-Meyer Assessment (+)</td>
</tr>
<tr>
<td></td>
<td>RCT (6)</td>
<td>NStart=24 NEnd=24</td>
</tr>
<tr>
<td>Saposnik et al. (2016)</td>
<td>E: Task-oriented using Nintendo Wii C: Traditional task-oriented training</td>
<td>Wolf Motor Function Test (-)</td>
</tr>
<tr>
<td></td>
<td>RCT (6)</td>
<td>NStart=141 NEnd=121</td>
</tr>
<tr>
<td>Jang et al. (2005)</td>
<td>E: Virtual reality training C: No Virtual reality training</td>
<td>Box and Block test (+)</td>
</tr>
<tr>
<td></td>
<td>RCT (5)</td>
<td>N=10</td>
</tr>
<tr>
<td>Lee et al. (2014)</td>
<td>E: Asymmetric training using virtual reality C: Symmetric movements with both hands and no virtual reality training</td>
<td>Fugl Meyer score (+)</td>
</tr>
<tr>
<td></td>
<td>RCT (5)</td>
<td>NStart=30 NEnd=24</td>
</tr>
<tr>
<td>Duff et al. (2013)</td>
<td>E: Virtual reality reaching therapy C: Control standard treatment</td>
<td>Fugl Meyer (+)</td>
</tr>
<tr>
<td></td>
<td>RCT (5)</td>
<td>NStart=25 NEnd=21</td>
</tr>
<tr>
<td>HyeonHui et al. (2013)</td>
<td>E: Virtual reality training C: Occupational therapy</td>
<td>Range of Motion: shoulder flexion (+), shoulder extension (+), shoulder abduction (+), elbow flexion (+), wrist flexion (+)</td>
</tr>
<tr>
<td></td>
<td>RCT (5)</td>
<td>NStart=40 NEnd=35</td>
</tr>
<tr>
<td>Shin et al. (2014)</td>
<td>E: Occupational therapy + virtual reality training C: Occupational therapy</td>
<td>Fugl Meyer Score (-)</td>
</tr>
<tr>
<td></td>
<td>RCT (5)</td>
<td>NStart=103 NEnd=93</td>
</tr>
<tr>
<td>Yin et al. (2014)</td>
<td>E: Virtual reality + conventional therapy C: Conventional therapy</td>
<td>Fugl Meyer Score (-)</td>
</tr>
<tr>
<td></td>
<td>RCT (5)</td>
<td>NStart=26 NEnd=21</td>
</tr>
<tr>
<td>Samuel et al. (2016)</td>
<td>E: Occupational and physical therapy + virtual reality training C: Occupational and physical therapy</td>
<td>Fugl-Meyer Assessment (-)</td>
</tr>
<tr>
<td></td>
<td>RCT (4)</td>
<td>NStart=8</td>
</tr>
</tbody>
</table>
| N<sub>End</sub>=6 | E: Motion gaming rehabilitation  
C: No gaming treatment | • Functional Independence Measure: Mobility (+), Transfers (+), Stairs (-)  
• 6 Minute Walk Test (+)  
• Functional Reach (-)  
• Motor Assessment Scale (-)  
• Step Test (-) |
|-----------------|------------------------|---------------------------------------------------------------|
| **Bower et al.** (2015) | RCT (4)  
N<sub>Start</sub>=20  
N<sub>End</sub>=16 | E1: 2DVR computer based training programme  
E2: Video modelling-based psychoeducational programme  
C: Control | • Mass Transit Railway: skills (-), self-efficacy (-) |
| **Lam et al.** (2006) | RCT (4)  
N=58 | E1: Home-based Nintendo Wii program  
C: Home-based exercise program | • Action Research Arm Test (-)  
• Quality of Life (-)  
• Occupational Performance (-) |
| **Adie et al.** (2017) | RCT (3)  
N<sub>Start</sub>=235  
N<sub>End</sub>=235 | E: Semi-immersive workbench with haptic and stereoscopic glasses  
C: No VR treatment | • Box and Block Test (-)  
• ABILHAND (-)  
• Trail Making Test (-)  
• Kinematics (+) |
| **Broeren et al.** (2008) | RCT (3)  
N=22 | E: Nintendo Wii-based movement therapy  
C: Modified constraint induced movement therapy | • Wolf Motor Function Test (-)  
• Motor Activity Log (-) |
| **Trinh et al.** (2016) | PCT  
N<sub>Start</sub>=46  
N<sub>End</sub>=46 | E: Robotic and virtually simulated arm and finger training  
C: Traditional arm and finger training (repetitive task practice) | • Wolf Motor Function Test (-)  
• Fugl-Meyer Assessment (-)  
• Finger extension (+)  
• Peak hand velocity (+)  
• Reach to lift time, reaching path length, reaching trajectory smoothness, trunk excursion, sagittal shoulder excursion, elbow excursion (-) |
| **Fluet et al.** (2015) | PCT  
N<sub>Start</sub>=21  
N<sub>End</sub>=21 | E: Robotic and virtually simulated arm and finger training  
C: Traditional arm and finger training (repetitive task practice) | • Wolf Motor Function Test (-)  
• Fugl-Meyer Assessment (-)  
• Finger extension (+)  
• Peak hand velocity (+)  
• Reach to lift time, reaching path length, reaching trajectory smoothness, trunk excursion, sagittal shoulder excursion, elbow excursion (-) |

* Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

**Discussion**

Virtual reality training is an innovative new treatment approach, which may enhance cortical reorganization following stroke. The studies evaluated in this review include patients from all phases of stroke, however, the majority evaluate the effects of virtual reality in chronic stroke patients. The RCTs of high quality (i.e. PEDro > 6) demonstrate conflicting results for certain outcomes of motor function such as the Fugl-Meyer Assessment, but no significant difference between a virtual reality intervention and a control on other measures of motor function such as the Action Research Arm Test, the Box and Block Test, and the Wolf Motor Function Test.

Two studies of high methodological quality and with large sample sizes detected no effect when comparing Nintendo Wii virtual reality training to conventional training on measures of upper limb motor function (Kong et al., 2016; Saposnik et al., 2016). Furthermore, many of the studies which found a significant difference on one measure of motor function found no significant difference on other measures of motor function (Lee et al., 2014; M. M. Lee et al., 2016; Saposnik et al., 2010; Standen et al., 2016). Overall, the evidence that virtual reality training is not superior to conventional therapy is stronger than the evidence suggesting that there is a significant difference.
Conclusions Regarding Virtual Reality Technology

There is level 1a evidence that virtual reality does not improve upper limb motor function in the chronic stroke phase.

Virtual reality therapy may not improve upper limb motor function in chronic stroke patients.

10.4.2 Computer Brain Interface Technology (CBI)

Computer-brain-interface (CBI) technology has only recently emerged as a potential rehabilitative treatment option for stroke patients. Thus far, only a few studies have evaluated the effects of this technology on upper limb motor impairments.

The results of controlled trials evaluating CBI are summarized in Table 10.4.2.1.

Table 10.4.2.1 Summary of Controlled Trials Evaluating Computer Brain Interface Technology for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ramos-Murguialday et al. (2013)</strong> RCT (8) NStart=32 NEnd=30</td>
<td>E: Brain machine interface C: Sham</td>
<td>• Modified Fugl Meyer Score: arm and hand (+) • Motor Activity Log (-) • Goal Assessment Scale (-) • Ashworth Scale (-)</td>
</tr>
<tr>
<td><strong>Ang et al. (2014)</strong> RCT (8) NStart=22 NEnd=21</td>
<td>E1: Brain-computer interface (BCI) with haptic knob (HK) E2: Haptic knob (HK) C: Standard Arm Therapy (SAT)</td>
<td>• Fugl Meyer Score (-)</td>
</tr>
<tr>
<td><strong>Ang et al. (2015)</strong> RCT (7) NStart=26 NEnd=25</td>
<td>E: Brain computer interface + robotic training C: Robotic training</td>
<td>• Fugl-Meyer Score (-)</td>
</tr>
<tr>
<td><strong>Young et al. (2016)</strong> RCT (5) NStart=19 NEnd=10</td>
<td>E: Brain computer interface training C: No training</td>
<td>• Stroke Impact Scale (-) • Action Research Arm Test (-) • 9 Hole Peg Test (-)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion

The use of CBI technology is still relatively new and largely untested. Studies by Ang et al. (2014), Ang et al. (2015), and Young et al. (2016) found that CBI was not superior to a control on outcomes of upper limb motor function. However, a study by Ramos-Murguialday et al. (2013) found that the group receiving brain machine interface improved more than the group receiving a sham on an assessment of arm and hand motor function. More studies are needed to determine how and if this technology is useful to facilitate upper limb recovery.

Conclusions Regarding Computer Brain Interface Technology
There is level 1a evidence that computer brain interface technology is not effective for improving upper limb motor function post-stroke.

Computer-brain-interface technology is likely not effective for improving upper limb motor function although more research is required to come to a more definitive result.

10.5 Treatment for Spasticity or Contracture in the Upper Extremity

Stroke survivors often display a constellation of signs and symptoms that together constitute the upper motor neuron syndrome. The syndrome consists of negative signs including weakness, loss of dexterity, fatigue, and positive signs including increased muscle stretch reflexes, abnormal cutaneous reflexes and spasticity. Spasticity is classically defined as a velocity dependent increase of tonic stretch reflexes (muscle tone) with exaggerated tendon jerks. Spasticity can be painful, interfere with functional recovery in the upper extremity and hinder rehabilitation efforts. However, Gallichio (2004) cautioned that a reduction in spasticity does not necessarily lead to improvements in function. Van Kuijk et al. (2002) noted that for most stroke patients, “...spasticity is a variable phenomenon in time and apparent in only certain muscle groups, and therefore, low threshold and “reversible” focal treatment techniques seem to be the preferable first option”.

A study by Watkins et al. (2002) reported that 39% of patients with a first-ever stroke were spastic 12 months after their stroke. Sommerfeld et al. (2004) reported that of 95 patients assessed initially (mean 5.4 days) after an acute stroke, 77 (81%) were hemiplegic and 20 (21%) were spastic. Overall, upper extremity spasticity alone (n=13) was more common than lower extremity spasticity alone (n=1) or spasticity in both upper and lower extremities (n=6). At three months post-stroke, 64 patients (67%) were still hemiparetic, and 18 (19%) were still spastic. At that point, there were more patients with spasticity in both extremities (n=10) than in the upper extremity alone (n=7) or in the lower extremity alone (n=1). The authors also reported that severe disabilities were found in almost the same number of nonspastic patients as spastic patients.

There are a number of interventions used for limb spasticity. These include oral antispasticity agents, injections of phenol to motor nerves or alcohol to muscle bellies, and physical modalities such as stretching, orthoses, casting, cold application and surgery. The mainstay of treatment for spasticity has been physical therapy. Traditional pharmacotherapies for spasticity include centrally acting depressants (baclofen, benzodiazepines, clonidine, and tizanidine) and muscle relaxants (dantrolene). There is evidence from RCTs published in the 1960’s and 1970’s that these treatments are only partially effective in treating spasticity and most have negative side effects of weakness and sedation with the exception of dantrolene. More recently, Tizanidine hydrochloride was used to successfully treat spasticity among 47 chronic stroke patients, although, due to a number of side effects (i.e. elevated transaminases, dizziness, lethargy, and hypertension), only a small percentage of patients reached the maximum daily dose (Gelber, Good, Dromerick, Sergay, & Richardson, 2001). Motor point or nerve blocks with phenol or alcohol have been used but are often associated with variable success rates, and high rates of neuropathic pain. Botulinum toxin type A, a potent neurotoxin that prevents the release of acetylcholine from the pre-synaptic axon, has more recently been studied as a potentially useful treatment for stroke related spasticity. Intrathecal drug therapy refers to the injection of a drug into the subarachnoid space of the central nervous system and requires the implantation of a programmable device into the subcutaneous tissue surrounding the abdominal wall. Intrathecal baclofen, the most commonly used intrathecal drug for relieving spasticity associated with stroke has not been well studied, particularly for spasticity of the upper extremity.
10.5.1 Splinting

Splints have been widely used in clinical practice with the aim of the prevention of contractures and reduction of spasticity; however, they have not been well studied to date.

In a systematic review by Steultjens et al. (2003), the authors concluded that based on the results of 2 RCTs (Langlois, Pederson, & MacKinnon, 1991; Rose & Shah, 1987), 2 case-controlled trials (McPherson, Kreimeyer, Aalderks, & Gallagher, 1982; Poole et al., 1990) and one uncontrolled trial (Gracies et al., 2000) there was insufficient evidence at the time of publication to support the effectiveness of splinting for decreasing muscle tone.

Tyson and Kent (2011) conducted a systematic review on the effect of upper limb orthotics following stroke, which included the results from 4 RCTs and represented 126 participants. Overall, the treatment effects associated with measures of disability, impairment, range of motion, pain, and spasticity were small and not statistically significant.

The results of RCTs evaluating splinting interventions are summarized in Table 10.5.1.1.

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lannin et al.</strong> (2003) RCT (8) N=28</td>
<td>E: Hand splint + conventional therapy C: Conventional therapy</td>
<td>• Contracture: wrist (-), finger flexor muscles (-)</td>
</tr>
<tr>
<td><strong>Lannin et al.</strong> (2007) RCT (7) N=63</td>
<td>E1: Extension splint E2: Neutral splint C: No splint</td>
<td>• Contracture: wrist (-)</td>
</tr>
<tr>
<td><strong>Basaran et al.</strong> (2012) RCT (6) N=39</td>
<td>E1: Volar splint E2: Dorsal splint C: No splint</td>
<td>• Modified Ashworth Scale (-) • Passive range of motion (-)</td>
</tr>
<tr>
<td><strong>Suat et al.</strong> (2011) RCT (6) NStart=19 NEnd=19</td>
<td>E: Hand splint C: No splint</td>
<td>• Functional Reach Test (-)</td>
</tr>
<tr>
<td><strong>Rose et al.</strong> (1987) RCT (4) N=30</td>
<td>E1: Dorsal orthosis E2: Volar orthosis C: No orthosis</td>
<td>• Passive range of motion: dorsal/volar vs. control (+) • Spontaneous flexion: dorsal vs. control (+), volar vs. control (-)</td>
</tr>
<tr>
<td><strong>Jung et al.</strong> (2011) RCT (4) NStart=21 NEnd=21</td>
<td>E: Hand stretching/splint device C: No splint</td>
<td>• Modified Ashworth Scale (+)</td>
</tr>
<tr>
<td><strong>Langlois et al.</strong> (1991) RCT (3) N=9</td>
<td>E1: Spint 22hr/d E2: Splint 12hr/d E3: Splint 6hr/d</td>
<td>• Spasticity (-)</td>
</tr>
<tr>
<td><strong>Amini et al.</strong> (2016) PCT NStart=39 NEnd=29</td>
<td>E1: Splint E2: Botulinum Toxin-A E3: Splint and Botulinum Toxin-A</td>
<td>• Active Range of Motion: E2 vs E1 (+) • Fugl-Meyer Assessment (+) • Modified Ashworth Scale for elbow and wrist (+) • Passive Range of Motion for elbow and wrist (-)</td>
</tr>
</tbody>
</table>

*Indicates non-statistically significant differences between treatment groups*
Discussion
Seven RCTs were identified examining the benefits of splinting. The focus of each of these studies was different (finger, wrist and elbow). Most of the studies failed to support the benefit of splinting in reducing spasticity, avoiding contracture and improving arm reach (Basaran et al., 2012; Langlois et al., 1991; Lannin et al., 2007; Lannin et al., 2003; Rose & Shah, 1987; Suat et al., 2011). Results should be taken with caution due to short treatment periods, typically between 4-6 weeks, along with low power.

Conclusions Regarding Splinting

There is level 1a evidence that splinting does not reduce the development of contracture nor reduce spasticity in the upper extremity.

Hand splints alone likely do not reduce spasticity or prevent contracture.

10.5.2 Stretching Programs to Prevent Contracture Formation
Spastic contracture following stroke relates to hypertonicity or increased active tension of the muscle. Contracture may also occur as a result of atrophic changes in the mechanical properties of muscles. Since surgery is the only treatment option once a contracture has developed, prevention is encouraged. Stretching may help to prevent contracture formation and, although well-accepted as a treatment strategy, has not been thoroughly studied as of yet.

Table 10.5.2.1 Summary of RCTs Evaluating Stretching Programs to Prevent Contracture Formation in the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tseng et al. (2007)</td>
<td>RCT (7)</td>
<td>N=59</td>
<td>E1: RN assisting&lt;br&gt;E2: RN supervising&lt;br&gt;C: Usual care</td>
<td>• Joint angles: RN groups vs. usual are (+)&lt;br&gt;• Activity function: RN groups vs usual care (+)</td>
</tr>
<tr>
<td>Santamato et. al. (2015)</td>
<td>RCT (7)</td>
<td>NStart=70&lt;br&gt;NEnd=70</td>
<td>E: 50-200 U Botox + adhesive tape for 10d&lt;br&gt;C: 50-200 U Botox + manual muscle stretching</td>
<td>• MAS (finger): 2wk (+), 1mo (+)&lt;br&gt;• MAS (wrist): 2wk (+), 1mo (+)&lt;br&gt;• Finger position scores: 2wk (+), 1mo (+)&lt;br&gt;• Disability Assessment Scale: 1mo (+)</td>
</tr>
<tr>
<td>Kim et al. (2013)</td>
<td>RCT (6)</td>
<td>NStart=15&lt;br&gt;NEnd=15</td>
<td>E: Hand modified stretching device&lt;br&gt;C: Control</td>
<td>• Modified Ashworth Scale (+)</td>
</tr>
<tr>
<td>Jang et al. (2016)</td>
<td>RCT (5)</td>
<td>NStart=21&lt;br&gt;NEnd=21</td>
<td>E: Additional hand and wrist stretching using a device&lt;br&gt;C: Standard outpatient care</td>
<td>• Modified Ashworth Scale (+)&lt;br&gt;• Fugl-Meyer Assessment (+)&lt;br&gt;• Active Range of Motion (-)</td>
</tr>
<tr>
<td>You et al. (2014)</td>
<td>RCT (5)</td>
<td>NStart=45&lt;br&gt;NEnd=41</td>
<td>E1: Stretching program + joint stabilizing exercise (combo)&lt;br&gt; E2: Stretching program&lt;br&gt;C: Traditional therapy</td>
<td>• Muscle thickness: E1 vs. C (+), E1 vs. E2 (+), E2 vs. C (-)&lt;br&gt;• Arm function: E1 vs. C (+), E1 vs. E2 (+), E2 vs. C (-)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups
Discussion

Few studies have been published examining the benefit of stretching regimen for the prevention of contracture formation. Tseng et al. (2007) found that having a nurse assisting with or supervising exercises was significantly more beneficial than the provision of usual care in terms of improvement in joint angles and activity function. Spasticity was also improved following use of a hand modified stretching device compared to the control group which did not receive a device (E. H. Kim et al., 2013). Stretching with joint stabilization improved muscle thickness and arm function compared to traditional therapy; however, a stretching program delivered alone was not significantly different compared to conventional therapy (You et al., 2014). Interestingly, all of the studies described above evaluated participants who were in the chronic phase post stroke. Additional hand and wrist stretching using a device improved spasticity and upper limb motor function, but not range of motion, compared to standard outpatient care (Jang et al., 2016).

Conclusions Regarding Stretching Programs to Prevent Contracture Formation

There is level 1b evidence that a nurse-led stretching program may improve range of motion in the upper extremity and reduce pain in the chronic stage of stroke.

There is level 1b and 2 evidence that a hand stretching device may improve spasticity in the upper limb.

10.5.3 Botulinum Toxin Injections

Botulinum toxin works by weakening spastic muscles through blocking the release of acetylcholine at the neuromuscular junction. The benefits of botulinum toxin injections are generally dose-dependent and last approximately 2 to 4 months (Brashear et al., 2002; Francisco, Boake, & Vaughn, 2002; Simpson et al., 1996; Smith, Ellis, White, & Moore, 2000). One of the advantages of botulinum toxin is that it is safe to use on small, localized areas or muscles, such as those in the upper extremity. Unlike chemical neurolysis with phenol or alcohol, botulinum toxin is not associated with skin sensory loss or dysesthesia (Suputtitada & Suwanwela, 2005). Dynamic EMG studies can be helpful in determining which muscles should be injected (Bell & Williams, 2003).

Van Kuijk et al. (2002) evaluated the benefit of botulinum toxin for the treatment of upper extremity spasticity with focal neuronal or neuromuscular blockade. This review included 10 studies (4 RCTs and 6 uncontrolled observational studies). The authors found that there was evidence of the effectiveness of botulinum toxin treatment on reducing muscle tone (as measured by the modified Ashworth Scale) and improving passive range of motion at all arm-hand levels in chronic patients for approximately 3 to 4 months. However, the authors concluded that, while overall the effectiveness of botulinum toxin for improving functional abilities was not justified, specific stroke groups may benefit from botulinum toxin injections in the upper extremity.

While many controlled studies have demonstrated a reduction in spasticity following treatment with botulinum toxin, it is less clear whether treatment is associated with improvement in upper extremity function. Francis et al.(2004) suggested several reasons for these results, including that underlying muscle weakness and not spasticity contribute to the limitation in function. However, it is speculated that the most likely reasons were insufficiently sensitive outcome measures and under-powered studies.
A meta-analysis by the same authors included the results from two RCTs (Bakheit et al., 2001; Bakheit et al., 2000) which suggested that there was a benefit, albeit modest, of BTX-A on improved function. The authors of this review pooled the data and assessed the effect using the arm section of the Barthel Index (dressing, grooming and eating), and reported a modest improvement in upper arm function following botulinum toxin. Pooling was only possible for two RCTs due to heterogeneity of interventions and outcomes.

Cardoso et al. (2005) conducted a meta-analysis investigating BTX-A as a treatment for upper limb spasticity following stroke. They included five RCTs (Bakheit et al., 2001; Bakheit et al., 2000; Brashear et al., 2002; Simpson et al., 1996; Smith et al., 2000) and reported that there was a significantly greater reduction in spasticity for patients who underwent BTX-A treatment compared to patients receiving the placebo treatment, as measured by the modified Ashworth Scale and the Global Assessment Scale. The authors concluded that BTX-A reduces spasticity and that the treatment was tolerated well, although the effects of long-term use of BTX-A are unknown. Levy et al. (2007) reported additional benefits when a course of constraint-induced movement therapy followed treatment with BTX-A. Unfortunately the gains in motor function were lost at the end of 24 weeks at which point spasticity returned.

A summary of the results from RCTs investigating Botulinum toxin for spasticity is presented in Table 10.5.3.1.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seo et al. (2015)</td>
<td>RCT (10)</td>
<td>E1: 360 U Neu-BoNT-A E2: 360 U Botox</td>
<td>• MAS: 4, 8, and 12 wk (-) • Disability Assessment Scale (-) • Carer burden Scale (-) • Global Assessment of intervention benefit (-)</td>
</tr>
<tr>
<td>Kaji et al. (2010)</td>
<td>RCT (9)</td>
<td>E1: 120 U Botox C1: Placebo E2: 200 U Botox C2: Placebo</td>
<td>• Modified Ashworth Scale: E2 vs. C2 (+), E1 vs. C1 (-) • Disability Assessment Scale: both groups (+)</td>
</tr>
<tr>
<td>McCrory et al. (2009)</td>
<td>RCT (9)</td>
<td>E: 500-1,000U of Dysport C: Placebo x 2 occasions</td>
<td>• The Assessment of Quality of Life scale: 20wk (-)</td>
</tr>
<tr>
<td>Wolf et al. (2012)</td>
<td>RCT (9)</td>
<td>E: 300U Botox + therapy C: Placebo + therapy</td>
<td>• Wolf Motor Function test (-)</td>
</tr>
<tr>
<td>Gracies et al. (2014)</td>
<td>RCT (9)</td>
<td>E1: 10000 U Botox E2: 15000 U Botox C: Placebo</td>
<td>• Modified Frenchay Scale (-)</td>
</tr>
<tr>
<td>Wissel et al. (2016)</td>
<td>RCT (8)</td>
<td>E: OnabotulinumtoxinA + standard care C: Placebo injection + standard care</td>
<td>• Pain Numeric Rating Scale (+) • Goal Attainment Scale (-)</td>
</tr>
<tr>
<td>Picelli et al. (2014)</td>
<td>RCT (8)</td>
<td>E1: Injections under sonographic guidance E2: Injection using electrical stimulation guidance</td>
<td>• MAS (wrist): all groups (+) • Tardieu Spasticity angle: all groups (+) • PROM (wrist): all groups (+) • PROM (proximal interphalangeal joints): all groups (+)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>N</td>
<td>Intervention Details</td>
</tr>
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<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Shaw et al. (2011)</td>
<td>RCT (8)</td>
<td>333</td>
<td>C: Injection using manual needle placement E: 100-200 U Dysport + 4 weeks therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>C: Therapy only</td>
</tr>
<tr>
<td>Bakheit et al. (2000)</td>
<td>RCT (8)</td>
<td>82</td>
<td>E1: 500 U of Dysport E2: 1000 U of Dysport E3: 1500 U of Dysport C: Placebo</td>
</tr>
<tr>
<td>Bakheit et al. (2001)</td>
<td>RCT (8)</td>
<td>59</td>
<td>E: Total of 1000 IU of BtxA (Dysport) into 5 muscles of the affected arm C: Placebo injections</td>
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<tr>
<td>Simpson et al. (1996)</td>
<td>RCT (8)</td>
<td>37</td>
<td>E1: Single treatment of 75 U E2: 150 U E3: 300 units of BTX-A C: Placebo</td>
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<tr>
<td>Simpson et al. (2009)</td>
<td>RCT (8)</td>
<td>60</td>
<td>E1: Up to 500 U of BT-X E2: Tinzanidine C: Placebo</td>
</tr>
<tr>
<td>Hesse et al. (2012)</td>
<td>RCT (7)</td>
<td>18</td>
<td>E: 150U Xeomin + therapy C: Therapy only</td>
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<tr>
<td>Bhakata et al. (2000)</td>
<td>RCT (7)</td>
<td>40</td>
<td>E: Total of 1000 IU Dysport (n=20) C: Placebo (n=20) divided between elbow, wrist, and finger flexors</td>
</tr>
<tr>
<td>Bhakata et al. (2008)</td>
<td>RCT (7)</td>
<td>40</td>
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<tr>
<td>Brashear et al. (2002)</td>
<td>RCT (7)</td>
<td>126</td>
<td>E: Botulinum toxin A (50 U) C: Placebo</td>
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<tr>
<td>Francisco et al. (2002)</td>
<td>RCT (7)</td>
<td>13</td>
<td>E1: High volume BTX-A (50 units/1 mL saline:1.2 mL delivered per 4 muscles) E2: Low volume BTX-A (100 units/1 mL saline)</td>
</tr>
<tr>
<td>Brashear et al. (2004)</td>
<td>RCT (7)</td>
<td>25</td>
<td>E: 10000 U of BTX-B C: Placebo</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Subjects</td>
<td>Interventions</td>
</tr>
<tr>
<td>-----------------------------</td>
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<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Pennati et al. (2015)</td>
<td>RCT</td>
<td>NStart=15, NEnd=15</td>
<td>E: Robot and Botulinum toxin neurolysis with dose dependant on muscle group affected C: Robotic training</td>
</tr>
<tr>
<td>Nam et al. (2015)</td>
<td>RCT</td>
<td>NStart=197, NEnd=177</td>
<td>E: New botulinum type A (NABOTA) up to 360 U depending on degree of spasticity and muscle group C: Omabotulinum toxin A (Botox) up to 360 U depending on degree of spasticity and muscle group</td>
</tr>
<tr>
<td>Elovic et al. (2016)</td>
<td>RCT</td>
<td>NStart=317, NEnd=299</td>
<td>E: 400U incobotulinumtoxinA C: Placebo</td>
</tr>
<tr>
<td>Meythaler et al. (2009)</td>
<td>RCT</td>
<td>N=21</td>
<td>E: 100 U Botox + therapy C: Saline + therapy</td>
</tr>
<tr>
<td>Jahangir et al. (2007)</td>
<td>RCT</td>
<td>N=27</td>
<td>E: 50 U Botox C: Placebo</td>
</tr>
<tr>
<td>Ward et al. (2014)</td>
<td>RCT</td>
<td>NStart=274, NEnd=273</td>
<td>E: Onabotulinumtoxin A + standard care (varying dosages) C: placebo injections + standard care (varying dosages)</td>
</tr>
<tr>
<td>Werner et al. (2013)</td>
<td>RCT</td>
<td>NStart=18, NEnd=18</td>
<td>E: 150 U BTX-A C: No injections</td>
</tr>
<tr>
<td>Santamato et al. (2014)</td>
<td>RCT</td>
<td>NStart=30, NEnd=30</td>
<td>E: BoNT-A injection using ultrasound guidance (dosages determined by investigator) C: BoNT-A manual injection via palpitation and anatomical landmarks (dosages determined by investigator)</td>
</tr>
<tr>
<td>Dressler et al. (2015)</td>
<td>PCT</td>
<td>NStart=218, NEnd=194</td>
<td>E: IncobotulinumtoxinA (BTX-A) (215±114 MU) and additional conventional treatment C: Conventional treatment (268±155 MU)</td>
</tr>
<tr>
<td>Lim et al. (2016)</td>
<td></td>
<td></td>
<td>E1: Subacute 200U of botulinum</td>
</tr>
</tbody>
</table>
PCT
N_{Start}=19
N_{End}=18
toxin
E2: Chronic 200U of botulinum toxin
- Modified Tardieu Scale: E1 vs. E2 (+)
- Manuel Muscle Testing (-)
- Wrist Range of Motion: E1 vs. E2 (+)
- Brunnstrom Stage (-)
- Modified Barthel Index (-)
- Fugl-Meyer Assessment (-)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion
Assessing the effectiveness of botulinum toxin in the treatment of upper limb spasticity is difficult owing to the broad range of doses and types of agents administered. Among the RCTs reviewed, many assessed a single dose, administered to several sites, of botulinum toxin A as either Dysport®, Botox® or Xeomin® versus placebo. A single trial assessed the benefit of BT-type B (10,000 U BT-B) (Childers et al., 2004). The dose equivalent is approximately 300-500 Units of Dysport which is equal 100 units of Botox (O’Brien, 2002). Among the trials of relatively high methodological quality, the majority of studies found an improvement in spasticity between those receiving Botulinum and those not, as well as between groups receiving higher and lower dosages. Specifically, Kaji et al. (2010), Shaw et al. (2011), Bakheit et al. (2001), Hesse et al. (2012), Bhakta et al. (2000), Bhakta et al. (2008), Brashear et al. (2004), Pennati et al. (2015), Elović et al. (2016), Meythaler et al. (2009) and Jahangir et al. (2007), found that measures of spasticity were higher in those receiving Botulinum toxin in comparison to those receiving a control. Studies by Bakheit et al. (2000), Gracies et al. (2015), Smith et al. (2000), and Suputtitada & Suwanwela (2005) also found significant differences in improvement of spasticity between groups receiving varying dosages of Botulinum toxin.

In terms of studies that didn’t find a significant difference in spasticity outcomes between groups, Seo et al. (2015) and Nam et al. (2015) compared different types of Botulinum toxin at the same dosages. Francisco et al. (2002) found no difference in spasticity between varying dosages of Botulinum toxin A.

Studies by Wolf et al. (2012), Gracies et al. (2014), Shaw et al. (2011), and Pennati et al. (2015) found that there was no significant improvement on measures of motor function after treatment with Botulinum toxin A when compared to a control.

Rosales et al. (2008) conducted a meta-analysis to evaluate the effect of Botulinum Toxin Type A on upper limb spasticity following stroke. A total of 11 studies were included in the analysis, revealing that at the 4-6 week follow-up, treatment with Botulinum Toxin Type A was favoured over the control for treating spasticity as measured by the Modified Ashworth Scale (MAS). Furthermore, the studies that evaluated a change in the MAS score of more than 1 point were pooled for analysis, with results demonstrating a significant effect favouring Botox. The same effect was found when the Global Assessment Scale was measured.

Another review by Ivanhoe & Eaddy-Rose (2009) found 13 articles which when analyzed indicated that BTX-A statistically improved spasticity of the elbow, wrist, fingers, and shoulder, with the duration of treatment lasting from 10 to 20 weeks.

**Conclusion Regarding Botulinum Toxin Injections**

*There is level 1a evidence that treatment with botulinum toxin significantly reduces spasticity in the upper extremity in stroke survivors.*
There is level 1a evidence that treatment with botulinum toxin does not improve upper limb motor function.

**Botulinum toxin likely decreases spasticity, but likely does not improve upper limb motor function.**

### 10.5.4 Electrical Stimulation Combined with Botulinum Toxin Injection

Three studies were found which evaluated the efficacy of botulinum toxin injection combined with therapies such as electrical stimulation, occupational therapy, and modified constraint induced movement therapy, summarized in Table 10.5.4.1.

**Table 10.5.4.1 Summary of RCT(s) Evaluating Combined Therapy with Botulinum Toxin Injection in the Upper Extremity**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hesse et al.</strong> (1998)</td>
<td>RCT (7) N=24</td>
<td>E1: 1000 U Btx A + electrical stimulation E2: 1000 U of Btx A E3: Placebo + electrical stimulation C: Placebo</td>
<td>• Muscle Tone Reduction: elbow joint for E1 (-) • Reduction in difficulties while cleaning palm: E1 vs. E2/C (+) • Difficulties putting arm through sleeve: reduction between botox groups vs. C (+)</td>
</tr>
<tr>
<td><strong>Marvulli et al.</strong> (2016)</td>
<td>RCT (6) NStart=36 NEnd=36</td>
<td>E: Botulinum toxin A therapy (118±34 U) + occupational therapy + electrical stimulation C: Botulinum toxin A therapy (116±36 U)+ occupational therapy</td>
<td>• Modified Ashworth Scale (+) • Range of Motion (+) • Action Research Arm Test (+)</td>
</tr>
<tr>
<td><strong>Sun et al.</strong> (2010)</td>
<td>RCT (6) N=32</td>
<td>E: 1,000 U Dysport + mCIMT C: 1,000 U Dysport + conventional rehab</td>
<td>• MAS (+) • Motor Activity Log: Amount of Use (+)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

**Discussion**

Botulinum toxin A with occupational therapy and electrical stimulation was found to improve spasticity, range of motion and upper limb motor function in comparison to receiving Botox A with occupational therapy (Marvulli et al., 2016). Similarly, Hesse et al. (1998) found that those receiving 1000 U Btx A along with electrical stimulation had fewer difficulties on some tasks than those who had only received Btx A and those receiving placebo. Lastly, a study by Sun et al. (2010) also found that 1000 U of Dysport with modified constraint induced movement therapy (mCIMT) improved spasticity compared to the same dosage of Dysport with conventional therapy.

**Conclusions Regarding Other Therapies Combined with Botulinum Toxin Injections**

**There is level 1a evidence that electrical stimulation combined with botulinum toxin injection is associated with reductions in spasticity.**

**There is level 1b evidence that modified constraint induced movement therapy combined with botulinum toxin injection is associated with reductions in spasticity.**
Botulinum toxin in combination with electrical stimulation or modified constraint-induced movement therapy likely improves muscle tone in the upper extremity.

10.5.5 Nerve Block and Spasticity
One method of decreasing spasticity is by injecting alcohol or phenol into a specific nerve (i.e., the musculocutaneous nerve) thus decreasing spasticity of the innervated muscles. One of the side effects of this treatment is a loss of sensation; therefore, this treatment is not widely used in clinical practice. A commonly reported side effect is pain (Kong & Chua, 1999).

Thus far, no RCTs were found which have investigated nerve block therapy for spasticity. However, two pre-post studies reported that spasticity was improved from baseline to post-therapy along with elbow passive range of motion following intramuscular nerve block on the hemiplegic upper limb (Kong & Chua, 1999, 2002).

Conclusions Regarding Nerve Block Treatment

*There is level 4 evidence that nerve blocks with ethyl alcohol improves elbow and finger passive range of motion and can decrease spasticity in the upper extremity in stroke survivors.*

*More research is needed to determine whether nerve block treatment decreases spasticity in the upper extremity.*

10.5.6 Physical Therapy in the Treatment of Spasticity
As previously mentioned, physical therapy is a mainstay in the treatment of spasticity. Common physical modalities used in the treatment of spasticity include stretching, orthoses, casting, and cold application.

The results of RCTs evaluating physical therapy are summarized in Table 10.5.6.1.

<table>
<thead>
<tr>
<th>Table 10.5.6.1 Summary of Physical Therapy in the Upper Extremity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author, Year Study Design (PEDro Score) Sample Size</strong></td>
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<tr>
<td>---------------------------------------------------------------</td>
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<tr>
<td>Horsley et al. (2007) RCT (8) N=40</td>
</tr>
<tr>
<td>Carey (1990) RCT (4) N=24</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion
Two RCTs evaluated the effect of stretching therapy on spasticity and upper limb function. The results showed no benefit of the treatment over the control regarding contracture, pain, and upper limb motor function (Carey, 1990; Horsley et al., 2007).

Conclusions Regarding Physical Therapy
There is level 1a evidence that physical therapy may not improve motor function or contracture.

Physical therapy may not decrease spasticity, or pain, or contracture, or improve upper extremity motor function.

10.5.7 Electrical Stimulation

Electrical stimulation provided as an adjunct to physical therapy has been found to be an effective treatment for lower-limb spasticity (see Chapter 9). The mechanism of action appears to be relaxation of agonist muscles and strengthening of antagonist muscles (Sahin, Ugurlu, & Albayrak, 2012). This treatment has also been well studied in the upper extremity and to date, there are a number of RCTs that have evaluated the effects of electrical stimulation on upper limb spasticity (Table 10.5.7.1).

Table 10.5.7.1 Summary of RCTs Evaluating Electrical Stimulation for spasticity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
</table>
| De Jong et al. (2013) | RCT (8) | N=46 | E: Arm stretch positioning + NMES  
C: Sham stretch positioning + Sham NMES | Modified Ashworth Scale (-) |
| Barker et al. (2008) | RCT (7) | N=33 | E1: SMART Arm + NMES  
E2: SMART Arm  
C: Conventional therapy | Modified Ashworth Scale: E1 vs. C (+); E2 vs. C (+) |
| Boyaci et al. (2013) | RCT (7) | N=31 | E1: Active NMES  
E2: Passive NMES  
C: Conventional therapy | Spasticity (wrist flexor): E1 vs. C (-); E2 vs. C (+);  
E1 vs. E2 (-)  
Spasticity (finger flexor): E1 vs C (-); E2 vs C (-); E1 vs E2 (-) |
| Chan et al. (2009) | RCT (7) | N=20 | E: Occupational therapy + NMES  
C: Occupational therapy + placebo NMES | Modified Ashworth Scale: shoulder (-), elbow (-), wrist (-) |
| Gharib et al. (2015) | RCT (7) | NStart=40  
NEnd=40 | E: Repetitive task practice + electrical stimulation  
C: Repetitive task practice | Jebsen Taylor Hand Function Test (+)  
Modified Ashworth Scale (+)  
Range of Motion (+) |
| Karakus et al. (2013) | RCT (7) | N=28 | E: Standard therapy + NMES  
C: Standard therapy | Modified Ashworth Scale: elbow (-), wrist (-), finger (-) |
| Mangold et al. (2009) | RCT (6) | N=23 | E: Conventional therapy + NMES  
C: Conventional therapy | Modified Ashworth Scale: finger flexor (-), wrist flexor (-) |
| De Kroon et al. (2004) | RCT (6) | N=28 | E: NMES on wrist flexors + extensors  
C: NMES on wrist extensors | Modified Ashworth Scale (-) |
| Sahin et al. (2012) | RCT (5) | N=42 | E: Stretching + NMES  
C: Stretching | Modified Ashworth Scale (+) |
| Hara et al. (2006) | RCT (5) | N=14 | E: Standard therapy + NMES  
C: Standard therapy | Modified Ashworth Scale: E (+) |
Hara et al. (2008)  
RCT (5)  
N=20  
E: Standard therapy + NMES  
C: Standard therapy  
- Modified Ashworth Scale: E (+)

Hesse et al. (1998)  
RCT (5)  
N=24  
E1: Botulinum toxin A  
E2: Placebo Botulinum toxin A  
E3: Placebo Botulinum toxin A + NMES  
- Modified Ashworth Scale: elbow (-), wrist (-), finger (-)

Kim & Lee (2014)  
RCT (5)  
N=29  
E1: BF-NMES + mirror therapy  
E2: NMES + mirror therapy  
C: Usual care  
- Modified Ashworth Scale: wrist extensor (-), wrist flexor (-), elbow extensor (-), elbow flexor (-)

Lin & Yan (2011)  
RCT (4)  
N=37  
E: Standard therapy + NMES  
C: Standard therapy  
- Modified Ashworth Scale: 2wk (-), 3wk (+), 1mo (+), 3mo (-), 6mo (-)

Ring & Rosenthal (2005)  
RCT (3)  
N=22  
E: Standard therapy + NMES  
C: Standard therapy  
- Modified Ashworth Scale (-)

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

Discussion
Neuromuscular electrical stimulation (NMES) has been used in rehabilitation of both upper and lower limb function and spasticity after stroke. A recent systematic review and meta-analysis incorporating the studies included above evaluated the effects of NMES on upper limb spasticity (Stein et al., 2004). Findings show that NMES was not more efficacious at improving wrist or elbow spasticity compared to conventional therapy (Barker et al., 2008; Boyaci et al., 2013; Chan et al., 2009; de Kroon et al., 2004; Hesse et al., 1998; Kim & Lee, 2014; Mangold et al., 2009). Combining NMES with mirror therapy, botulinum toxin A, or robotic devices (SMART Arm device) also showed no superior effect over the comparator therapy (Barker et al., 2008; Hesse et al., 1998; Kim & Lee, 2014).

Conclusions Regarding Electrical Stimulation Combined with Physical Therapy

There is level 1a evidence that neuromuscular electrical stimulation does not reduce wrist or elbow spasticity.

Neuromuscular electrical stimulation (NMES) may not reduce wrist or elbow spasticity.

10.5.8 Shock Wave Treatment
Shock wave therapy has been demonstrated to effectively treat a variety of bone and tendon diseases by reducing hypertonia and may be an attractive treatment option for stroke patients compared to botulinum toxin.

The results of one RCT evaluating shock wave therapy are summarized in Table 10.5.8.1.

Table 10.5.8.1 Summary of RCT(s) Evaluating Shockwave Therapy in the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
</table>
| Santamato et al. (2013) Italy | E: Botox + extracorporeal shockwave therapy | - Modified Ashworth Scale (MAS) (+)  
- Spasm Frequency Scale (+) |
Discussion

Two studies have been found indicating the effectiveness of shock wave therapy for improving spasticity in the upper limb post stroke (Dymarek et al., 2016; Santamato et al., 2013). A single treatment of shock wave therapy and botox was compared among a small group of patients to botox with electrical stimulation therapy (Santamato et al., 2013). Spasticity in the hand was effectively reduced for a period of more than 12 weeks, with no adverse effects. In the study by Dymarek et al. (2016), extracorporeal shock wave stimulation was found to improve upper limb spasticity in comparison to a placebo.

Conclusions Regarding Shock Wave Therapy

There is level 1a evidence that extracorporeal shock wave therapy improves upper limb spasticity.

Extracorporeal shockwave therapy likely improves upper limb spasticity.

10.5.9 Centrally Acting Muscle Relaxants

Tolperisone is a centrally acting muscle relaxant, similar in action to lidocaine, which acts by reducing sodium influx through nerve membranes. It may be superior to other muscle relaxants in that it does not cause sedation or muscle weakness, nor does it impair attention-related brain functions. Tolperisone and its analogue eperisone have been used successfully in patients with spinal cord injury.

The results of one RCT evaluating tolperisone for spasticity in the upper extremity post stroke are summarized in Table 10.5.9.1.

Table 10.5.9.1 Summary of RCT(s) Evaluating Tolperisone Therapy for Spasticity in the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
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</thead>
<tbody>
<tr>
<td>Stamenova et al. (2005) RCT (8) N=120</td>
<td>E: Daily dose of 300-900 mg of tolperisone C: Placebo</td>
<td>Modified Ashworth Scale (MAS) (+)</td>
</tr>
</tbody>
</table>

Discussion

One RCT found that a daily dose of tolperisone was significantly more effective at reducing upper limb spasticity than placebo injections when delivered over a period of 12 weeks (Stamenova et al., 2005). Further research is needed to determine the effect of tolperisone for improving upper limb impairments and contracture. Eperisone, was found to improve upper limb muscle tone in 75% of patients, while only...
44% of patients improved in tone when receiving only physiotherapy (Tariq et al., 2005). Currently, it is unclear whether eperisone is significantly beneficial for tone reduction in the upper extremity.

**Conclusions Regarding Centrally Acting Muscle Relaxants**

*There is level 1b evidence that tolperisone can reduce spasticity following stroke.*

*Further research is needed to determine the benefits of tolperisone on upper limb muscle tone.*

### 10.6 EMG/Biofeedback

EMG/biofeedback uses instrumentation applied to an individual’s muscle(s) with external electrodes to capture motor unit electrical potentials. As the instrumentation converts the potentials into visual or audio information, the individual has a visual depiction or auditory indication of how much they are activating their muscle(s). Moreland and Thomson (1994) published a research overview and meta-analysis on the efficacy of electromyographic biofeedback compared with conventional physical therapy for upper extremity function in stroke patients. They concluded that neither therapy was superior over the other.

The results of RCTs evaluating EMG/biofeedback therapy are presented in Table 10.6.1.

**Table 10.6.1 Summary of RCTs Evaluating EMG/Biofeedback Therapy for the Upper Extremity**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crow et al.</strong> (1989)</td>
<td>RCT (8) N=40</td>
<td>E: EMG/Biofeedback Therapy C: Sham EMG/biofeedback</td>
<td>• Action Research Arm test: post (+), 6wk follow-up (-)</td>
</tr>
<tr>
<td><strong>Garrido-Montenegro et al.</strong> (2016)</td>
<td>RCT (8) N&lt;sub&gt;Start&lt;/sub&gt;=14 N&lt;sub&gt;End&lt;/sub&gt;=14</td>
<td>E: EMG/Biofeedback + conventional occupational therapy C: Occupational therapy</td>
<td>• Barthel Index (+) • Instrumental Activities of Daily Living (+) • Action Research Arm Test (+) • Motor Activity Log (+)</td>
</tr>
<tr>
<td><strong>Hemmen &amp; Seelen</strong> (2007)</td>
<td>RCT (7) N=27</td>
<td>E: EMG biofeedback + movement imagery C: Conventional electrostimulation</td>
<td>• Fugl-Meyer Score (-) • Action Research Arm test (-)</td>
</tr>
<tr>
<td><strong>Armagan et al.</strong> (2003)</td>
<td>RCT (7) N=27</td>
<td>E: EMG/Biofeedback Therapy C: Sham EMG/biofeedback</td>
<td>• Active range of motion (+) • Changes in EMG surface potentials (+) • Brunnstrom stages (-) • Complex movement (-)</td>
</tr>
<tr>
<td><strong>Dorsch et al.</strong> (2014)</td>
<td>RCT (7) N&lt;sub&gt;Start&lt;/sub&gt;=33 N&lt;sub&gt;End&lt;/sub&gt;=30</td>
<td>E: EMG stimulation C: Usual therapy</td>
<td>• MAS (-) • Manual Muscle Test (-)</td>
</tr>
<tr>
<td><strong>You et al.</strong> (2013)</td>
<td>RCT (7) N&lt;sub&gt;Start&lt;/sub&gt;=18 N&lt;sub&gt;End&lt;/sub&gt;=16</td>
<td>E: Mental training + EMG stimulation C: FES</td>
<td>• Range of Motion (-) • MAS (-) • Fugl Meyer Score (+) • Motor Activity Log: Amount of Use (-),Quality of Movement (-)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>N Start</td>
<td>N End</td>
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<tr>
<td>Chang-Yong et al. (2015)</td>
<td>RCT (7)</td>
<td>44</td>
<td>40</td>
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<tr>
<td>Thielbar et al. (2017)</td>
<td>RCT (6)</td>
<td>23</td>
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<tr>
<td>Basmajian et al. (1987)</td>
<td>RCT (6)</td>
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<td>Cordo et al. (2013)</td>
<td>RCT (6)</td>
<td>46</td>
<td>43</td>
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<tr>
<td>Hurd et al. (1980)</td>
<td>RCT (6)</td>
<td>24</td>
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<tr>
<td>Basmajian et al. (1982)</td>
<td>RCT (6)</td>
<td>37</td>
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<tr>
<td>Inglis et al. (1984)</td>
<td>RCT (5)</td>
<td>30</td>
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<tr>
<td>Kim et al. (2015)</td>
<td>RCT (5)</td>
<td>33</td>
<td>29</td>
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<tr>
<td>Greenberg &amp; Fowler (1980)</td>
<td>RCT (5)</td>
<td>29</td>
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<tr>
<td>Mroczek et al. (1978)</td>
<td>RCT (5)</td>
<td>9</td>
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<td>Rayegani et al. (2014)</td>
<td>RCT (5)</td>
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<tr>
<td>Lee et al. (1976)</td>
<td>RCT (4)</td>
<td>18</td>
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<tr>
<td>Prevo et al. (1982)</td>
<td>RCT (3)</td>
<td>28</td>
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</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
Discussion
Over the past few years, more studies have attempted to delineate the potential benefit of EMG/biofeedback technology within the stroke rehabilitation field. Various studies have found a significant effect of EMG/Biofeedback during rehabilitation, predominantly for improved motor function (Armagan et al., 2003; Chang-Yong et al., 2015; Crow et al., 1989; Garrido-Montenegro et al., 2016; You & Lee, 2013) although a study by Armagan et al. (2003) found that EMG/Biofeedback therapy improved active range of motion when compared to those receiving sham EMG/Biofeedback. The largest trial of these was that by Chang-Yong et al. (2015) which compared target reaching training with biofeedback to routine therapy in a total of 40 patients. Both the Fugl-Meyer score and the Wolf Motor Function Test were found to be superior in the intervention group.

However, there were more studies that found no significant difference between EMG/Biofeedback and conventional therapy than studies that found one (Basmajian et al., 1982; Basmajian et al., 1987; Dorsch et al., 2014; Hemmen & Seelen, 2007; Hurd et al., 1980; Thielbar et al., 2017). In a study by Cordo et al. (2013) AMES robot with torque biofeedback was not found to be superior to AMES robot with EMG biofeedback in a total of 43 patients on the Fugl Meyer score and the Box and Block Test, both measures of upper limb motor function.

Overall, the evidence suggests that biofeedback through EMG technology, either delivered alone or in combination with other treatments, may not improve upper limb motor function, manual dexterity, or spasticity. More high-powered RCTs are required to determine whether or not this method of rehabilitation is beneficial for improving other aspects of upper limb function.

Conclusions Regarding Efficacy of EMG/Biofeedback Therapy

There is level 1a evidence that EMG/biofeedback therapy does not improve upper extremity motor function or spasticity.

EMG/biofeedback therapy is likely not effective for improving upper limb motor function or spasticity.

10.7 Neuromuscular Electrical Stimulation (NMES)
Neuromuscular electrical stimulation (NMES) can be used to improve motor recovery, reduce pain and spasticity, strengthen muscles and increase range of motion following stroke. NMES is a technique that uses trains of electrical pulses to generate muscle contraction by stimulating motor axons. Three forms of NMES are available: 1) cyclic NMES, which contracts paretic muscles on a pre-set schedule and does not require participation on the part of the patient; 2) electromyography (EMG) triggered NMES, which may be used for patients who are able to partially activate a paretic muscle and may have a greater therapeutic effect; 3) Functional electrical stimulation (FES), which refers to the application of NMES to help achieve a functional task. FES can be used to improve or restore volitional grasp and manipulation functions required for typical ADLs (Popovic, Popovic, & Keller, 2002), or can be intended as a permanent assistive device (i.e., neuroprosthesis) for helping patients perform ADL.

RCTs evaluating electrical stimulation were categorized according to chronicity of stroke. Patients were considered to be suacute if they had suffered a stroke within 6 months and chronic if their stroke had
occurred greater than 6 months prior to inclusion in the study. The results are presented in Tables 10.8.2 and 10.8.3.

**Table 10.8.2 Summary of Studies Evaluating Electrical Stimulation (FES, NMES) for the Hemiparetic Upper Extremity in Subacute Stroke (<6 months)**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
</table>
| **Karakus et al. (2013)** | RCT (8) | N<sub>Start</sub>=28 N<sub>End</sub>=28 | E: FES + standard rehabilitation  
C: Standard rehabilitation | Brunnstrom (+)  
Motricity Index (+)  
Modified Ashworth Scale (-) |
| **Shimodozono et al. (2014)** | RCT (8) | N<sub>Start</sub>=27 N<sub>End</sub>=24 | E1: Continuous NMES + repetitive facilitative exercise  
E2 Repetitive facilitative exercise  
C: Conventional therapy | Fugl Meyer Score: all (+)  
Range of Motion: all elbow extension (+), all shoulder flexion (-), wrist flexion (-) |
| **Kojima et al. (2014)** | RCT crossover (7) | N<sub>Start</sub>=13 N<sub>End</sub>=13 | E: Mirror therapy + EMG-triggered NMES first  
C: Mirror therapy + EMG-triggered NMES delayed | Fugl Meyer Score (+)  
Range of Motion: 4wk (+) |
| **Kwakkel et al. (2016)** | RCT (7) | N<sub>Start</sub>=159 N<sub>End</sub>=159 | E1: EMG-NMES (unfavourable prognosis)  
E2: Modified constraint-induced movement therapy (favourable prognosis)  
C1: Unfavourable prognosis based on preservation or return of voluntary finger extension early after stroke (received usual care)  
C2: Favourable prognosis based on preservation or return of voluntary finger extension early after stroke (received usual care) | Action Research Arm Test: E1 vs. C1 (-), E2 vs. C2 (+)  
Fugl-Meyer Assessment: E1 vs. C1 (-), E2 vs. C2 (-)  
Motricity Index: E1 vs. C1 (-), E2 vs. C2 (-)  
Stroke Impact Scale: E1 vs. C1 (-), E2 vs. C2 (+)  
Wolf Motor Function Test: E1 vs. C1 (-), E2 vs. C2 (-)  
Motor Activity Log: E1 vs. C1 (-), E2 vs. C2 (-) |
| **Powell et al. (1999)** | RCT (7) | N=60 | E: Cyclic electrical stimulation + standard rehabilitation  
C: Standard rehabilitation | Action Research Arm test: grasp (+), grip (+) |
| **Manigandan et al. (2014)** | RCT (7) | N<sub>Start</sub>=24 N<sub>End</sub>=24 | E1: Cyclic electrical stimulation to supraspinatus and posterior deltoid  
E2: Cyclic electrical stimulation to supraspinatus, posterior deltoid, and long head of biceps | Shoulder subluxation (+)  
Active abduction range: without elbow flexion (+), with flexion (+) |
| **Wilson et al. (2016)** | RCT (6) | N<sub>Start</sub>=122 N<sub>End</sub>=96 | E1: Cyclic Neuromuscular Electrical Stimulation  
E2: Electromyographically-triggered Neuromuscular Electrical Stimulation  
E3: Sensory Stimulation | Fugl-Meyer Assessment (-)  
Modified Arm Motor Assessment Task (-) |
| **Hayward et al. (2013)** | 6 (RCT) | N=8 | E: SensoriMotor Active Rehabilitation Training (SMART) with outcome trigger electrical stimulation (OT-stim)  
C: SensoriMotor Active Rehabilitation Training (SMART) | Motor Assessment Scale (-)  
Upper Arm Function (-) |
| **Shindo et al. (2011)** | RCT (6) | N=24 | E: EMG-triggered NMES + splint  
C: Splint | Fugl-Meyer Score: wrist/hand distal (+), wrist/hand proximal (-)  
Motor Activity Log (-) |
<table>
<thead>
<tr>
<th>Study</th>
<th>Interventions</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knutson et al. (2012)</td>
<td>E1: Contralaterally controlled FES</td>
<td>Action Research Arm Test (+)</td>
</tr>
<tr>
<td></td>
<td>E2: Cyclic NMES</td>
<td>Maximum finger extension angle (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tracking error (% of AROM) (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fugl Meyer Score (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Box and Block Test (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm Motor Abilities Test Score (-)</td>
</tr>
<tr>
<td>Lin &amp; Yan (2011)</td>
<td>E: Cyclic NMES + standard rehabilitation</td>
<td>Fugl-Meyer Score (+)</td>
</tr>
<tr>
<td></td>
<td>C: Standard rehabilitation</td>
<td>Barthel Index (+)</td>
</tr>
<tr>
<td>Hsu et al. (2010)</td>
<td>E1: High dose NMES (60 minutes/session)</td>
<td>Fugl Meyer Assessment: E1/E2 vs. C (+); E1 vs. E2 (-)</td>
</tr>
<tr>
<td></td>
<td>E2: Low dose NMES (30 minutes/session)</td>
<td>Action Research Arm Test: E1/E2 vs. C (+); E1 vs. E2 (-)</td>
</tr>
<tr>
<td></td>
<td>C: No treatment</td>
<td>Grasp: E1/E2 vs. C (+); E1 vs. E2 (-)</td>
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<td></td>
<td></td>
<td>Grip: E1/E2 vs. C (+); E1 vs. E2 (-)</td>
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<tr>
<td></td>
<td></td>
<td>Pinch: E1/E2 vs. C (+); E1 vs. E2 (-)</td>
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<tr>
<td></td>
<td></td>
<td>Gross Movement: E1/E2 vs. C (+); E1 vs. E2 (-)</td>
</tr>
<tr>
<td>Kowalczewski et al. (2007)</td>
<td>E1: High intensity FES exercise therapy</td>
<td>Wolf Motor Function Test (+)</td>
</tr>
<tr>
<td></td>
<td>E2: Low intensity FES exercise therapy</td>
<td>Motor Activity Log (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fugl-Meyer Score (-)</td>
</tr>
<tr>
<td>Popovic et al. (2004)</td>
<td>E: Early (acute) FES</td>
<td>Upper Extremity Function test: acute (+)</td>
</tr>
<tr>
<td></td>
<td>C: Delayed (chronic) FES</td>
<td>Drawing test: acute (+)</td>
</tr>
<tr>
<td>Popovic et al. (2003)</td>
<td>E: FES</td>
<td>Upper Extremity Function test (+)</td>
</tr>
<tr>
<td></td>
<td>C: Standard therapy</td>
<td>Drawing test (+)</td>
</tr>
<tr>
<td>Chae et al. (1998)</td>
<td>E: Cyclic NMES or EMG-triggered NMES or EMG</td>
<td>Fugl-Meyer Score: post (+), 12wk follow-up (-)</td>
</tr>
<tr>
<td></td>
<td>controlled NMES + routine rehabilitation</td>
<td></td>
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<tr>
<td></td>
<td>C: Sham stimulation + routine rehabilitation</td>
<td></td>
</tr>
<tr>
<td>Miyasaka et al. (2016)</td>
<td>E: NMES + robotic training</td>
<td>Fugl-Meyer Assessment (-)</td>
</tr>
<tr>
<td></td>
<td>C: Robotic training</td>
<td>Range of Motion (-)</td>
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<tr>
<td>Mangold et al. (2009)</td>
<td>E: FES</td>
<td>ADL subscore of Extended Barthel Index (-)</td>
</tr>
<tr>
<td></td>
<td>C: Conventional therapy</td>
<td>Chedoke McMaster Stroke Assessment (-)</td>
</tr>
<tr>
<td>Thrasher et al. (2008)</td>
<td>E: FES + conventional therapy</td>
<td>Rehabilitation Engineering Laboratory Hand Function Test (+)</td>
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<td>C: Conventional therapy</td>
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<tr>
<td>Alon et al. (2007)</td>
<td>E: FES + task specific training</td>
<td>Box and Block Test (+)</td>
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<tr>
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<td>C: Task specific training</td>
<td>Jebsen-Taylor light object lift (+)</td>
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<td></td>
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<td>Modified Fugl-Meyer: 12wk (+)</td>
</tr>
<tr>
<td>Francisco et al. (1998)</td>
<td>E: EMG-triggered NMES + standard therapy</td>
<td>Fugl-Meyer Score (+)</td>
</tr>
<tr>
<td></td>
<td>C: Conventional Therapy</td>
<td>Upper extremity FIM scores (+)</td>
</tr>
<tr>
<td>Malhotra et al. (2013)</td>
<td>E: NMES</td>
<td>Passive Range of Motion (-)</td>
</tr>
<tr>
<td></td>
<td>C: No stimulation</td>
<td></td>
</tr>
<tr>
<td>Faghri &amp; Rodgers (1997)</td>
<td>E: FES + conventional therapy</td>
<td>Range of motion (+)</td>
</tr>
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<td></td>
<td>C: Conventional therapy</td>
<td></td>
</tr>
<tr>
<td>Author, Year</td>
<td>Study Design (PEDro Score)</td>
<td>Sample Size</td>
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<tr>
<td>Gharib et al. (2014)</td>
<td>RCT (9)</td>
<td>N Start=40 N End=40</td>
</tr>
<tr>
<td>Chae et al. (2009)</td>
<td>RCT (8)</td>
<td>N=26</td>
</tr>
<tr>
<td>Lee et al. (2015)</td>
<td>RCT (8)</td>
<td>N Start=39 N End=39</td>
</tr>
<tr>
<td>Barker et al. (2008)</td>
<td>RCT (8)</td>
<td>N Start=42 N End=33</td>
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<tr>
<td>Chan et al. (2009)</td>
<td>RCT (7)</td>
<td>N=20</td>
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<tr>
<td>Weber et al. (2010)</td>
<td>RCT (7)</td>
<td>N=23</td>
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<tr>
<td>De Kroon &amp; Ijzerman (2008)</td>
<td>RCT (7)</td>
<td>N=22</td>
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</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimberley et al. (2004)</td>
<td>RCT (7)</td>
<td>N=16</td>
<td>EMG-triggered NMES vs. Sham</td>
<td>Box &amp; Block test (+), Motor Activity Log (+), Jebsen Taylor Hand Function test (+)</td>
</tr>
<tr>
<td>Hu et al. (2015)</td>
<td>RCT (6)</td>
<td>N_{Start}=26, N_{End}=26</td>
<td>EMG-driven NMES robot vs. EMG-driven robot</td>
<td>Fugl-Meyer Assessment (+), Action Research Arm Test (+), Modified Ashworth Scale (-)</td>
</tr>
<tr>
<td>Ring &amp; Rosenthal (2005)</td>
<td>RCT(6)</td>
<td>N=22</td>
<td>Neuroprosthetic FES vs. Control</td>
<td>Modified Ashworth Scores (+), Box &amp; Block test (+), Jebsen Taylor Hand Function test (+)</td>
</tr>
<tr>
<td>De Kroon et al. (2004)</td>
<td>RCT (6)</td>
<td>N=30</td>
<td>Electrical stimulation to the extensor and flexor muscles vs. Electrical stimulation to the extensors only</td>
<td>Arm Research Arm test (-), Motricity Index (-), Ashworth Scale (-)</td>
</tr>
<tr>
<td>Knutson et al. (2016)</td>
<td>RCT (5)</td>
<td>N_{Start}=80, N_{End}=64</td>
<td>Contralaterally controlled FES (CCFES) vs. Cyclic NMES</td>
<td>Fugl-Meyer Assessment (-), Arm Motor Abilities Test (-), Box and Block Test (+)</td>
</tr>
<tr>
<td>Kim et al. (2015)</td>
<td>RCT (5)</td>
<td>N_{Start}=33, N_{End}=29</td>
<td>FES with biofeedback + mirror therapy vs. FES + mirror therapy</td>
<td>Box and Block Test (+), Jebsen Taylor Hand test (+), Stroke Specific Quality of Life (+), Grip strength (+)</td>
</tr>
<tr>
<td>Baygutalp et al. (2014)</td>
<td>RCT (5)</td>
<td>N_{Start}=30, N_{End}=30</td>
<td>NMES + conventional therapy vs. Conventional therapy</td>
<td>Modified Ashworth Scale: post (-), 2mo follow-up (-), Barthel Index (-), Brunnstrom (-), Pain: post (+), at discharge (+), at 2mo follow-up (+)</td>
</tr>
<tr>
<td>Doucet and Griffin (2013)</td>
<td>RCT (5)</td>
<td>N_{Start}=16, N_{End}=16</td>
<td>High frequency NMES (40Hz) vs. Low frequency NMES (20Hz)</td>
<td>Lateral pinch strength (+), Minnesota Manual Dexterity Test (+), Endurance of thumb adduction (+)</td>
</tr>
<tr>
<td>Hara et al. (2008)</td>
<td>RCT (5)</td>
<td>N=20</td>
<td>FES vs. Control</td>
<td>ROM (+), Modified Ashworth Scale (+)</td>
</tr>
<tr>
<td>Mann et al. (2005)</td>
<td>5 (RCT)</td>
<td>N=22</td>
<td>Neuromuscular Electrical Stimulation vs. Passive Extension Exercises</td>
<td>Action Research Arm Test (+)</td>
</tr>
<tr>
<td>Gabr et al. (2005)</td>
<td></td>
<td></td>
<td>EMG-triggered NMES</td>
<td>Fugl Meyer Score (+)</td>
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</tbody>
</table>
RCT (4)  
N=12  
C: Home exercise  
• Action Research Arm test (-)

Hara et al. (2006)  
RCT (4)  
N=14  
E: FES  
C: Control  
• Modified Ashworth Scale (-)  
• Range of Motion (+)

Cauraugh et al. (2000)  
RCT (4)  
N=11  
E: EMG-triggered NMES + passive range of motion + stretching exercises  
C: Passive range of motion + stretching exercises  
• Box and Block test (+)  
• Motor Assessment scale (-)  
• Fugl-Meyer upper extremity (-)

King (1996)  
RCT (4)  
N=21  
E: NMES  
C: Passive stretch  
• Tone reduction (+)

Bhatt et al. (2007)  
RCT (3)  
N=20  
E1: EMG-triggered ES  
E2: Tracking training  
E3: EMG-triggered ES + tracking training  
• Jebson Taylor tests (-)  
• Box & Block test (-)  
• Finger tracking test (-)

Inobe et al. (2013)  
PCT  
N_{start}=7  
N_{end}=7  
E: ES  
C: Sham ES  
• Fugl Meyer Score: upper extremities (+), distal and proximal upper extremities (+)

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

Discussion

Among the studies evaluating FES/NMES in the subacute stage of stroke, most assessed the same treatment comparison, electrical stimulation versus physical therapy alone or sham stimulation. The results indicated that FES/NMES was associated with improvements in motor function, range of motion, ADL and dexterity in acute to subacute strokes (Alon et al., 2007; Faghri, 1997; Faghri et al., 1994; Francisco et al., 1998; Heckmann et al., 1997; Karakus et al., 2013; Lin & Yan, 2011; Popovic et al., 2003; Powell et al., 1999; Thrasher et al., 2008). In the chronic phase, FES/NMES may be advantageous at recovering impaired manual dexterity, coordination and range of motion however, improvements in motor function in general following FES/NMES are less clear (Bhatt et al., 2007; Cauraugh et al., 2000; Conforto et al., 2002; de Kroon & Ijzerman, 2008; de Kroon et al., 2004; Inobe & Kato, 2013; Kim & Lee, 2015; Ring & Rosenthal, 2005; Weber et al., 2010; Wu et al., 2006). Despite improvements observed during both phases of stroke recovery, limited evidence indicates that recovery may be more significant when FES was delivered early (<6 months) compared to when it was delivered at a later chronic stage (>6 months) (Popovic et al., 2004). More research is needed to verify this effect. Furthermore, in unfavourable patients, EMG-NMES was found to have no effect when compared to those receiving usual care on measures of upper limb motor function and dexterity (Kwakkel et al., 2016).

Two studies compared a high intensity NMES or FES exercise therapy (60 minutes) against a low intensity exercise program (Hsu et al., 2010; Kowalczyewski et al., 2007). Both studies found that there was no significant difference between groups in upper limb motor function in patients during the acute/subacute phase post stroke.

EMG-triggered and cyclic neuromuscular electrical stimulation (NMES)/electrical stimulation delivered to patients in the acute-subacute stroke phase led to improvements in upper limb functional impairments (Chae et al., 1998; Kojima et al., 2014; Shimodozono et al., 2014; Shindo et al., 2011). However, the findings are less clear when range of motion is considered given that only elbow extension
was found to improve and not shoulder/wrist flexion when continuous NMES was delivered in combination with repetitive facilitative exercise in the subacute phase of stroke (Shimodozono et al., 2014). In individuals with chronic stroke, a similar beneficial effect on upper limb motor function was found following EMG-triggered NMES or electrical stimulation (Chan et al., 2009; Gharib et al., 2014; Hu et al., 2015; Kim, Lee, & Lee, 2015; Kimberley et al., 2004; Y. H. Lee et al., 2015; Ring & Rosenthal, 2005). Unlike in subacute stroke patients however, EMG-triggered NMES was not found to be superior to cyclic or passive NMES at improving upper limb motor function in the chronic phase (Boyaci et al., 2013; de Kroon & Ijzerman, 2008; Wilson et al., 2016). Contralaterally controlled FES (FES) was also not found to be superior to cyclic NMES on measures of upper limb motor function, although it did show a benefit for dexterity. Furthermore, Wilson et al. (2016) also found that neither cyclic NMES nor EMG-triggered NMES were superior to sensory stimulation. Delivering higher frequency NMES (40Hz) evoked greater improvements in manual dexterity relative to lower frequency NMES (20Hz) (Doucet & Griffin, 2013).

Three recent meta-analyses have investigated the effect of NMES on functional recovery post-stroke. These studies include patients in the acute to chronic stage post-stroke and protocols involving upper and lower limbs. Nascimento, (2014) analyzed data from 16 RCTs and concluded that there were significant improvements associated with cyclic NMES on both strength and activity level after stroke (Nascimento et al., 2014). This review used a broader definition of cyclic NMES that included EMG-triggered NMES. The effects were maintained up to 36 weeks after 6 weeks of therapy when compared to no treatment or a placebo (Nascimento et al., 2014). This review did not provide separate analysis for the upper extremity studies.

A review of 18 RCTs by Howlett et al. (2015) included 9 RCTs of FES targeted for improvement of upper limb function however, only 8 were analyzed. Outcomes used for analyses include those that reflect the International Classification of Function domain of activity performance (i.e. Motor Assessment Scale for Stroke (Barker et al., 2008), Arm Motor Ability Test (Daly et al., 2005), Box and Block Test (S.J. Page et al., 2012), Action Research Arm Test (Mann et al., 2005), Upper Extremity Function Test (Popovic et al., 2004; Popovic et al., 2003), and the Wolf Motor Function Test (Tarkka, Pitkanen, Popovic, Vanninen, & Kononen, 2011). Due to the variation in outcomes included, the results were measured in terms of “activity”. Pooled analyses demonstrate a significant effect favouring the FES treatment over the control therapy (i.e. no treatment or placebo) on upper limb activity. Despite the positive findings, results are to be interpreted with caution since all studies were poorly powered, and the methodological quality averaged to 5.5 (out of a total score of 10 on the PEDro scale). Furthermore, 3 studies included patients in the acute phase of stroke, while the remainder 5 studies evaluated patients in the chronic stage with a time post-stroke ranging from 6 to 46 months. Lastly, although all outcomes measured “activity”, not all outcomes assess the same aspects of “activity” or function. For instance, the Box and Block Test assesses manual dexterity, while the Upper Extremity Function Test measures general upper limb function. Combining all measures does not provide an accurate representation of the effect of FES on upper limb impairment following stroke.

Analyses involving only the upper limb in the most recent review showed that various NMES treatments had no effect on spasticity in the wrist or elbow, or on range of motion in the wrist when combined with other treatments (Stein, Fritsch, Robinson, Sbruzzi, & Plentz, 2015). The only significant result was a positive relationship of NMES on range of motion in the elbow. Among the limitations of these studies, a lack of blinding of therapists and participants was most prevalent. However, the authors noted that this may be considered as an inherent drawback to studies involving a physically active intervention such as electrical stimulation. Other problematic factors included a lack of allocation concealment and intention-to-treat analysis, and the inclusion of studies of low methodological quality and statistical power.
Conclusions Regarding FES/NMES Therapy for Upper Extremity

There is level 1a and level 2 evidence that FES/NMES may improve upper limb motor function, range of motion, and manual dexterity when offered in combination with conventional therapy or delivered alone in subacute stroke. The evidence is also indicative of a beneficial effect on range of motion and manual dexterity when FES/NMES was offered to chronic stroke patients either alone or in combination with other therapies.

Despite improvements in both stages of stroke recovery, level 1b evidence indicates that delivering FES early (<6 months) may be more beneficial at recovering impaired motor function than delivering FES after 6 months post-stroke.

There is level 1b evidence that EMG-NMES in the subacute phase is not more effective than usual care for patients with an unfavourable prognosis based on voluntary finger extension.

There is level 1a evidence that high intensity NMES or FES exercise is no more effective for improving upper limb motor function than low intensity NMES or FES in the subacute phase.

There is level 1a and level 2 evidence that both EMG-triggered and cyclic approaches to NMES/electrical stimulation may improve upper limb motor function and range of motion in subacute and chronic stroke patients; however, evidence indicates no superior benefit of EMG-triggered NMES over cyclic or passive NMES at improving upper limb motor function in chronic (level 1a) and subacute (level 1b) stroke patients.

There is level 1b evidence that Contralaterally Controlled FES is not superior to cyclic NMES for improving upper limb motor function, although it may improve dexterity.

There is level 1b evidence that coupling continuous NMES with repetitive facilitative exercise may be beneficial at improving general upper extremity function and range of motion during elbow extension but not during shoulder or wrist flexion in subacute stroke patients.

There is level 1b evidence that high frequency NMES may be superior to low frequency NMES at improving endurance of thumb adduction, lateral pinch strength and manual dexterity in chronic stroke individuals.

Both functional electrical stimulation (FES) and neuromuscular electrical stimulation (NMES) may help improve impaired upper extremity motor function during all phases of stroke (i.e. from acute to chronic).

FES may be more beneficial at improving impaired motor function when delivered early (<6 months) than late (>6 months).

There is no significant difference in the benefits observed following different NMES delivery modalities (i.e. cyclic, EMG-triggered, and passive).
10.8 Brain Stimulation

Brain stimulation has been increasingly studied as a means to improve motor recovery, particularly in the hand, and to alleviate pain in chronic stroke. Both invasive and non-invasive methods are available.

10.8.1 Invasive Motor Cortex Stimulation (MCS)

Since Tsubokawa et al. (1991) discovered that stimulation of the motor cortex via implanted electrodes was sufficient to induce muscle contraction, its use was extended to potentially treat various neurological conditions including stroke. However, due to the invasive nature of this technique and the complications associated with the procedure, the evidence for its use in the stroke population is limited. The trials that have evaluated the use of invasive motor cortex stimulation for improving motor function post stroke are summarized in table 10.8.1.1.

Table 10.8.1.1 Summary of RCTs Evaluating Invasive Stimulation for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dawson et al. (2016)</td>
<td>RCT (7)</td>
<td>N_{Start}=20 N_{End}=20</td>
<td>E: Implanted vagus nerve stimulation + upper limb therapy C: Upper limb therapy</td>
<td>Fugl-Meyer Assessment (+) Action Research Arm Test (-) Grip Strength (-) 9 Hole Peg Test (-) Box and Block Test (-)</td>
<td></td>
</tr>
<tr>
<td>Brown et al. (2006)</td>
<td>RCT (6)</td>
<td>N=10</td>
<td>E: Motor cortex stimulation C: Rehabilitation</td>
<td>Fugl Meyer Scale (+) Stroke Impact Scale (+)</td>
<td></td>
</tr>
<tr>
<td>Levy et al. (2016)</td>
<td>RCT (6)</td>
<td>N_{Start}=164 N_{End}=128</td>
<td>E: Cortical implant with epidural 6-contact lead perpendicular to the primary motor cortex and a pulse generator C: No implant</td>
<td>Upper Extremity Fugl-Meyer (-) Arm Motor Ability Test (-)</td>
<td></td>
</tr>
<tr>
<td>Huang et al. (2008)</td>
<td>RCT (5)</td>
<td>N=24</td>
<td>E1: Motor cortex stimulation (50Hz) C1: Rehabilitation therapy E2: Motor cortex stimulation (101Hz) C2: Rehabilitation therapy</td>
<td>Fugl Meyer Score (+) Box and Block Test (+) Stroke Impact Scale (-) Arm Motor Ability Test (-) Grip strength (-)</td>
<td></td>
</tr>
<tr>
<td>Levy et al. (2008)</td>
<td>RCT (5)</td>
<td>N=24</td>
<td>E: Motor cortex stimulation C: Control</td>
<td>Fugl Meyer Score (+) Arm Motor Ability Test (+)</td>
<td></td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion

Motor Cortex Stimulation (MCS) was found to improve upper limb motor function post stroke in some studies, but not in others. Brown et al. (2006) reported efficacious gains in upper limb motor function in patients who received MCS compared to a control group who received standard care. However, the results of this study are to be interpreted with caution because the study was highly underpowered, with only 10 patients included.
In another study, Huang et al. (2008) reported a significant effect of group, with significantly favourable gains for the treatment groups on the Fugl-Meyer Assessment and Box and Block Test (BBT), but no significant improvement on the Arm Motor Ability Test (AMAT). Huang et al. (2008) suggest that the difference in BBT and AMAT may also have been due to sensitivity of proximal performance. Although grip strength did not show any improvement, the authors suggest that gains may have been more proximal than distal.

Dawson et al. (2016) also found an improvement in those receiving implanted vagus nerve stimulation and upper limb therapy in comparison to those only receiving upper limb therapy on the Fugl-Meyer Assessment for upper limb motor function. However, no significant difference between groups was found on the Action Research Arm Test, Nine Hole Peg Test, and the Box and Block Test. This suggests that vagus nerve stimulation may improve overall upper limb motor function, but not dexterity or grip strength.

Lastly, a large study by Levy et al. (2016) found no significant difference on upper limb motor function outcomes between patients receiving a cortical implant providing primary motor cortex stimulation with a pulse generator when compared to those not receiving an implant.

Adverse events have also been reported in patients receiving MCS. Brown et al. (2006) evaluated the safety of MCS and did not report any deaths or neurological deterioration, and although there were two cases of infection, the authors stated that these were due to a protocol violation and a faulty lead and therefore are not typical of the MCS itself. One seizure also occurred in the study conducted by Huang et al. (2008), but the authors believe that it was caused by the anesthetic rather than the treatment. Additional prospective multicenter double-blind RCTs are needed to establish definitive data regarding the use of MCS for the recovery of impaired motor function post stroke.

**Conclusions Regarding Invasive Motor Cortex Stimulation (MCS)**

*There is level 1a evidence that motor cortex stimulation does not improve upper limb motor function.*

*There is level 1b evidence that vagus nerve stimulation can improve overall upper limb motor function, but not dexterity or grip strength.*

Motor Cortex Stimulation via implanted electrodes may not improve upper limb function in patients post-stroke. More studies are needed to conclude on the effectiveness of vagus nerve stimulation for upper limb motor function.

**10.8.2 Non-Invasive Motor Cortex Stimulation**

In the preceding section, the efficacy of motor cortex stimulation by surgically implanted devices in the relief of central pain following stroke, is reviewed. Cortical stimulation can also be achieved non-invasively through the use of single or repetitive transcranial magnetic stimulation (TMS and rTMS) and transcranial direct-current stimulation (tDCS) to help improve motor recovery.
10.8.2.1 Repetitive Transcranial Magnetic Stimulation (rTMS)

TMS is a novel approach to neurorehabilitation following stroke. TMS may be delivered in a single pulse, in paired pulses or as repetitive trains of stimulation. Repetitive TMS (rTMS) produces effects which last longer than the period of stimulation. When TMS is applied in the form of trains of stimuli (rTMS) to the motor cortex, it can facilitate or suppress targeted regions of the brain, depending on the stimulation parameters. Low stimulation frequencies (1 Hz or lower) decrease cortical excitability and inhibit the targeted cortex, while high frequency (10 to 20Hz) stimulation increases excitability and has a facilitatory effect.

The stimulation process is both painless and non-invasive, and involves the use of a coil that produces a magnetic field which passes through the skull to the cerebral cortex. Repetitive TMS induces sustained increases in cortical excitability through mechanisms that are still not well defined; however, inhibition of the unaffected hemisphere theoretically results in decreased inhibitory projections to the affected hemisphere, increasing intracortical excitability within the ipsilesional cortial tissue that ultimately would translate into an improvement in motor function (Fregni et al., 2006). Alternatively, excitatory rTMS may target the affected hemisphere directly, thereby increasing intracortical excitability (Hoyer & Celnik, 2011). Repetitive TMS has also been used to identify those patients who might benefit from long-term motor cortex stimulation long term using implantable devices.

A recent meta-analysis (Hsu, Cheng, Liao, Lee, & Lin, 2012) including the results of 18 RCTs and representing data from 392 patients, examined the effectiveness of rTMS for improving motor function following stroke. The authors reported a clinically significant treatment effect. The outcomes evaluated included finger tapping tasks, the Nine Hole Peg Test, hand grip strength and the Wolf Motor Function test. The treatment effects associated with treatment in the acute, subacute and chronic stages of stroke were 0.79, 0.63 and 0.66, respectively. Low-frequency rTMS (1 Hz) over the unaffected hemisphere appeared to be more effective than high-frequency rTMS (10 Hz) over the unaffected hemisphere (treatment effect =0.69 vs. 0.41).

A systematic review with meta-analysis by Graef et al. (2016) investigated whether there is a significant difference between rTMS with upper limb training in comparison to sham rTMS with upper limb training. The review included 11 studies, and overall found no significant difference between groups for upper limb motor function or spasticity.

A growing number of studies have investigated the effects of both single and repetitive TMS with the aim of improving function of the upper extremity and lower extremity. The results of RCTs evaluating rTMS for the upper extremity are presented in Table 10.8.2.1.1.

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Intervention</th>
<th>Outcome(s) and Result(s)</th>
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<tbody>
<tr>
<td>Wang et al. (2014) RCT (9) NStart=44 NEnd=44</td>
<td>E1: 1Hz rTMS premotor E2: 1Hz rTMS motor C: Sham</td>
<td>• Wolf Motor Function Test: E1 vs. E2 (+), E1 vs. C (+), E2 vs. C (+) • Fugl Meyer Score: E1 vs. E2 (+), E1 vs. C (+), E2 vs. C (+)</td>
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<tr>
<td>Lüdemann-Podubecká et al. (2015) RCT (9) NStart=40</td>
<td>E1: 1Hz contralesional rTMS + motor training, lesioned dominant hemisphere E2: 1Hz contralesional rTMS + motor training, lesioned non-dominant</td>
<td>• Wolf Motor Function Test: E2 vs. C2 (-), E1 vs. C1 (+) • Motor Evaluation Scale for Upper: E2 vs. C2 (-), E1 vs. C1 (+)</td>
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<tr>
<td>Study</td>
<td>Design</td>
<td>N Start</td>
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<tr>
<td>Hosomi et al. (2016)</td>
<td>RCT (8)</td>
<td>41</td>
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<tr>
<td>Yang et al. (2016)</td>
<td>RCT (8)</td>
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<tr>
<td>Seniów et al. (2012)</td>
<td>RCT (8)</td>
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<tr>
<td>Khedr et al. (2009)</td>
<td>RCT (8)</td>
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<tr>
<td>Khedr et al. (2010)</td>
<td>RCT (8)</td>
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<tr>
<td>Sasaki et al. (2013)</td>
<td>RCT (8)</td>
<td>29</td>
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<td>Barros Galvao et al. (2014)</td>
<td>RCT (8)</td>
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<tr>
<td>Sasaki et al. (2014)</td>
<td>RCT (8)</td>
<td>58</td>
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<tr>
<td>Pomeroy et al. (2007)</td>
<td>RCT (8)</td>
<td>27</td>
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<tr>
<td>Ludemann-Podubecka et al. (2015)</td>
<td>RCT (7)</td>
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<tr>
<td>Abo et al. (2014)</td>
<td>RCT (7)</td>
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<td>Study</td>
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</table>
| Higgins et al. (2013) | RCT (7) |        | 11                | 11              | E: Inhibitory rTMS  
C: Sham                                                  | • Box and Block Test (-)  
• Motor Activity Log (-)  
• Wolf Motor Function Test (-)                    |
| Emara et al. (2010)   | RCT (7) | N=60   |                   |                 | E1: 5Hz rTMS  
E2: 1Hz rTMS  
C: Sham                                                 | • Finger tapping test: rTMS vs. C (+)  
• Activities Index: rTMS vs. C (+)  
• Modified Rankin Scale: rTMS vs. C (+)               |
| Takeuchi et al. (2008)| RCT (7) | N=20   |                   |                 | E: Inhibitory rTMS + pinch force motor training  
C: Sham + pinch force motor training                     | • Pinch acceleration (+)  
• Pinch force (+)                                      |
| Liepert et al. (2007)| RCT (7) | N=12   |                   |                 | E: Inhibitory rTMS  
C: Sham                                                  | • Grip strength (-)  
• 9-hole peg test (+)                                 |
| Fregni et al. (2006)  | RCT (7) | N=15   |                   |                 | E: Inhibitory rTMS  
C: Sham                                                  | • Jebsen-Taylor Hand Function test (+)                 |
| Zheng et al. (2015)   | RCT (7) | NStart=112  
NEnd=108 |           |                 | E: 1 Hz rTMS + virtual reality (VR) training  
C: Sham + VR training                                  | • Fugl Meyer Score (+)  
• Wolf Motor Function Test (+)  
• Modified Barthel Index (+)  
• SF-36 (+)                                          |
| Cassidy et al. (2015) | RCT (7) | NStart=11  
NEnd=11 |           |                 | E1: 6Hz rTMS  
E2: 1Hz rTMS  
C: Sham                                                  | • Box and Block Test: E1/E2 vs. C (+)                  |
| Du et al. (2016)      | RCT (7) | NStart=69  
NEnd=55 |           |                 | E1: 1200 10s pulses 3Hz ipsilesional rTMS  
E2: 1200 30s pulses 1Hz contralesion rTMS  
C: Sham rTMS                                             | • Fugl-Meyer Assessment: E1/E2 vs. C (+)  
• Medical Research Council Score: E2 vs. C (+)  
• National Institute of Health Stroke Scale: E1/E2 vs. C (+)  
• Modified Rankin Scale: E1/E2 vs. C (+)  
• Barthel Index: E1/E2 vs. C (+)                        |
| Li et al. (2016)      | RCT (7) | NStart=127  
NEnd=127 |           |                 | E1: 1Hz rTMS  
E2: 10Hz rTMS  
C: Sham                                                  | • Fugl-Meyer Assessment: E1/E2 vs. C (+)  
• Wolf Motor Function Test (-)                         |
| Ludemann-Podubecka et al. (2016) | RCT (7) | NStart=10  
NEnd=10 |           |                 | E: 1 Hz rTMS  
C: Sham                                                  | • Jebsen Taylor Hand Function Test (+)  
• Box and Block Test (-)                                |
| D’Agata et al. (2016) | RCT (6) | NStart=34  
NEnd=34 |           |                 | E: Inhibitory tDCS + rTMS + Mirror Therapy  
C: Sham tDCS + Mirror Therapy                          | • Action Research Arm Test (+)                         |
| Ji et al. (2014)      | RCT (7) | NStart=35  
NEnd=35 |           |                 | E1: Mirror therapy+ excitatory rTMS  
E2: Mirror therapy  
C: Sham                                                  | • Fugl Meyer Score: E1 vs. E2 (+), E2 vs. C (+)  
• Box and Block Test: E1 vs. E2 (+), E2 vs. C (+)      |
| Sung et al. (2013)    | RCT (6) | NStart=54 |           |                 | E1: Inhibitory rTMS + iTBS  
E2: Sham rTMS + iTBS  
E3: Inhibitory rTMS + sham iTBS                          | • Wolf Motor Function test: E(all) vs. C (+), E1 vs. E2 (+), E1 vs. E3 (+)  
• Fugl-Meyer Assessment: E(all) vs. C (+), E1 vs. E2   |
<table>
<thead>
<tr>
<th>N&lt;sub&gt;End&lt;/sub&gt;=54</th>
<th>C: Sham rTMS + sham iTBS</th>
<th>(+), E1 vs. E3 (+) • FIM (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conforto et al. (2012)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N=29</td>
<td>E: Inhibitory rTMS&lt;br&gt;C: Sham</td>
<td>• Jebsen-Taylor Hand Function test (+)&lt;br&gt;• Pinch Force (+)&lt;br&gt;• Fugl-Meyer (upper) (+)&lt;br&gt;• Modified Ashworth (-)</td>
</tr>
<tr>
<td><strong>Malcolm et al. (2007)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N=19</td>
<td>E: Excitatory rTMS&lt;br&gt;C: Sham</td>
<td>• Wolf Motor Function Test (-)&lt;br&gt;• Motor Activity Log (-)</td>
</tr>
<tr>
<td><strong>Takeuchi et al. (2009)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N=30</td>
<td>E1: Bilateral (dual) rTMS + pinch force motor training&lt;br&gt;E2: Excitatory rTMS affected hemisphere + pinch force motor training&lt;br&gt;E3: Inhibitory rTMS unaffected hemisphere + pinch force motor training</td>
<td>• Pinch force: E1 vs. E3 (+), E1 vs. E2(+) • Acceleration: E1 vs. E3 (+), E1 vs. E2(+)</td>
</tr>
<tr>
<td><strong>Takeuchi et al. (2005)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N=20</td>
<td>E: Inhibitory rTMS&lt;br&gt;C: Sham</td>
<td>• Hand and pinch force (-)&lt;br&gt;• Hand acceleration (+)</td>
</tr>
<tr>
<td><strong>Kim et al. (2014)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N&lt;sub&gt;Start&lt;/sub&gt;=31&lt;br&gt;N&lt;sub&gt;End&lt;/sub&gt;=31</td>
<td>E: Excitatory rTMS&lt;br&gt;C: Sham</td>
<td>• Manual Function Test (+)</td>
</tr>
<tr>
<td><strong>Khedr et al. (2005)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N=52</td>
<td>E: rTMS&lt;br&gt;C: Sham</td>
<td>• Barthel Index (+)&lt;br&gt;• NIHSS (+)&lt;br&gt;• Scandinavian Stroke Impact Scale (+)</td>
</tr>
<tr>
<td><strong>Chang et al. (2010)</strong>&lt;br&gt;RCT (5)&lt;br&gt;N=28</td>
<td>E: rTMS&lt;br&gt;C: Sham</td>
<td>• Motricity Index (+)&lt;br&gt;• Fugl-Meyer (-)</td>
</tr>
<tr>
<td><strong>Rose et al. (2014)</strong>&lt;br&gt;RCT (5)&lt;br&gt;N&lt;sub&gt;Start&lt;/sub&gt;=22&lt;br&gt;N&lt;sub&gt;End&lt;/sub&gt;=19</td>
<td>E: rTMS + functional task practice (FTP)&lt;br&gt;C: Sham + FTP</td>
<td>• Wolf Motor Function Test (-)&lt;br&gt;• Lateral pinch (-)&lt;br&gt;• Palmar pinch (-)&lt;br&gt;• Fugl Meyer Assessment (-)&lt;br&gt;• Action Research Arm Test (-)&lt;br&gt;• Modified Ashworth Scale (-)&lt;br&gt;• Motor Activity Log: quality of movement (-)&lt;br&gt;• Motor Activity Log: amount of use (-)</td>
</tr>
<tr>
<td><strong>Lindenberg et al. (2010)</strong>&lt;br&gt;RCT (4)&lt;br&gt;N=20</td>
<td>E: rTMS&lt;br&gt;C: Sham</td>
<td>• Fugl Meyer (Upper) (+)&lt;br&gt;• Wolf Motor Function test (+)</td>
</tr>
<tr>
<td><strong>Mansur et al. (2005)</strong>&lt;br&gt;RCT (4)&lt;br&gt;N=10</td>
<td>E: rTMS&lt;br&gt;C: Sham</td>
<td>• Simple reaction time (+)&lt;br&gt;• Four-choice reaction time (+)&lt;br&gt;• Finger tapping test (-)&lt;br&gt;• Perdue Pegboard test (+)</td>
</tr>
<tr>
<td><strong>Kim et al. (2016)</strong>&lt;br&gt;PCT&lt;br&gt;N&lt;sub&gt;Start&lt;/sub&gt;=82&lt;br&gt;N&lt;sub&gt;End&lt;/sub&gt;=82</td>
<td>E1: rTMS responders based on self-care score of Modified Barthel Index&lt;br&gt;E2: rTMS non-responders based on self-care score of Modified Barthel Index&lt;br&gt;C: Usual care</td>
<td>• Modified Barthel Index: E1 vs. E2/C (+)&lt;br&gt;• National Institute of Health Stroke Scale: E1/E2 vs. C (+)&lt;br&gt;• Brunnstrom Stage: E1/E2 vs. C (+)&lt;br&gt;• Upper Limb Mobility: E1 vs. E2/C (+)</td>
</tr>
<tr>
<td><strong>Guo et al. (2016)</strong>&lt;br&gt;PCT</td>
<td>E: 10Hz rTMS + usual care&lt;br&gt;C: usual care</td>
<td>• National Institute for Health Stroke Scale (-)&lt;br&gt;• Barthel Index (-)</td>
</tr>
<tr>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=15</td>
<td>N&lt;sub&gt;End&lt;/sub&gt;=15</td>
<td>• Fugl-Meyer Assessment (+)</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------</td>
<td>-----------------------------</td>
</tr>
</tbody>
</table>
| **Etoh et al. (2016)** | PCT | E1: Exercise + rTMS  
E2: Exercise + NMES + Vibration  
E3: Exercise + NMES + Vibration + rTMS | • Fugl-Meyer Assessment (-)  
• Action Research Arm Test (-)  
• Modified Ashworth Scale (-) |

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

**Discussion**

Most of the trials evaluating rTMS or TMS examined the effect of brain stimulation on upper extremity motor function. Among these trials, treatment periods were short, usually lasting for 2 weeks, and were most often conducted on patients during the chronic stage of stroke. A number of studies also investigated the intensity of rTMS provided. Research from Khedr et al. (2009; 2010) investigated rTMS at frequencies of 1Hz versus 3Hz and 3Hz versus 10Hz, respectively. The results from the former study suggested that 10 consecutive days of 1Hz was more efficacious than 3Hz, with patients who received 1Hz performing better on the Pegboard Task and on the National Institutes of Health Stroke Scale (NIHSS); however, the authors were unable to provide an explanation for this difference (Khedr et al., 2009). In a later study, Khedr et al. (2010) compared 3Hz with 10Hz, and reported no significant differences between protocols but a significant improvement in favour of rTMS compared to a sham rTMS condition was found. The authors note that 3Hz was performed at 130% resting motor threshold (RMT) whereas 10Hz was performed at 100% RMT due to safety concerns which may have balanced the results between the two conditions. Khedr et al. (2010) also highlighted that misestimating the motor threshold, as well as the lack of a surrogatemarker informing clinicians when rTMS has activated the cortex, may lead to patients being stimulated suboptimally. Sasaki et al. (2013) reported greater functional improvements in patients who received high-frequency compared with low-frequency rTMS, and noted that patients in the acute stage of stroke may benefit from a high-frequency approach over the ipsilesional hemisphere, adding that developmental proteins reappear during the early phases of stroke and interhemisphere inhibition is abnormally high.

The location of rTMS application may also influence recovery. Wang et al. (2014) examined rTMS applied to the primary motor cortex (M1) and dorsal premotor cortex (PMd). The results suggest that rTMS over the M1 is more effective in promoting recovery than rTMS over the PMd; however, both intervention approaches were significantly more efficacious than sham rTMS over the M1. The discrepancy between these two regions of the brain may be explained by differences in excitability between pyramidal tract neurons and neurons with distant interconnected projections (C. C. Wang et al., 2014).

Emara et al. (2010) investigated the use of different intensities on the ipsilesional and contralesional areas of the brain. Although no direct comparisons were made between the ipsilesional and contralesional conditions, ANOVA analyses revealed a significant group by time interaction with greater improvement indicated in both rTMS groups compared to a sham rTMS condition. An increase in the cumulative number of sessions may also play a role; Emara et al. (2010) randomized participants to receive 10 daily sessions of either sham, 5Hz ipsilesional or 1Hz contralesional rTMS, and reported statistically significant improvement in upper extremity motor function in the active stimulation groups compared to the sham control group. The authors noted that patients in the contralesional 1Hz condition received twice as many treatment sessions as compared to previous studies, which may be important for sustaining the positive effect of rTMS. Further research is required to investigate the neurological reactions across different areas of the brain after rTMS therapy.
Lüdemann-Podubecka et al. (2015) compared 1Hz rTMS with a sham condition, targeting the contralesional hemisphere, for a total of 3 weeks. All participants also received daily 30-minute motor training sessions. In terms of participants with lesioned non-dominant hemispheres, the study did not find a significant difference between the two conditions for either the unaffected hand or the affected hand; however, in terms of participants with lesioned dominant hemispheres, changes in motor function of the affected hand differed significantly between groups as indicated by WMFT and Motor Evaluation Scale for Upper Extremity in Stroke Patients (MESUPES) scores at 3 weeks and 6 months, at and 1 week, respectively. Within-group analyses revealed that participants with lesioned dominant hemispheres receiving rTMS and participants with lesioned non-dominant hemispheres receiving either sham or rTMS therapy showed significant changes in motor function of the affected hand over the three-week training period and 6 months thereafter. The authors concluded that motor recovery of the affected upper extremity may depend on hemispheric dominance, and that 1Hz rTMS over the contralesional M1 area improves motor ability in the affected hand in patients with a lesion in the dominant hemisphere, but not in those with lesioned non-dominant hemispheres (Ludemann-Podubecka et al., 2015).

Other studies have sought to improve motor function by implementing a physiotherapy program alongside an rTMS intervention with varying intensities. Takeuchi et al. (2008) reported significant gains in pinch force and acceleration after rTMS and motor training compared to sham rTMS. A potential mechanism for this may be due to the lasting effects of rTMS with motor training during elevated levels of excitability in the motor cortex, allowing for reorganisation and therefore acquirement of functional ability (Takeuchi et al., 2008). Mixed results were reported by Chang et al. (2010), who combined rTMS with conventional physiotherapy and occupational therapy. Results indicated significant improvement in Motricity Index upper-extremity scores compared to a sham rTMS protocol, but no other between-group differences were observed. However, both Seniow et al. (2012) and Barros Galvao et al. (2014) investigated the effectiveness of rTMS in addition to physiotherapy, and reported that although both groups demonstrated significant improvements, there were no between-group differences on measures of upper extremity function. While it may be that physiotherapy was the common denominator in reducing spasticity and increasing motor function to a clinically meaningful degree, the study period may have been too short and patients may have experienced a time lag between changes in spasticity and function; therefore, studies including a longer follow-up time may be better able to detect functional improvements (Barros Galvão et al., 2014). Furthermore, Rose et al. (2014) also reported no significant between-group differences on all measures of upper extremity function in their study investigating rTMS coupled with functional task practice.

Zheng et al. (2015) combined low-frequency (1 Hz) rTMS and sham rTMS with a virtual reality training protocol and reported significantly higher scores on the WMFT, FMA, modified Barthel Index, and the SF-36 Physical Functioning subscale among those receiving low-frequency rTMS. It has been suggested that rTMS can change synaptic efficacy and facilitate practice-dependent plasticity, thereby improving motor regeneration, and when combined with VR training, may produce a synergistic effect (Zheng et al., 2015).

Studies investigating the effectiveness of low-frequency rTMS in comparison to sham found conflicting results on upper limb motor function and dexterity outcomes. For example, studies such as those by Wang et al. (2014), Ludemann-Podubecka et al. (2015), Zheng et al. (2015), Du et al. (2016) found a significant difference between groups. However, studies such as those by Hosomi et al. (2016), Yang et al. (2016), and Seniow et al. (2012), found no significant difference. Two studies (Barros Galvão et al., 2014; Liepert et al., 2007) found that low-frequency rTMS did not improve upper limb spasticity.
All studies investigating high-frequency rTMS found a significant effect when compared to sham rTMS, including on outcomes such as upper limb motor function, dexterity, and grip strength (Cassidy et al., 2015; Chang et al., 2010; Emara et al., 2010; Ji et al., 2014; Khedr et al., 2010; Kim, Lee, & Song, 2014; Li, Chai, Xu, & Li, 2016; Sasaki et al., 2013).

None of the studies comparing high-frequency and low-frequency rTMS found a significant difference on measures of motor function or grip strength (Cassidy et al., 2015; Emara et al., 2010; Khedr et al., 2010; J. Li et al., 2016; Sasaki et al., 2013).

Two studies investigated both high-frequency and low-frequency rTMS at the same time compared to high-frequency rTMS alone, specifically Sasaki et al. (2014) and Takeuchi et al. (2009). Based on the results from the study by Sasaki et al. (2014), there was an improvement in upper limb motor function, but not in grip strength between the groups.

Conclusions Regarding Repetitive Transcranial Magnetic Stimulation

_There is level 1a conflicting evidence regarding the effectiveness of low-frequency (1Hz) rTMS for the improvement of upper limb motor function and dexterity. There is also level 1a evidence that inhibiting rTMS does not improve upper limb spasticity when compared to sham stimulation._

_There is level 1a evidence that high-frequency rTMS (≥5 Hz) improves upper limb motor function, dexterity, and grip strength when compared to sham stimulation._

_There is level 1a evidence that there is no significant difference between inhibitory and excitatory rTMS for improving upper limb motor function or grip strength._

_There is level 1b evidence that dual rTMS (the combination of both inhibitory and excitatory rTMS) improves upper limb motor function, but not grip strength when compared to sham stimulation._

_It is unclear whether low-frequency (1 Hz) Repetitive Transcranial Magnetic Stimulation (RTMS) is effective, while high-frequency (5 Hz) and Dual RTMS Repetitive Transcranial Magnetic Stimulation is likely effective for improving upper limb motor function._

10.8.2.2 Theta Burst Stimulation (TBS)

Theta Burst Stimulation (TBS) is a novel form of rTMS that provides a low-intensity output that can incite or reduce cortical excitability (Talelli, Greenwood, & Rothwell, 2007). As poor upper limb recovery is associated with a reduction of excitability in the ipsilesional primary motor cortex M1 and increased excitability in the contralesional M1, TBS can be used to rebalance hemispheric activity. This can be achieved through the use of intermittent TBS (iTBS) which can facilitate M1 excitability, or continuous TBS (cTBS), which can suppress M1 excitability (Ackerley, Stinear, Barber, & Byblow, 2010). Individually, both are found to be successful despite the limited literature on TBS and upper limb function. The use of cTBS has been found to improve reaction times of the paretic limb (Meehan, Dao, Linsdell, & Boyd, 2011), although other studies have not reported any clinical effects despite a reduction in motor evoked potentials of the contralesional hemisphere (Talelli et al., 2007). Not only can TBS be used for functional or strength gains, but previous literature has also reported alleviation of spasticity. Research by Kim et al. (2016) revealed that intermittent TBS of the ipsilesional motor hotspot for the carpi radialis muscle resulted in a significant reduction in spasticity of the wrist with benefits lasting for at least 30 minutes post treatment. Furthermore, other studies have reported positive improvements of TBS in the...
treatment of other motor disorders such as ataxia, with decreases in intracortical inhibition and increases in intracortical facilitation observed (Bonni, Ponzo, Caltagirone, & Koch, 2014).

The results of controlled trials evaluating TBS are detailed in Table 10.8.2.2.1.

**Table 10.8.2.2.1 Summary of Controlled Trials Examining TBS for the Upper Extremity**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Intervention</th>
<th>Outcome(s) and Result(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sung et al. (2013)</td>
<td>RCT (9)</td>
<td>E1: rTMS + iTBS E2: sham rTMS + iTBS E3: rTMS + sham iTBS C: Sham rTMS + sham iTBS.</td>
<td>• Finger Flexor Medical Research Council Scale (+) • Wolf Motor Function test: E(all) vs. C (+), E1 vs. E2 (+), E1 vs. E3 (+) • Fugl-Meyer Assessment: E(all) vs. C (+), E1 vs. E2 (+), E1 vs. E3 (+) • Simple reaction time (+)</td>
</tr>
<tr>
<td>Ackerley et al. (2016)</td>
<td>RCT (8)</td>
<td>E: iTBS C: Sham TBS</td>
<td>• Action Research Arm Test (+) • Fugl-Meyer Assessment (-)</td>
</tr>
<tr>
<td>Kim et al. (2015)</td>
<td>RCT (8)</td>
<td>E: iTBS C: Sham TBS</td>
<td>• Modified Ashworth Scale (+) • Peak torque (+) • Peak torque angle (+) • Work (-) • Modified Tardieu Scale: R1 (+), R2 (-)</td>
</tr>
<tr>
<td>Di Lazzaro et al. (2016)</td>
<td>RCT (7)</td>
<td>E: cTBS + robotic therapy C: Sham TBS + robotic therapy</td>
<td>• Fugl-Meyer Assessment (-)</td>
</tr>
<tr>
<td>Talelli et al. (2012)</td>
<td>RCT (7)</td>
<td>E1: iTBS C1: Sham iTBS E2: cTBS C2: Sham cTBS</td>
<td>• Nine Hole Peg Test (-) • Jebsen Taylor Hand test (-)</td>
</tr>
<tr>
<td>Hsu et al. (2013)</td>
<td>RCT=7 N=12</td>
<td>E: iTBS C: Sham</td>
<td>• Fugl Meyer Assessment (upper) (+) • Action Research Arm Test (-)</td>
</tr>
<tr>
<td>Di Lazzaro et al. (2014)</td>
<td>RCT (6)</td>
<td>E: cTBS C: Sham</td>
<td>• Action Research Arm Test (-) • Nine Hole Peg Test (-) • Jebsen Taylor hand test (-) • Grasp strength (-) • Pinch strength (-)</td>
</tr>
<tr>
<td>Volz et al. (2016)</td>
<td>RCT (5)</td>
<td>E: iTBS C: Sham TBS</td>
<td>• Grip Strength (+) • Jebsen Taylor Hand Function Test (-)</td>
</tr>
<tr>
<td>Lai et al. (2015)</td>
<td>PCT</td>
<td>E1: iTBS (MEP+, MRC&gt;1) E2: iTBS (MEP-, MRC&gt;1) E3: iTBS (MEP-, MRC=0) C: Sham (MEP+, MRC&gt;1)</td>
<td>• Wolf Motor Function Test: E1 vs E2 (+); E1 vs C (+) • Finger Tapping: E1 v E2 (+); E1 vs E3 (+); E1 v C (+)</td>
</tr>
<tr>
<td>Kim et al. (2015)</td>
<td>PCT</td>
<td>E: iTBS C: Sham</td>
<td>• Modified Ashworth Scale (+) • Peak torque (+)</td>
</tr>
</tbody>
</table>
Discussion

Intermittent TBS was investigated by six RCTs and two prospective controlled trials. Two studies examined the effectiveness of iTBS in the acute/subacute phase (Hsu et al., 2013; Volz et al., 2016). The results of the studies indicated that while iTBS improved upper limb motor function when compared to sham, measures of dexterity were not improved in the iTBS group over the sham group.

Four RCTs examined the effectiveness of iTBS in the chronic phase in comparison to a sham group (Ackerley et al., 2016; D. H. Kim et al., 2015; Sung et al., 2013; Talelli et al., 2012). The results of the studies were conflicting, with Sung et al. (2013) finding positive outcomes for upper limb motor function, Ackerley et al. (2016) finding no improvement in upper limb motor function, but an improvement in dexterity, Hsu et al. (2013) finding an improvement in upper limb motor function, but not dexterity, and Kim et al. (2015) finding an improvement in upper limb spasticity. Kim et al. (2015) observed a transient reduction of spasticity for up to 30 minutes after iTBS over the hotspot of the affected flexor carpi radialis muscle within the ipsilesional hemisphere. Although the mechanism for this remains unclear, iTBS may encourage neural activity projection to local inhibitory interneurons of the spinal cord (D. H. Kim et al., 2015). A reduction in spasticity was not observed according to electrophysiological measurements which suggested that the H-reflex has high variability and low reliability, and interneurons at the spinal level may not be directly involved (D. H. Kim et al., 2015).

Three RCTs examined the effectiveness of continuous TBS (cTBS) in comparison to sham, and three studies were conducted during the chronic phase post stroke (Di Lazzaro et al., 2016; Di Lazzaro et al., 2014; Talelli et al., 2012). All three found no significant differences between groups on measures of upper limb motor function and dexterity.

Although the studies by Hsu et al. (2013) and Kim et al. (2015) evaluated stimulation of the ipsilesional hemispheres, other studies have investigated stimulation of both the affected and unaffected hemispheres. Sung et al. (2013) reported that 1Hz of rTMS over the contralesional M1 followed by iTBS (three pulses of 50Hz) over the ipsilesional M1 was more effective than iTBS plus sham rTMS and 1Hz rTMS plus sham iTBS. This would suggest that doubling treatment load is beneficial in enhancing upper extremity function with no adverse events reported. In particular, the authors noted a decrease in excitability in the contralesional M1 and an increase in the ipsilesional M1, supporting the suggestion that an inhibitory-facilitatory approach might be most efficacious (Sung et al., 2013).

Lai et al. (2015) reported that predictors for the success of iTBS interventions on upper extremity motor enhancement depend on hand grip strength at pre-treatment and the presence of positive motor-evoked potentials (MEPs). The authors note that these predictors were independent of stroke type, time post stroke, and size of lesion. Patients who exhibited no MEPs nor any movement in the paretic hand may have experienced disruption of the key motor pathway and contralesional inhibition (C. J. Lai et al., 2015). It was suggested by Lai et al. (2015) that patients fitting this criteria may benefit from training-dependent neuroplasticity such as robot-training, nerve stimulation, or behavioural interventions alongside rTMS/TBS in order to maximise enhancements.

Conclusions Regarding Theta Burst Stimulation
There is level 1b and level 2 evidence that iTBS improves upper limb motor function, but not dexterity, in the acute or subacute period after stroke.

There is conflicting level 1a evidence that iTBS improves upper limb motor function and dexterity in the chronic phase after stroke. There is level 1b and level 2 evidence that iTBS improves spasticity in the chronic phase after stroke.

There is level 1a evidence that cTBS does not improve upper extremity motor function or dexterity following stroke.

Intermittent Theta Burst Stimulation (iTBS) may improve upper limb motor function in the acute/subacute phase as well as during the chronic phase post stroke. While iTBS may not be effective for improving dexterity in the acute/subacute phase, it is likely effective during the chronic phase.

Continuous Theta Burst Stimulation (cTBS) may not be effective for improving upper limb motor function or dexterity after stroke.

10.8.2.3 Transcranial Direct Current Stimulation (tDCS)

Another form of noninvasive electrical stimulation is transcranial direct-current stimulation (tDCS). This procedure involves the application of mild electrical currents (1-2 mA) conducted through 2 saline soaked, surface electrodes applied to the scalp, overlaying the area of interest and the contralateral forehead above the orbit. Anodal stimulation increases cortical excitability while cathode stimulation decreases it (Alonso-Alonso, Fregni, & Pascual-Leone, 2007). In contrast to TMS, tDCS does not induce action potentials, but instead modulates the resting membrane potential of the neurons (Alonso-Alonso et al., 2007). tDCS is a good candidate for study since unlike TMS, it does not elicit somatosensory changes that would alert a subject to the fact a real, rather than sham treatment was being applied.

A meta-analysis (Bastani & Jaberzadeh, 2012) examined the effectiveness of tDCS to improve motor function in both healthy individuals and those following stroke. Four RCTs were included (Boggio et al., 2007; Fregni et al., 2005; Hummel et al., 2005; Kim, Ohn, Yang, Park, & Jung, 2009). All but the Kim et al. (2009) included subjects in the chronic stage of stroke and all subjects exhibited mild to moderate baseline hand impairment. The pooled standardized mean difference for hand function was 0.39 (95% CI -0.17 to 0.9, p=0.17) indicating a small but non-significant treatment effect.

Another review and meta-analysis authored by Butler et al. (2013), restricted to the examination of anodal tDCS, included the results from 8 RCTs, all of which examined motor function in the upper extremity following stroke (Butler et al., 2013). Outcomes assessed among the trials included the Jebsen-Taylor Hand Function test, BBT, pinch and grip strength and reaction time. Overall, compared with sham stimulation, anodal tDCS was associated with a small to moderate significant treatment effect (SMD=0.49, 95% CI 0.18 to 0.81, p=0.005).

The results of trials evaluating tDCS are detailed in Tables 10.8.2.3.1 to 10.8.2.3.4.

Table 10.8.2.3.1 Summary of Studies Examining Anodal tDCS for the Upper Extremity
<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hesse et al.</strong> (2011) RCT (10) N=96</td>
<td>E1: Anodal tDCS  E2: Cathodal tDCS  C: Sham</td>
<td>• Fugl Meyer score (-): E1 vs E2 (-); E1 vs C (-); E2 vs C (-)</td>
</tr>
<tr>
<td><strong>Viana et al.</strong> (2014) RCT (9) NStart=20 NEnd=20</td>
<td>E: Virtual reality + anodal tDCS  C: Virtual reality + sham</td>
<td>• Fugl Meyer Assessment (-)  • Wolf Motor Function Test (-)  • Modified Ashworth Scale (-)  • Stroke Specific Quality of Life (+)  • Grip strength (-)</td>
</tr>
<tr>
<td><strong>Khedr et al.</strong> (2013) RCT (9) NStart=40 NEnd=40</td>
<td>E1: Anodal tDCS  E2: Cathodal tDCS  C: Sham</td>
<td>• Orgogozo’s MCA Scale: E1 vs. C (+), E2 vs. C (-), E1 vs. E2 (-)  • Barthel Index: E1 vs. C (+), E2 vs. C (-), E1 vs. E2 (-)  • Muscle strength (-)</td>
</tr>
<tr>
<td><strong>Triccas et al.</strong> (2015) RCT (8) NStart=23 NEnd=22</td>
<td>E: Anodal tDCS + robotic ArmeoSpring  C: Sham tDCS + robotic ArmeoSpring</td>
<td>• Fugl-Meyer Assessment (-)  • Action Research Arm Test (-)  • Motor Activity Log (-)  • Stroke Impact Scale (-)</td>
</tr>
<tr>
<td><strong>Ilic et al.</strong> (2016) RCT (8) NStart=26 NEnd=25</td>
<td>E: Anodal tDCS + occupational therapy  C: Sham tDCS + occupational therapy</td>
<td>• Modified Jezben-Taylor Hand Function Test (+)  • Fugl-Meyer Assessment (-)  • Grip Strength (-)</td>
</tr>
<tr>
<td><strong>Powell et al.</strong> (2016) RCT (8) NStart=11 NEnd=10</td>
<td>E1: Anodal tDCS followed by peripheral nerve stimulation  E2: Peripheral nerve stimulation followed by tDCS</td>
<td>• Fugl-Meyer Assessment (-)  • Stroke Impact Scale (-)</td>
</tr>
<tr>
<td><strong>Au-Yeung et al.</strong> (2014) RCT (8) NStart=10 NEnd=10</td>
<td>E1: Anodal tDCS  E2: Cathodal tDCS  C: Sham</td>
<td>• Purdue Pegboard Test (-)  • Pinch strength (-)</td>
</tr>
<tr>
<td><strong>Figlewski et al.</strong> (2016) RCT (7) NStart=44 NEnd=44</td>
<td>E: Constraint-induced movement therapy + Anodal tDCS  C: Constraint-induced movement therapy + Sham tDCS</td>
<td>• Wolf Motor Function Test: Functional Ability (+), Grip Strength (-), Arm Strength (-)</td>
</tr>
<tr>
<td><strong>Lee et al.</strong> (2014) RCT (7) NStart=64 NEnd=59</td>
<td>E1: cathodal tDCS  E2: Virtual reality  E3: tDCS + virtual reality</td>
<td>• Manual Function Test: E1 vs. E2 (+)  • Fugl Meyer Assessment (+)  • Modified Barthel Index (-)  • Manual Muscle Test (-)  • Modified Ashworth Scale (-)  • Box and Block Test (-)</td>
</tr>
<tr>
<td><strong>Mortensen et al.</strong> (2016) RCT (7) NStart=16 NEnd=15</td>
<td>E: Anodal tDCS + occupational therapy  C: Sham tDCS + occupational therapy</td>
<td>• Grip Strength (+)  • Activities of Daily Living (-)  • Jezben-Taylor Hand Function Test (-)</td>
</tr>
<tr>
<td><strong>Hendy &amp; Kidgell</strong> (2014) RCT (7) NStart=10 NEnd=10</td>
<td>E1: Anodal tDCS + strength training  E2: sham tDCS + strength training  C: Anodal tDCS</td>
<td>• Extensor carpi radialis strength (+)</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Design</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
<td>--------</td>
</tr>
<tr>
<td>Kim et al. (2009)</td>
<td>RCT (7)</td>
<td>N=10</td>
</tr>
<tr>
<td>Kim et al. (2010)</td>
<td>RCT (7)</td>
<td>N=18</td>
</tr>
<tr>
<td>Wang et al. (2014)</td>
<td>RCT (7)</td>
<td>N Start=9</td>
</tr>
<tr>
<td>Hendy et al. (2014)</td>
<td>RCT (7)</td>
<td>N Start=10</td>
</tr>
<tr>
<td>Sattler et al. (2015)</td>
<td>RCT (7)</td>
<td>N Start=20</td>
</tr>
<tr>
<td>Fregni et al. (2005)</td>
<td>RCT (7)</td>
<td>N=6</td>
</tr>
<tr>
<td>Kim et al. (2009)</td>
<td>RCT (7)</td>
<td>N=10</td>
</tr>
<tr>
<td>Straudi et al. (2016)</td>
<td>RCT (6)</td>
<td>N Start=23</td>
</tr>
<tr>
<td>Ang et al. (2015)</td>
<td>RCT (6)</td>
<td>N Start=19</td>
</tr>
<tr>
<td>Bolognini et al. (2015)</td>
<td>RCT (6)</td>
<td>N Start=12</td>
</tr>
<tr>
<td>Cunningham et al. (2015)</td>
<td>RCT (6)</td>
<td>N Start=12</td>
</tr>
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Table 10.8.2.3.2 Summary of Controlled Trials Examining Cathodal tDCS for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hesse et al. (2011)</td>
<td>RCT (10)</td>
<td>N=96</td>
<td>E1: Anodal tDCS E2: Cathodal tDCS C: Sham</td>
<td>Fugl Meyer score (-): E1 vs E2 (-); E1 vs C (-); E2 vs C (-)</td>
</tr>
<tr>
<td>Wu et al. (2013)</td>
<td>RCT (9)</td>
<td>NStart=90 NEnd=90</td>
<td>E: Cathodal tDCS C: Sham</td>
<td>Modified Ashworth Scale (+)</td>
</tr>
</tbody>
</table>
| Khedr et al. (2013) | RCT (9) | NStart=40 NEnd=40 | E1: Anodal tDCS E2: Cathodal tDCS C: Sham | Orgogozo’s MCA Scale: E1 vs. C (+), E2 vs. C (-), E1 vs. E2 (-) 
Barthel Index: E1 vs. C (+), E2 vs. C (-), E1 vs. E2 (-) 
Muscle strength (-) |
| Rocha et al. (2016) | RCT (8) | NStart=21 NEnd=21 | E1: Anodal tDCS E2: Cathodal tDCS C: Sham | Fugl-Meyer Assessment: E1/E2 vs. C (+) 
Motor Activity Log (-) 
Grip Strength (-) |
| Au-Yeung et al. (2014) | RCT (8) | NStart=10 NEnd=10 | E1: Anodal tDCS E2: Cathodal tDCS C: Sham | Purdue Pegboard Test (-) 
Pinch strength (-) |
| Del Felice et al. (2016) | RCT (8) | NStart=10 | E1: Cathodal tDCS E2: Dual tDCS C: Sham tDCS | Motor Assessment Scale (-) 
European Stroke Scale (-) 
Action Research Arm Test (-) |
### Table 10.8.2.3.3 Summary of Studies Examining Anodal versus Cathodal tDCS for the Upper Extremity

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N Start</th>
<th>N End</th>
<th>Treatment 1</th>
<th>Treatment 2</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lee et al.</strong> (2014)</td>
<td>RCT</td>
<td>64</td>
<td>59</td>
<td>E1: cathodal tDCS</td>
<td>E2: Virtual reality</td>
<td>• Manual Function Test: E1 vs. E2 (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>E3: tDCS + virtual reality</td>
<td></td>
<td>• Fugl Meyer Assessment (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Modified Barthel Index (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Manual Muscle Test (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Modified Ashworth Scale (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Box and Block Test (-)</td>
</tr>
<tr>
<td><strong>Fregni et al.</strong> (2005)</td>
<td>RCT</td>
<td>6</td>
<td>59</td>
<td>E1: Anodal tDCS</td>
<td>E2: Cathodal tDCS</td>
<td>• Jebsen-Taylor Hand Function test: E1 vs C (+); E2 vs C (+); E1 vs E2 (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Fugl-Meyer Score (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Barthel Index (-)</td>
</tr>
<tr>
<td><strong>Kim et al.</strong> (2010)</td>
<td>RCT</td>
<td>18</td>
<td>18</td>
<td>E1: Anodal tDCS</td>
<td>E2: Cathodal tDCS</td>
<td>• Movement Accuracy (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Movement time: E1 vs E2 (+); E1 vs C (+)</td>
</tr>
<tr>
<td><strong>Kwon et al.</strong> (2016)</td>
<td>RCT</td>
<td>20</td>
<td>20</td>
<td>E1: Cathodal tDCS + rTMS</td>
<td>E2: Anodal tDCS + rTMS</td>
<td>• 9-hole peg test: E vs. C (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Grasp force (-)</td>
</tr>
<tr>
<td><strong>Fusco et al.</strong> (2013)</td>
<td>RCT</td>
<td>9</td>
<td>9</td>
<td>E1: Dual tDCS (anodal and cathodal)</td>
<td>E2: Anodal tDCS</td>
<td>• Canadian Neurologic Scale (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Nine Hole Peg Test (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Barthel Index (-)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Fugl Meyer Assessment (-)</td>
</tr>
<tr>
<td><strong>Zimerman et al.</strong> (2012)</td>
<td>RCT</td>
<td>12</td>
<td>12</td>
<td>E: Cathodal tDCS</td>
<td>C: Sham</td>
<td>• Grip strength (-)</td>
</tr>
<tr>
<td><strong>Hummel et al.</strong> (2005)</td>
<td>RCT</td>
<td>6</td>
<td>6</td>
<td>E: Cathodal tDCS</td>
<td>C: Sham</td>
<td>• Jebsen-Taylor Hand Function test (+)</td>
</tr>
<tr>
<td><strong>Fusco et al.</strong> (2014)</td>
<td>RCT</td>
<td>14</td>
<td>11</td>
<td>E: Cathodal tDCS + active electrode</td>
<td>C: Sham</td>
<td>• Manual Function Test (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Fugl Meyer Score (+)</td>
</tr>
<tr>
<td><strong>Lee &amp; Chun</strong> (2014)</td>
<td>RCT</td>
<td>64</td>
<td>59</td>
<td>E1: Cathodal tDCS</td>
<td>E2: Virtual reality</td>
<td>• Fugl Meyer Assessment (+)</td>
</tr>
<tr>
<td><strong>Lee et al.</strong> (2015)</td>
<td>RCT</td>
<td>24</td>
<td>24</td>
<td>E1: Cathodal tDCS + physical therapy</td>
<td>C: Physical therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Stagg et al.</strong> (2012)</td>
<td>RCT</td>
<td>13</td>
<td>13</td>
<td>E1: Anodal tDCS</td>
<td>E2: Cathodal tDCS</td>
<td>• Grip strength: E1 vs C (+); E2 vs C (+); E1 vs E2 (-)</td>
</tr>
<tr>
<td><strong>Boggio et al.</strong> (2007)</td>
<td>RCT</td>
<td>4</td>
<td>4</td>
<td>E1: Anodal tDCS</td>
<td>E2: Cathodal tDCS</td>
<td>• Jebsen-Taylor Hand Function test: E1 vs, C (+); E2 vs C (+)</td>
</tr>
</tbody>
</table>

*Indicates non-statistically significant differences between treatment groups

+ Indicates statistically significant differences between treatment groups
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hesse et al. (2011)</td>
<td>RCT (10)</td>
<td>N=96</td>
<td>E1: Anodal tDCS E2: Cathodal tDCS C: Sham</td>
<td>Fugl Meyer score (-): E1 vs E2 (-); E1 vs C (-); E2 vs C (-)</td>
</tr>
<tr>
<td>Khedr et al. (2013)</td>
<td>RCT (9)</td>
<td>NStart=40 NEnd=40</td>
<td>E1: Anodal tDCS E2: Cathodal tDCS C: Sham</td>
<td>Orgogozo’s MCA Scale: E1 vs. C (+), E2 vs. C (-), E1 vs. E2 (-) Barthel Index: E1 vs. C (+), E2 vs. C (-), E1 vs. E2 (-) Muscle strength (-)</td>
</tr>
<tr>
<td>Rocha et al. (2016)</td>
<td>RCT (8)</td>
<td>NStart=21 NEnd=21</td>
<td>E1: Anodal tDCS + CIMT E2: Cathodal tDCS + CIMT C: Sham tDCS + CIMT</td>
<td>Fugl-Meyer Assessment: E1/E2 vs. C (+) Motor Activity Log (-) Grip Strength (-)</td>
</tr>
<tr>
<td>Au-Yeung et al. (2014)</td>
<td>RCT (8)</td>
<td>NStart=10 NEnd=10</td>
<td>E1: Anodal tDCS E2: Cathodal tDCS C: Sham</td>
<td>Purdue Pegboard Test (-) Pinch strength (-)</td>
</tr>
<tr>
<td>Ochi et al. (2013)</td>
<td>RCT (7)</td>
<td>N=18</td>
<td>E: Anodal tDCS on affected hemisphere + robot assisted arm training C: Cathodal tDCS on unaffected hemisphere + robot assisted arm training</td>
<td>Modified Ashworth Scale: finger (+) Fugl Meyer Score (-) Motor Activity Log (-)</td>
</tr>
<tr>
<td>Kwon et al. (2016)</td>
<td>RCT (7)</td>
<td>NStart=20 NEnd=20</td>
<td>E1: Cathodal tDCS + rTMS E2: Anodal tDCS + rTMS C: Sham tDCS + rTMS</td>
<td>Movement Accuracy (-) Movement time: E1 vs E2 (+); E1 vs C (+)</td>
</tr>
<tr>
<td>Fusco et al. (2013)</td>
<td>RCT (7)</td>
<td>N=9</td>
<td>E1: Dual tDCS (anodal and cathodal) E2: Anodal tDCS E3: Cathodal tDCS C: Sham</td>
<td>9-hole peg test: E vs. C (+) Grasp force (-)</td>
</tr>
<tr>
<td>Kim et al. (2010)</td>
<td>RCT (7)</td>
<td>N=18</td>
<td>E1: Anodal tDCS E2: Cathodal tDCS C: Sham</td>
<td>Fugl-Meyer Score (-) Barthel Index (-)</td>
</tr>
<tr>
<td>Fregni et al. (2005)</td>
<td>RCT (7)</td>
<td>N=6</td>
<td>E1: Anodal tDCS E2: Cathodal tDCS C: Sham</td>
<td>Jebsen-Taylor Hand Function test: E1 vs C (+); E2 vs C (+); E1 vs E2 (-)</td>
</tr>
<tr>
<td>Sik et al. (2015)</td>
<td>RCT (6)</td>
<td>NStart=36 NEnd=31</td>
<td>E1: Anodal tDCS + PT + OT E2: Anodal-cathodal tDCS + PT + OT C: Sham tDCS + PT + OT</td>
<td>Wolf Motor Function Test (-) Jebsen Taylor Hand Function Test (-) Kocaeli Functional Evaluation Test (-)</td>
</tr>
<tr>
<td>Stagg et al. (2012)</td>
<td>RCT (6)</td>
<td>N=13</td>
<td>E1: Anodal tDCS E2: Cathodal tDCS C: Sham</td>
<td>Grip strength: E1 vs C (+); E2 vs C (+); E1 vs E2 (-)</td>
</tr>
<tr>
<td>Boggio et al. (2007)</td>
<td>RCT (6)</td>
<td>N=4</td>
<td>E1: Anodal tDCS E2: Cathodal tDCS C: Sham</td>
<td>Jebsen-Taylor Hand Function test: E1 vs C (+); E2 vs C (+)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

**Table 10.8.2.3.4 Summary of Studies Examining Dual tDCS for the Upper Extremity**
<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lefebvre et al. (2013)</strong>&lt;br&gt;RCT (8)&lt;br&gt;N_{Start}=18&lt;br&gt;N_{End}=18</td>
<td>E: Dual tDCS (anodal and cathodal) C: Sham</td>
<td>• Learning Index (+)&lt;br&gt;• Performance Index (-)&lt;br&gt;• Purdue Pegboard Test (+)&lt;br&gt;• Maximal hand grip force (+)</td>
</tr>
<tr>
<td><strong>Lefebvre et al. (2014)</strong>&lt;br&gt;RCT (8)&lt;br&gt;N_{Start}=19&lt;br&gt;N_{End}=19</td>
<td>E: Dual tDCS (anodal and cathodal) C: Sham</td>
<td>• Purdue Pegboard Test (+)&lt;br&gt;• Precision grip (+)&lt;br&gt;• Dexterity (+)</td>
</tr>
<tr>
<td><strong>Del Felice et al. (2016)</strong>&lt;br&gt;RCT (8)&lt;br&gt;N_{Start}=10&lt;br&gt;N_{End}=10</td>
<td>E1: Anodal or Cathodal tDCS&lt;br&gt;E2: Dual tDCS&lt;br&gt;C: Sham tDCS</td>
<td>• Medical Research Council Scale: E2 vs. E1 (+)&lt;br&gt;• Motor Assessment Scale (-)&lt;br&gt;• European Stroke Scale (-)&lt;br&gt;• Action Research Arm Test (-)&lt;br&gt;• Barthel index (-)</td>
</tr>
<tr>
<td><strong>Goodwill et al. (2016)</strong>&lt;br&gt;RCT (7)&lt;br&gt;N_{Start}=16&lt;br&gt;N_{End}=15</td>
<td>E: dual tDCS + upper limb training&lt;br&gt;C: Sham tDCS + upper limb training</td>
<td>• Tardieu Scale (-)&lt;br&gt;• Grip Strength (-)</td>
</tr>
<tr>
<td><strong>Fusco et al. (2013)</strong>&lt;br&gt;RCT (7)&lt;br&gt;N=9</td>
<td>E1: Dual tDCS (anodal and cathodal)&lt;br&gt;E2: Anodal tDCS&lt;br&gt;E3: Cathodal tDCS&lt;br&gt;C: Sham</td>
<td>• 9-hole peg test: E vs. C (+)&lt;br&gt;• Grasp force (-)</td>
</tr>
<tr>
<td><strong>D’Agata et al. (2016)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N_{Start}=34&lt;br&gt;N_{End}=34</td>
<td>E1: rTMS + tDCS (dual) + mirror therapy&lt;br&gt;E2: dual-tDCS + mirror Therapy + rTMS&lt;br&gt;C: Sham tDCS + mirror Therapy</td>
<td>• Action Research Arm Test (-)</td>
</tr>
<tr>
<td><strong>Sik et al. (2015)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N_{Start}=36&lt;br&gt;N_{End}=31</td>
<td>E1: Anodal tDCS + PT + OT&lt;br&gt;E2: Anodal-cathodal tDCS + PT + OT&lt;br&gt;C: Sham tDCS + PT + OT</td>
<td>• Wolf Motor Function Test: E1/E2 vs. C (+), E1 vs. E2 (-)&lt;br&gt;• Jebsen Taylor Hand Function Test (-)&lt;br&gt;• Kocaeli Functional Evaluation Test (-)</td>
</tr>
<tr>
<td><strong>Cha et al. (2014)</strong>&lt;br&gt;RCT (6)&lt;br&gt;N_{Start}=20&lt;br&gt;N_{End}=20</td>
<td>E: Dual tDCS (anodal and cathodal) C: Conventional training</td>
<td>• Fugl Meyer Assessment (+)&lt;br&gt;• Box and Block Test (+)</td>
</tr>
<tr>
<td><strong>Lefebvre et al. (2015)</strong>&lt;br&gt;RCT Crossover (5)&lt;br&gt;N_{Start}=19&lt;br&gt;N_{End}=19</td>
<td>E: Dual tDCS C: Sham tDCS</td>
<td>• Purdue Pegboard Test (+)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups 
+ Indicates statistically significant differences between treatment groups

**Discussion**

Similar to rTMS, the majority of tDCS studies were directed at improving movement or function of the upper extremity. The length and intensity of stimulation was consistent across most studies (20 minutes at 1 mA). Many of the studies examined a one-time session of either anodal and/or cathodal stimulation compared with sham treatment and the majority did not include concurrent therapy.
Studies examining the effectiveness of anodal tDCS when compared to sham tDCS indicated that there was no significant difference between the groups on outcomes of motor function, spasticity, or grip strength. As an example, a study by Hesse et al. (2011) with a large sample size and high methodological quality compared anodal tDCS to sham and found no significant difference on measures of upper limb motor function. However, outcomes related to dexterity were mixed between studies (Allman et al., 2016; Au-Yeung et al., 2014; Boggio et al., 2007; Bolognini et al., 2015; Fregni et al., 2005; Fusco et al., 2014; Ilic et al., 2016; Kim et al., 2009; Lee & Chun, 2014; Mortensen et al., 2016; Sattler et al., 2015; Şik et al., 2015; Straudi et al., 2016; Triccas et al., 2015; C. C. Wang et al., 2014).

Studies examining the effectiveness of cathodal tDCS when compared to sham tDCS found that outcomes were conflicting for upper limb motor function, grip strength, dexterity, and for measures of independence or daily living. For example, two of the trials examining spasticity had relatively large sample sizes in comparison to the other studies, although Wu et al. (2013) found an improvement in spasticity between cathodal tDCS sham, whereas Lee et al. (2014) did not. Although patients in the cathodal tDCS condition demonstrated significant improvement in bilateral arm function over the course of the study, Hesse et al. (2011) did not report any differences between groups in function or muscle strength. It was noted that the majority of patients in the study presented with infarcts with both cortical and subcortical involvement whereas the majority of tDCS literature with positive results focusing mostly on patients with only subcortical deficits and therefore intact cortical connectivity (Hesse et al., 2011). Similarly, the results from Au-Yeung et al. (2014) did not yield any differences in dexterity or pinch strength. The application of tDCS to only one motor area may not have been sufficient in improving dexterity which requires motor function and coordination (Au-Yeung et al., 2014). The authors also note that patients did not receive any additional motor training and so a combination with tDCS may allow for greater dexterity and an increase in strength (Au-Yeung et al., 2014).

Various studies also examined whether anodal and cathodal tDCS differed significantly. Studies by Hesse et al. (2011), Rocha et al. (2016), Ochi et al. (2013), Kim et al. (2010), Fregni et al. (2005), Sik et al. (2015) found no significant difference between anodal and cathodal tDCS on measures of upper limb motor function. Various studies also found that there was no significant difference between anodal and cathodal tDCS on measures of dexterity (Fregni et al., 2005; Fusco et al., 2013; Şik et al., 2015), grip strength (Rocha et al., 2016; Stagg et al., 2012), and measures of independence or daily living (Khedr et al., 2013; Kim et al., 2010).

An emerging approach is the combination of both anodal and cathodal tDCS, also known as dual tDCS. Based on the studies examining dual tDCS in comparison to sham tDCS, various studies indicated a significant improvement in those receiving dual tDCS on measures of dexterity (Fusco et al., 2013; Lefebvre et al., 2015; Lefebvre et al., 2013; Lefebvre et al., 2014). Two studies found that dual tDCS improved grip force (Lefebvre et al., 2013; Lefebvre et al., 2014) while two studies found that dual tDCS did not improve grip force (Fusco et al., 2013; Goodwill et al., 2016). There was insufficient evidence to investigate other outcomes, so additional studies are needed to establish conclusions for other outcome measures. As performance on the PPT continued to improve, the authors suggest that dual tDCS may be useful in facilitating patients in an optimal state for training (Lefebvre et al., 2014). This optimal state could be achieved through enhancement of synaptic plasticity and neural activity in the motor cortex (Cha et al., 2014). However, Fusco et al. (2013) reported that anodal tDCS was the most effective in the improvement of dexterity while cathodal and dual tDCS demonstrated little effect. Lefebvre et al. (2013) suggest that dual tDCS may induce a reduction in cortical excitability in the contralesional hemisphere and facilitation of excitability within the ipsilesional hemisphere thereby improving motor functioning through a rebalancing of interhemispheric interaction.
A more novel approach of combining and comparing tDCS with virtual reality (VR) training was conducted by two RCTs with mixed results. Viana et al. (2014) reported significant improvements in spasticity of the wrist and quality of life in patients who received VR and tDCS compared to those who received VR and a sham tDCS. The authors suggest that application of tDCS over the injured hemisphere, specifically, the primary motor cortex, may have increased neural activity. It was also noted that there may have been a ceiling effect in responsiveness on the FMA and the insufficient sample size could potentially have affected the between group differences (Viana et al., 2014). In contrast, Lee and Chun (2014) reported significant improvements on the FMA and Manual Function Test (MFT) for VR and tDCS combined compared to VR and tDCS alone but moreover, patients in the VR-only group outperformed patients in the tDCS-only group on the FMA and MFT. However, the tDCS group demonstrated greater hand functionality than the VR condition. It was noted by the authors that the VR protocol required movement of the proximal arm and a task facilitating hand movement may lead to even greater improvements. The observed efficacy of the combined condition may have been the result of cortical reorganisation after VR and receptor activity of N-methyl-D-aspartate, and sodium and calcium voltage-dependent channels mediated after tDCS (Lee & Chun, 2014).

A systematic review conducted by Elsner et al. (2016) revealed evidence favouring the use of tDCS over sham tDCS or a differing control condition, but there was no evidence of lasting effects at follow-up. It was also reported that ADLs were found to improve after tDCS treatment, but this effect was not maintained after excluding studies that were at a high risk for bias (Elsner et al., 2016). Another meta-analysis, authored by Butler et al. (2013), was restricted to the examination of anodal tDCS and included the results from eight RCTs, all of which examined motor function in the upper extremity following stroke. Outcomes assessed included the Jebsen-Taylor Hand Function test, BBT, pinch and grip strength, and reaction time. Butler et al. (2013) reported a significant increase in pooled scores favouring tDCS from baseline to post-treatment, although only a small to moderate effect size (0.40) was obtained. Furthermore, a small to moderate effect size (0.49) was found in the improvement of the contralateral limb favouring tDCS compared to sham tDCS despite a significant increase in pooled scores. Future meta-analyses are needed to determine the efficacy of cathodal and dual tDCS as well as anodal. Butler et al. (2013) also recommend that future reviews and meta-analyses should investigate additional factors such as the intensity of tDCS, lesion location, and time post stroke.

Conclusions Regarding Transcranial Direct Current Stimulation

There is level 1a evidence that anodal tDCS does not improve upper limb motor function, spasticity, or grip strength. There is conflicting level 1a evidence regarding whether anodal tDCS improves dexterity.

There is level 1a conflicting evidence for the effectiveness of cathodal tDCS for improving upper limb motor function, dexterity grip strength, and activities of daily living.

There is level 1a evidence that anodal and cathodal tDCS do not significantly differ on measures of motor function, dexterity, or on measures of independence/daily living.

There is level 1a evidence that dual tDCS (both anodal and cathodal tDCS administered at the same time) is effective for improving dexterity. There is level 1a conflicting evidence regarding the effectiveness of dual tDCS for improving grip force.

There is level 1b evidence that coupling methylphenidate with tDCS may improve hand function relative to when tDCS or methylphenidate are delivered alone.
There is level 1b evidence that combining tDCS with computer brain interface training may not improve spasticity or upper extremity motor function.

**Anodal Transcranial Direct Current Stimulation (tDCS) is likely not effective for improving upper limb motor function, spasticity, and grip strength, with uncertainty regarding its effectiveness for dexterity.**

**The effectiveness of Cathodal Transcranial Direct Current Stimulation (tDCS) remains uncertain for upper limb motor function, dexterity, and activities of daily living.**

**Dual Transcranial Direct Current Stimulation is likely effective for dexterity.**

### 10.9 Drugs and Medical Interventions

Medications used to augment the rehabilitation process following stroke have mainly been examined for their potential benefit in terms of global recovery and depression. The results from these trials have been published in other chapters (Mobility, Depression, and Aphasia). However, a small group of studies that evaluated the efficacy of drugs for their effect on the upper extremity has also been identified. These drugs include stimulants (amphetamines and methylphenidate), Levodopa and anti-depressants (citalopram and reboxetine). A systematic review (Berends et al., 2009) evaluated the benefit of drugs influencing neurotransmitters on motor recovery following stroke. Six studies evaluating a broad range of drugs were included (antidepressant, amphetamine/methylphenidate and Levodopa). The outcomes assessed included the Barthel Index and the FIM. Methylphenidate, tarazadone and nortriptyline were associated with improved motor function. While recognizing that the studies differed in many respects, the authors concluded that there was insufficient evidence to recommend their use.

#### 10.9.1 Stimulants

Amphetamines have shown promise in aiding recovery following stroke as they have the potential to accelerate motor recovery following motor cortex lesions in the rat model (Feeney, Gonzalez, & Law, 1982), especially when combined with task-specific training. Stimulants such as amphetamines have been reported to enhance plasticity through axonal sprouting (Papadopoulos et al., 2009). Four RCTs have examined the effects of either amphetamine or methylphenidate on motor recovery in the upper extremity, the results of which are detailed in Table 10.9.1.1.

### Table 10.9.1.1. Summary of RCTs Examining Stimulants for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score)</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Platz et al.</strong> (2005) RCT (9) N=31</td>
<td>E: d-amphetamine (10mg) + arm training C: Placebo + arm training</td>
<td>• TEMPA: post (+), follow-up (-)</td>
</tr>
<tr>
<td><strong>Tardy et al.</strong> (2006) RCT (9) N=8</td>
<td>E: Methylpenidate (20mg) C: Placebo</td>
<td>• Finger tapping scores (+) • Hand grip strength (-)</td>
</tr>
<tr>
<td><strong>Schuster et al.</strong> (2011) RCT (9) N=16</td>
<td>E: Dexamphetamine + physiotherapy C: Placebo + physiotherapy</td>
<td>• Chedoke-McMaster Stroke Assessment: ADL (+) • Chedoke-McMaster Stroke Assessment: hand scores (+)</td>
</tr>
<tr>
<td><strong>Wang et al.</strong> (2011)</td>
<td>E1: Real tDCS + methylphenidate</td>
<td>• Purdue Pegboard Test: E1 vs. E2 (+), E1 vs. E3 (+)</td>
</tr>
</tbody>
</table>
RCT (7)  
N=9  
E2: Real tDCS + placebo drug  
E3: Sham tDCS + methylphenidate  
C: Sham tDCS + placebo drug

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

Discussion

Amphetamines were investigated for their effect on upper extremity function in two RCTs. Platz et al. (2005) compared dextroamphetamine (d-amphetamine) with a placebo and tested effects of upper extremity function using the TEMPA, a timed test of upper-extremity performance with tasks based on ADLs. Both groups received arm ability training which may lead to gains in motor recovery, however, no differences were found between groups. Furthermore, there was no new acquisition or facilitation of skills associated with d-amphetamine use which may have been due to its effect on attentional systems with high arousal, resulting in non-clinical attentional difficulties (Platz, Kim, et al., 2005). Short-term gains in favour of amphetamines were reported by Schuster et al. (2011) on the CMSA Hand and ADL subscales after 1 week, but these were not sustained at 6 month and 12 month follow-ups. Despite the lack of statistical significance, there was trend in favour of the experimental group. Timing may have been a causal factor, with previous studies reporting positive results with a start date of less than 30 days post stroke, whereas this study began intake at a mean of 37.9 days post stroke (Schuster et al., 2011). The authors also noted that the small sample size may have influenced the results, particularly as the types of physiotherapy were specific to each patient.

One RCT also examined the effect of methylphenidate (Tardy et al., 2006), which is in the same class of drug as amphetamines, but it does not produce the same side effect profile as amphetamines (insomnia, lack of appetite). In comparison with a placebo group, Tardy et al. (2006) reported significantly higher finger tapping scores, with the authors explaining this effect as the result of dopaminergic and noradrenergic modulation. Further research is required to understand the neuronal reactions of methylphenidate in post-stroke patients.

Wang et al. (2014) combined the use of methylphenidate with tDCS whilst also studying each intervention separately. The results indicated that methylphenidate plus tDCS was most effective in restoring hand function compared to each intervention separately. Furthermore, post-hoc analyses revealed that methylphenidate alone did not result in significant improvements, whereas tDCS and methylphenidate in combination with tDCS did. Interestingly, all three groups did not differ with regards to evoked potentials of cortical excitability. Although the authors conclude the mechanism behind these results remains unclear, they propose that methylphenidate strengthened and enhanced the effects of tDCS.

Conclusions Regarding Stimulants

There is level 1a evidence that delivering stimulants in combination with additional therapy may improve upper extremity function; however, level 1b evidence suggests that grip strength may not improve.

There is Level 1b evidence that stimulants may only be effective at improving impaired upper limb function in the short term.

Stimulants may help improve impaired upper limb function; however, the effects may not be observed in the long term.
### 10.9.2 Levodopa

Levodopa is a dopamine precursor which, once it crosses the blood-brain barrier, is converted to dopamine (which cannot cross the blood-brain barrier). Levodopa is used as a prodrug to increase dopamine levels, most commonly in the treatment of Parkinson’s disease. However, there have been two RCTs conducted evaluating Levodopa for upper extremity function post stroke, the details of which are detailed in Table 10.9.2.1.

#### Table 10.9.2.1 Summary of RCTs Examining Levodopa for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restemeyer et al. (2007)</td>
<td>RCT (9)</td>
<td>N=10</td>
<td>E: Levodopa (100mg) C: Placebo (100mg)</td>
<td>Nine Hole Peg Test (-) Grip strength (-) Action Research Arm Test (-)</td>
</tr>
<tr>
<td>Rosser et al. (2008)</td>
<td>RCT (5)</td>
<td>N=18</td>
<td>E: Levodopa (100mg) + cabidopa (25mg) C: Placebo</td>
<td>Reaction time (+)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

#### Discussion

Mixed results were reported from the two RCTs conducted to investigate the effect of Levodopa on upper extremity functions. Rosser et al. (2008) reported a significant improvement in reaction time performance after patients were treated with three consecutive doses of Levodopa compared to performance after receiving a placebo. The mechanism for this improvement may be the result of dopamine release leading to a strengthening of task-relevant synapses and suppression of task-irrelevant synapses (Rosser et al., 2008). However, this study did not include a follow-up assessment; therefore potential long-term benefits were not evaluated. Restemeyer et al. (2007) did not report any significant differences in function when comparing patients’ performance after receiving 100mg of Levodopa or placebo. However, the authors note that patients were prescribed only a single dose of Levodopa and this may not be sufficient to support or induce changes in neuroplasticity. Furthermore, baseline Action Research Arm Test scores were high, thereby indicating a ceiling effect and that prior function was at a sufficient level (Restemeyer et al., 2007). Further research with varying dosage over extended periods of time is recommended.

#### Conclusions Regarding Levodopa

There is level 1b evidence that Levodopa may not improve arm and hand function however, level 2 evidence suggests that reaction time may be improved.

More research is needed to determine the effects of Levodopa on impaired upper limb motor function.

### 10.9.3 Antidepressants

Beyond their ability to improve depression following stroke, antidepressants can be used to enhance upper extremity motor recovery through changes in neurotransmission. There is evidence suggesting that serotonergic modulation may be involved in motor recovery post stroke. Previous research has
suggested that patients who have reacted well to antidepressant treatment may also demonstrate improvements in upper limb motor functioning (Chemerinski, Robinson, & Kosier, 2001). Furthermore, there are reports that single doses of selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine and paroxetine, have resulted in activation of the motor cortices (Dam et al., 1996; Pariente et al., 2001) therefore, manipulation of neurochemicals may influence aspects of function other than psychological distress. Moreover, there is evidence to suggest that noradrenergic reuptake inhibitors (NRIs) increase motor cortex excitability (Plewnia et al., 2002). Results of RCTs evaluating antidepressants for upper extremity outcomes are reported in Table 10.9.3.1 and results regarding the lower extremities are presented in Chapter 9.

### Table 10.9.3.1 Summary of RCTs Examining Antidepressants for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chollet et al. (2011)</td>
<td>RCT (9)</td>
<td>N=118</td>
<td>E: Fluoxetine (20mg) C: Placebo</td>
<td>• Fugl Meyer Motor Scale (+) • NIHSS (-) • Modified Rankin Scale (+)</td>
</tr>
<tr>
<td>Robinson et al. (2000)</td>
<td>RCT (8)</td>
<td>N=104</td>
<td>E1: Nortriptyline (100mg) E2: Fluoxetine (40mg) C: Placebo</td>
<td>• FIM: E1 vs. E2 (+), E1 vs. C (+)</td>
</tr>
<tr>
<td>Zittel et al. (2008)</td>
<td>RCT (8)</td>
<td>N=8</td>
<td>E: Citalopram C: Placebo</td>
<td>• Nine Hole Peg Test (+) • Hand grip strength (-)</td>
</tr>
<tr>
<td>Mikami et al. (2011)</td>
<td>RCT (8)</td>
<td>N=104</td>
<td>Additional analysis of Robinson et al. 2000 E1: Nortriptyline (100mg) E2: Fluoxetine (40mg) C: Placebo</td>
<td>During 1yr follow-up: • Modified Rankin Scale: E1 vs. C (+), E2 vs. C (+)</td>
</tr>
<tr>
<td>Zittel et al. (2007)</td>
<td>RCT (6)</td>
<td>N=10</td>
<td>E: Reboxetine C: Placebo</td>
<td>• Tapping speed (+) • Grip strength (+)</td>
</tr>
<tr>
<td>Mohammadianinejad et al. (2014)</td>
<td>RCT (6)</td>
<td>NStart=80 NEnd=66</td>
<td>E: Lithium carbonate (300mg) C: Placebo</td>
<td>• NIHSS (+) • Fugl Meyer Scores: Hand (+)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

### Discussion

SSRIs have long been used in the treatment of depression. Zittel et al. (2008) revealed a significant improvement in dexterity after patients had received Citalopram compared to a placebo. Furthermore, the authors revealed a trend towards even greater improvement among patients who also received physiotherapy. The results did not yield any significant improvement in strength, suggesting that Citalopram’s modification of serotonergic transmission is associated with coordination and dexterity. In a multicentre RCT assessing the effect of Fluoxetine on motor recovery compared to a placebo, Chollet et al. (2011) reported significantly greater improvement on the Fugl-Meyer Motor Scale (FMMS) and Modified Rankin Scale (mRS) among patients receiving Fluoxetine. A potential explanation for these results could be that the main function of the serotonergic system is to facilitate motor output which would allow for greater efficiency, especially when combined with physical training (Chollet et al., 2011). No side effects were reported for Citalopram (Zittel et al., 2008) but transient digestive disorders such as
nausea, diarrhea and pain were reported in more patients treated with Fluoxetine than placebo (Chollet et al., 2011).

In comparison with Nortriptyline, a Tricyclic antidepressant, Robinson et al. (2000) reported greater improvements on the FIM in patients who received Nortriptyline compared to who received Fluoxetine or a placebo. Interestingly, there were no significant differences between patients with or without depression regardless of the type of treatment provided (Nortriptyline, Fluoxetine or placebo). Robinson et al. (2000) suggest that the 12 week study period may have been insufficient to observe improvements in impairment between depressed and non-depressed patients. Further analyses of this dataset by Mikami et al. (2011) revealed that patients receiving antidepressant treatment, regardless of type (Nortriptyline or Fluoxetine), outperformed patients given a placebo on the mRS at 1-year follow-up. Mikami et al. (2011) note that previous literature suggests that both tricyclic antidepressants and SSRIs inhibit microglial production of proinflammatory cytokines thereby resulting in neurogenesis and synaptic plasticity. The authors propose that both types of antidepressant may be of benefit to stroke patients independent of presence of depression.

A single dose of an NRI such as Reboxetine was found to be efficacious in improving grip strength and tapping speed compared to a placebo (Zittel et al., 2007). In contrast with their 2008 study of SSRIs, Zittel et al. (2007) did not report a significant difference between groups on the 9HPT, suggesting that NRIs may not be as effective in treating dexterity. Reboxetine was well-tolerated with only one patient experiencing transient nausea. It is worth noting that this study only recruited chronic stroke patients; future research may be advised to explore the effects of Reboxetine in acute and sub-acute populations.

Mohammadianinejad et al. (2014) investigated the use of Lithium Carbonate and reported no differences in improvement in upper limb motor function when compared with a placebo. However, a subgroup analysis of patients with a lesion located near the middle cerebral artery revealed a significant improvement on the NIHSS and FMA Hand subscale compared to placebo patients. Previous research suggests that Lithium enhances neuronal growth in cortical grey matter and increases grey matter volume; therefore, if the motor cortex was affected by a cortical stroke, this may explain improvements in motor ability (Mohammadianinejad et al., 2014). It was proposed by Mohammadianinejad et al. (2014) that further research with longer study periods is required to investigate whether patients with non-cortical strokes could benefit from Lithium treatment.

Conclusions Regarding Antidepressants

There is level 1a evidence that fluoxetine and nortriptyline may improve overall disability and upper extremity motor function.

There is level 1a that citalopram, reboxetine and lithium carbonate may enhance impaired arm and hand function however, level 1b evidence indicates that citalopram may not be effective at improving hand grip strength.

Antidepressants may help improve impaired upper extremity motor function following a stroke.
10.9.4 Steroids
Corticosteroids have been used to treat pain and functional limitations in hemiplegic patients, with pain potentially hindering the rehabilitation of physical functioning (Dogan, Demirtas, & Ozgirgin, 2013). Previous literature has reported significant gains in muscle mass and strength in terms of lower limb recovery after administration of anabolic steroids (Okamoto et al., 2011), but literature concerning upper limb function is limited. Only two studies, one RCT and one prospective controlled trial, have investigated the use of steroids on upper limb recovery; results of the controlled trials are summarized in Table 10.9.4.1.

Table 10.9.4.1 Summary of Controlled Trials Examining Steroids for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yasar et al. (2011)</strong> RCT (9) N&lt;sub&gt;Start&lt;/sub&gt;=26 N&lt;sub&gt;End&lt;/sub&gt;=26</td>
<td>E1: Intra-Articular Steroid Injection E2: Suprascapular Nerve Block Injection</td>
<td>• VAS (-) • Range of Motion (Passive) (-) • Range of Motion (at onset of pain) (-)</td>
</tr>
<tr>
<td><strong>Doğan et al. (2013)</strong> PCT N&lt;sub&gt;Start&lt;/sub&gt;=60 N&lt;sub&gt;End&lt;/sub&gt;=60</td>
<td>E1: Steroid injection + physical therapy E2: Hydraulic distension + steroid injection + physical therapy E3: Physical therapy C: Physical therapy</td>
<td>• Range of Motion (shoulder joint): E2 vs. E1 (+), E2 vs. C (+) • Shoulder pain: E2 vs. E1 (+), E2 vs. C (+) • Self care: E2 vs. E1 (+), E2 vs. C (+)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion
Yasar et al. (2011) found steroid and nerve block injections to be equivalently effective, as patients demonstrated significant improvements in range of motion and decreases in shoulder pain after receiving either intervention. Previous research suggests that steroids may have anti-inflammatory properties while suprascapular nerve block may provide transient cessation of nociceptive signals from the shoulder (Yasar et al., 2011). Despite no side effects being reported, this study adopted a short follow-up time and recruited a small group of patients with no placebo group, so the results should be interpreted with caution. Dogan et al. (2013) reported that patients who received hydraulic distension, steroid injection and physical therapy combined into a triple-intervention approach demonstrated even greater improvements in upper limb motor outcomes than those who received steroid injection plus physical therapy or physical therapy only. Although spasticity was more prevalent in both experimental groups compared to the control group, greater range of motion was also reported in both at 1 month post-intervention. The authors suggest that the suppression of pain may have influenced the pain experienced from any spasticity that may have been present. By combining steroid injections with hydraulic distension, inflammation may have been suppressed and joint volume increased, thereby leading to decreased pressure on the supraspinatus and periarticular soft tissue (Dogan et al., 2013).

Conclusions Regarding Steroids

*There is level 1b evidence that intra-articular steroid injections may not improve pain or range of motion of the upper extremity; however, limited level 2 evidence provides conflicting findings.*

*Further research is needed to determine if steroid injections are beneficial at reducing upper limb pain and improving range of motion following a stroke.*
10.9.5 Antibiotics

Although no studies have been conducted exploring the use of antibiotics, their use as an adjuvant alongside other rehabilitative therapies has been proposed. D-cycloserine, an antibiotic used in the treatment of tuberculosis, was found to be a high-affinity agonist of the N-methyl-D-aspartate (NMDA) glutamate receptor which was identified as an important component in long-term learning and potentiation (Nadeau et al., 2014). There is one RCT investigated the combination of constraint induced movement therapy (CIMT) with D-cycloserine, the results of which are summarized in Table 10.9.5.1.

Table 10.9.5.1 Summary of RCT(s) Examining Antibiotics for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nadeau et al. (2014)</td>
<td>RCT (7)</td>
<td>N_{Start}=24, N_{End}=22</td>
<td>Group A: E: CIMT (6hr/d, 5d/wk, 2wk) + d-cycloserine C: CIMT (6hr/d, 5d/wk, 2wk) + placebo Group B: E: CIMT (2hr/d, 3d/wk, 10wks) + d-cycloserine C: CIMT (2hr/d, 3d/wk, 10wks) + placebo</td>
<td>• Fugl Meyer Score (-) • Wolf Motor Function Test (-) • Motor Activity Log (-) • Stroke Impact Scale (-) • Geriatric Depression Scale (-) • Caregiver Strain Index (-)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion

Nadeau et al. (2014) reported no significant differences between d-cycloserine and placebo groups, nor between the more-condensed and less-condensed CIMT conditions on all outcome measures; however, all four groups demonstrated significant decreases in WMFT scores. The lack of treatment efficacy may have been the result of a ceiling effect on neuroplasticity, which may in turn have limited the amount of recovery achieved as previous studies have suggested that loss of corticospinal and corticobulbar fibers may impose limitations on recovery (Nadeau et al., 2014). The authors also suggest that the dosage of d-cycloserine administered may have been too low. Further research with different dosages and types of antibiotics may be warranted.

Conclusions Regarding Antibiotics

There is level 1b evidence that d-cycloserine delivered in combination with constraint-induced movement therapy may not improve upper extremity motor function.

Further research is needed to determine the effects of d-cycloserine on post-stroke upper extremity motor function.

10.9.6 Ozonated Autohemotherapy

Ozonated autohemotherapy is a novel treatment that involves the transfusion of oxidated blood. Previous research suggests that ozone therapy can improve circulation, decrease blood viscosity, and maintain energy metabolism in brain tissues thereby reducing cellular apoptosis (X. N. Wu et al., 2013). There is currently a lack of literature assessing the use of ozonated autohemotherapy in stroke patients, and even more so in terms of post-stroke motor function. Only one prospective controlled trial
investigated the use of ozonated autohemotherapy for upper extremity function, as detailed in Table 10.9.6.1.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wu et al. (2013)</td>
<td>PCT</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=86 N&lt;sub&gt;End&lt;/sub&gt;=86</td>
<td>E: Ozonated autohemotherapy C: Conventional rehabilitation</td>
<td>• NIHSS (+)  • Modified Rankin Scale (+)  • Central motor conduction time (+)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion
Wu et al. (2013) reported significant increases in motor-evoked potential of the upper limb and shorter central motor conduction times for those in the intervention group compared to the control group. However, it should be noted this intervention can induce pain and has technical limitations (X. N. Wu et al., 2013). Further studies are required to investigate the use of ozonated autohemotherapy in treating upper extremity dysfunction and to seek clarification on the biological mechanisms as to why this may be a potentially successful approach. Despite the efficacious nature of ozonated autohemotherapy on upper extremity motor function post stroke, the mechanisms underlying its beneficial effect remain unclear (X. N. Wu et al., 2013).

Conclusions Regarding Ozonated Autohemotherapy

There is limited level 2 evidence that ozonated autohemotherapy may improve general motor disability.

Evidence for the use of ozonated autohemotherapy for improving post-stroke upper limb motor function is currently limited.

10.9.7 Peptides

Cerebrolysin contains low molecular weight neuropeptides and free amino acids which are believed to have neuroprotective properties and to reduce excitotoxicity, inhibit free radical formation, reduce neuroinflammation, and activate calpain apoptosis (Muresanu et al., 2016).

Randomized controlled trials investigating the effectiveness of Cerebrolysin are summarized in Table 10.9.7.1.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muresanu et al. (2016)</td>
<td>RCT (9)</td>
<td></td>
<td>E: Cerebrolysin + physical/occupational therapy</td>
<td>Fugl-Meyer Assessment (+)</td>
</tr>
</tbody>
</table>
10. Upper Extremity Interventions

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

### Discussion

Two studies were found to investigate cerebrolysin in stroke patients (Chang et al., 2016; Muresanu et al., 2016). The study by Muresanu et al. (2016) had a large sample size and was a multi-center trial with high methodological quality. The study found that cerebrolysin in combination with physical/occupational therapy was superior to placebo with physical/occupational therapy for improving upper limb motor function, based on the Fugl-Meyer Assessment (Muresanu et al., 2016). The other study by Chang et al. (2016), which also had a moderately large sample size, found that cerebrolysin with conventional therapy improved upper limb motor function and dexterity through the Action Research Arm Test, and also that it improved measures of independence/daily living through improvements on the Barthel Index and the Modified Rankin Scale.

#### Conclusions Regarding Cerebrolysin

**There is level 1a evidence that Cerebrolysin improves upper limb motor function.**

**There is level 1b evidence that Cerebrolysin improves dexterity and measures of independence/daily living.**

**Cerebrolysin may improve upper limb motor function, dexterity, and measures of independence/daily living.**

### 10.9.8 Neuroprotectants

NeuroAid is made of 9 herbal and 5 animal components and is widely used after stroke in China, as it is believed to protect neurons and encourage plasticity (Kong et al., 2009).

The mechanism behind the possible action of Phosphodiesterase-5 Inhibitor (PF-3049423) is unknown but it has been suggested that it may upregulate neurogenesis, synaptogenesis, angiogenesis, and improve regional blood flow (Di Cesare, Mancuso, Woodward, Bednar, & Loudon, 2016).

The studies examining the effectiveness of neuroprotectants including NeuroAid and PF-3049423 are summarized in Table 10.10.8.1.

<table>
<thead>
<tr>
<th>Author, Year Study Design (PEDro Score) Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kong et al. (2009) RCT (8)</td>
<td>E: NeuroAid C: Placebo</td>
<td>Fugl Meyer Score (-) NIHSS (-)</td>
</tr>
</tbody>
</table>
N=40

<table>
<thead>
<tr>
<th>Study</th>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Di Cesare et al. (2016)</td>
<td>RCT (6)</td>
<td>N_Start=139, N_End=137</td>
<td>E: PF-3049423 (phosphodiesterase-5 inhibitor) C: Placebo</td>
<td>Modified Rankin Scale (-) Barthel Index (-) National Institute of Health Stroke Scale (-) Box and Block Test (-) Grip Strength (-)</td>
</tr>
<tr>
<td></td>
<td>Venketasubramanian et al. (2015)</td>
<td>Cohort</td>
<td>N_Start=880, N_End=862</td>
<td>E: MLC601 - Chinese Medicine NeuroAid C: Placebo</td>
<td>Modified Rankin Scale (-)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

**Discussion**
Both Kong et al. (2009) and Venketasubramanian et al. (2015) investigated the effectiveness of NeuroAid, and both found that it was no more effective than placebo for improving level of independence or activities of daily living. Kong et al. (2009) also found that it did not improve upper limb motor function.

Di Cesare et al. (2016) examined the effectiveness of phosphodiesterase-5 inhibitor, and found that it did not significantly improve dexterity, grip strength, or level of independence or activities of daily living.

Further studies are required to gain further knowledge regarding the effectiveness of neuroprotectants and to further understand the mechanism of action.

**Conclusions Regarding Neuroprotectants**

*There is level 1b evidence that NeuroAid does not improve upper limb motor function.*

*There is level 1b evidence that phosphodiesterase-5 inhibitor does not improve dexterity, grip strength, or level of independence/daily living.*

**NeuroAid may not improve upper limb motor function and phosphodiesterase-5 inhibitor may not improve dexterity, grip strength, or level of independence/daily living.**

**10.9.9 Statins**

Statins are also believed to have a neuroprotective function, and in the table below the effectiveness of statins are examined.

**Table 10.9.9.1 Summary of Controlled Trial(s) Examining Statin Use in Stroke Recovery**

<table>
<thead>
<tr>
<th>Study</th>
<th>Author, Year</th>
<th>Study Design (PEDro Score)</th>
<th>Sample Size</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zhang et al. (2017)</td>
<td>RCT (6)</td>
<td>N_Start=78, N_End=75</td>
<td>E: Atorvastatin C: Placebo</td>
<td>Modified Rankin Scale (+) Barthel Index (+)</td>
</tr>
</tbody>
</table>
Discussion

Only Zhang et al. (2017) explored the effectiveness of statins such as Atorvastatin against a placebo, and found that Atorvastatin led to improvements in the level of independence/activities of daily living. Serum brain-derived neurotrophic factor (BDNF) levels and functional recovery were both assessed.

**Conclusions Regarding Statins**

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

**There is level 1b evidence that Atorvastatin improves level of independence / activities of daily living.**

**Evidence for the use of Atorvastatin for improving outcomes after stroke is limited.**

10.10 Alternative and Complementary Medicine

Traditional Chinese Medicine (TCM) includes a variety of treatments including acupuncture, massage and Chinese herbal medicines. Several studies have been conducted on the use of TCM, mostly in the acute stage of stroke (Wang et al., 2013). The majority of these studies have been written in the Chinese language and published in Chinese journals, though Wang et al. (2013) found that institutions in the United Kingdom are among the top 10 locations of first authors of articles written in English.

10.10.1 Acupuncture

The use of acupuncture has recently gained attention as an adjunct to stroke rehabilitation in Western countries even though acupuncture has been a primary treatment in China for about 2000 years (Baldry, 2005). In China, acupuncture is an acceptable, time-efficient, simple, safe and economical form of treatment used to ameliorate motor, sensation, verbal communication and further neurological functions in post-stroke patients,” (Wu et al., 2002). According to Rabinstein and Shulman (2003), “Acupuncture is a therapy that involves stimulation of defined anatomic locations on the skin by a variety of techniques, the most common being stimulation with metallic needles that are manipulated either manually or that serve as electrodes conducting electrical currents”. The traditional concept is that life energy flows through channels that connect all organs to each other. Disease is explained as an imbalance in the energy flow, and acupuncture treatment is believed to restore the healthy energy by stimulating specific points along the channels (Rabinstein & Shulman, 2003). There is a range of possible acupuncture mechanisms that may contribute to the effects experienced by stroke patients (Park, James, & White, 2006). For example, acupuncture may stimulate the release of neurotransmitters (Han & Terenius, 1982) and have an effect on the deep structure of the brain (Wu et al., 2002). Lo et al. (2005) established acupuncture, when applied for at least 10 minutes, led to long-lasting changes in cortical excitability and plasticity even after the needle stimulus was removed. A study using positron emission tomography (PET) to observe cerebral function after electroacupuncture treatments showed that glucose metabolism changed significantly immediately after treatment, and after three weeks of daily electroacupuncture treatments in multiple cerebral motor areas (Fang, Ning, Xiong, & Shulin, 2012). From these results, Fang et al. (2012) concluded that electroacupuncture participated in modulating motor plasticity.

De Qi is a numbness or tingling sensation experienced by patients and considered to be an important aspect of TCM. When De Qi is not achieved, it is suggested that the effects of acupuncture are
diminished. De Qi has been suggested to be a relatively stable predictor of therapeutic effectiveness of acupuncture for stroke recovery (Bai, Cui, Zou, & Lao, 2013).

While the exact mechanisms are not all well-defined, there are biological responses that occur both at local areas being stimulated and at remote areas of the body. With respect to stroke rehabilitation, the benefit of acupuncture has been evaluated most frequently for pain relief and recovery from hemiparesis. Evidence from several RCTs and meta-analyses shows the effectiveness of acupuncture remains unclear.

Syndrome differentiation, one of the most important principles of TCM diagnosis and treatment, is a way of classifying patients’ symptoms and determines the disharmony in the body and consequent treatment. A meta-analysis of an acute stroke subgroup of 44 RCTs showed no differences between trials using fixed acupoints prescriptions and trials using individualized treatment prescriptions based on patients’ symptoms (Cao, Bourchier, & Liu, 2012).

Sze et al. (2002) included 14 RCTs in a meta-analysis of the efficacy of acupuncture. This study found that acupuncture in conjunction with stroke rehabilitation had no additional effect on motor recovery compared to stroke rehab alone, but small positive effect on disability was found. However, it was noted that the benefits reported could be explained by a placebo effect, or poor study quality. Similar to the previous reviews, the authors concluded that the efficacy of acupuncture alone remains uncertain, mainly because of the poor quality of available studies.

A review of the effectiveness of acupuncture as a specific treatment for shoulder pain included the results from 7 RCTs, all published in China (J. A. Lee et al., 2012). The treatment contrasts included acupuncture + exercise vs. exercise, acupuncture + exercise vs. drug treatment, acupuncture + exercise vs. exercise + drug treatment and electroacupuncture vs. TENS. Duration of treatment ranged from 10 to 32 days. Measures of motor function, range of motion and pain were assessed. Across the studies, patients in the treatment group reported significantly greater reductions in pain and improvement in motor function compared with patients in the control group.

A large number of studies examining acupuncture were identified, although a number of RCTs not included in this review were published in non-English languages. The methodological quality of the RCTs are generally poor (Zhao, Du, Liu, & Wang, 2012), leading to inconclusive evidence. The results of RCTs with PEDro scores greater than 3 are presented in Table 10.11.1.1.

Table 10.11.1.1 Summary of RCTS with PEDro Scores >3 Assessing Acupuncture for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>PEDro Score</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wayne et al.</strong> (2005)</td>
<td>RCT (9) E: Acupuncture C: Sham</td>
<td>N=33</td>
<td></td>
<td>Fugl-Meyer (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Modified Ashworth scores (-)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ROM (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BI (-)</td>
<td></td>
</tr>
<tr>
<td><strong>Bai et al.</strong> (2013)</td>
<td>RCT (9) NStart=120 NEnd=120</td>
<td>E1: Acupuncture E2: Physical therapy E3: Acupuncture + physical therapy</td>
<td></td>
<td>Fugl-Meyer Assessment (-),</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fugl-Meyer Assessment (28d follow-up, E1 vs. E2) (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Modified Barthel Index (-)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Modified Barthel Index (28d follow-up, E1 vs. E2) (+)</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Study Design</td>
<td>Start N</td>
<td>End N</td>
<td>Intervention(s)</td>
<td>Primary Outcomes</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------</td>
<td>---------</td>
<td>-------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Chen et al. (2016)</td>
<td>RCT (8)</td>
<td>250</td>
<td>250</td>
<td>E: Acupuncture</td>
<td>National Institute of Health Stroke Scale (+)&lt;br&gt;Fugl-Meyer Assessment (+)</td>
</tr>
<tr>
<td>Zhuang et al. (2012)</td>
<td>RCT (7)</td>
<td>295</td>
<td></td>
<td>E1: Acupuncture&lt;br&gt;E2: Physiotherapy&lt;br&gt;E3: Acupuncture + physiotherapy</td>
<td>Fugl-Meyer (-)&lt;br&gt;BI (-)&lt;br&gt;Neurologic Defect Scale (-)</td>
</tr>
<tr>
<td>Gosman-Hedstom et al. (1998)</td>
<td>RCT (7)</td>
<td>104</td>
<td></td>
<td>E1: Superficial acupuncture&lt;br&gt;E2: Deep acupuncture&lt;br&gt;C: No acupuncture</td>
<td>At 3 and 12 month follow-up:&lt;br&gt;Neurological Score (-)&lt;br&gt;Barthel Index (-)&lt;br&gt;Sunnaas Index (-)&lt;br&gt;Nottingham Health Profile (-)</td>
</tr>
<tr>
<td>Sze et al. (2002)</td>
<td>RCT (7)</td>
<td>106</td>
<td></td>
<td>E: Acupuncture + Standard Therapy&lt;br&gt;C: Standard Therapy</td>
<td>At 0, 5 and 10 weeks:&lt;br&gt;Fugl-Meyer (-)&lt;br&gt;Barthel Index (-)&lt;br&gt;FIM(-)&lt;br&gt;Abbreviated Mental Test (-)&lt;br&gt;NHI stroke scale(-)</td>
</tr>
<tr>
<td>Hopwood et al. (2008)</td>
<td>RCT (7)</td>
<td>105</td>
<td></td>
<td>E: Acupuncture + usual care&lt;br&gt;C: Mock TENS + usual care</td>
<td>Barthel Index (-)&lt;br&gt;Motricity Index (-)&lt;br&gt;NHP (-)</td>
</tr>
<tr>
<td>Ni et al. (2013)</td>
<td>RCT (7)</td>
<td>165</td>
<td>165</td>
<td>E: Standard Acupuncture with Shixuan &amp; Xiaohai acupoints&lt;br&gt;C: Standard Acupuncture only</td>
<td>Finger grip strength (+)&lt;br&gt;Fugl Meyer Assessment (+)</td>
</tr>
<tr>
<td>Liu et al. (2016)</td>
<td>RCT (6)</td>
<td>38</td>
<td>31</td>
<td>E: Manual acupuncture + standard care&lt;br&gt;C: Standard care</td>
<td>National Institute of Health Stroke Scale (-)&lt;br&gt;Fugl-Meyer Assessment (-)&lt;br&gt;Functional Independence Measure (-)&lt;br&gt;Barthel Index (-)&lt;br&gt;Modified Ranking Scale (-)</td>
</tr>
<tr>
<td>Han et al. (2015)</td>
<td>RCT (6)</td>
<td>488</td>
<td>488</td>
<td>E: Meridian sinew row needling combined with dermal needling&lt;br&gt;C: Cerebroprotein hydrolysate and piracetam injections</td>
<td>Fugl-Meyer Assessment (+)&lt;br&gt;Modified Ashworth Scale (+)</td>
</tr>
<tr>
<td>Fragoso &amp; Ferreira (2012)</td>
<td>RCT (6)</td>
<td>32</td>
<td></td>
<td>E1: Acupuncture at Tianquan (PC2)&lt;br&gt;E2: Acupuncture at Quchi (LI11)</td>
<td>Maximal Isometric Voluntary Contraction during elbow flexion (-)</td>
</tr>
<tr>
<td>Kjendhal et al. (1997)</td>
<td>RCT (6)</td>
<td>41</td>
<td></td>
<td>E: Acupuncture&lt;br&gt;C: Standard Therapy</td>
<td>Motor Assessment Scale (+)&lt;br&gt;Sunnaas Index (+)&lt;br&gt;Nottingham Health Profile (+)</td>
</tr>
<tr>
<td>Naeser et al. (1992)</td>
<td>RCT (6)</td>
<td>16</td>
<td></td>
<td>E: Acupuncture&lt;br&gt;C: Sham Acupuncture</td>
<td>Boston Motor Inventory (+ for patients with lesions in less than half of the motor pathways areas)</td>
</tr>
<tr>
<td>Cui et al. (2014)</td>
<td>RCT (6)</td>
<td>60</td>
<td>60</td>
<td>E: Yin Yang manipulation&lt;br&gt;C: Conventional needling manipulation</td>
<td>Elbow spasm (+)&lt;br&gt;Clinical Spasticity Index (+)&lt;br&gt;Integral electric discharge of involved muscle (+)</td>
</tr>
</tbody>
</table>
Upper Extremity

Interventions

Song et al. (2016)  
RCT (5)  
N_{Start}=30  
N_{End}=30  
E: Scalp cluster acupuncture + constraint-induced movement therapy  
C: Body acupuncture + traditional rehabilitation  
• Fugl-Meyer Assessment (-)

Zhao et al. (2009)  
RCT (5)  
N=131  
E: Experimental acupuncture  
C: Traditional acupuncture  
• Spasticity (+)  
• Fugl-Meyer (+)  
• Barthel Index (+)

Sallstrom et al. (1996)  
RCT (5)  
N=45  
E: Acupuncture + Multidisciplinary rehabilitation  
C: Multidisciplinary rehabilitation  
• Motor Assessment Scale (+)  
• ADL scores (+)  
• Nottingham Health Profile (+)

Hu et al. (1993)  
RCT (4)  
N=30  
E: Acupuncture  
C: Supportive Therapy + Conventional Rehabilitation  
• Neurological Scoring used by Scandinavian Stroke Group: day 28 (+)  
• Neurological Scoring used by Scandinavian Stroke Group: day 90 (+)  
• Barthel Index (-)

Li et al. (2015)  
PCT  
N_{Start}=14  
N_{End}=14  
E: Acupuncture with a twisting angle less than 90° + blood circulation medication  
C: Blood circulation medication  
• Fugl-Meyer Assessment (-)

- Indicates non-statistically significant differences between treatment groups  
+ Indicates statistically significant differences between treatment groups

Discussion

A large number of RCTs were reviewed. The majority of them assessed outcomes associated with motor recovery, ADLs and spasticity. There was also great variation in the treatment contrasts examined.

The majority of studies investigating the effectiveness of acupuncture for improving upper limb motor function found that there was no significant benefit to acupuncture when compared to a control (Alexander et al., 2004; Bai et al., 2013; Li et al., 2015; C. H. Liu et al., 2016; Sze et al., 2002; Wayne et al., 2005; Zhuangl et al., 2012). Chen et al. (2016) found a significant improvement in upper limb motor function in those receiving acupuncture, although the therapy that the control group received was not specified. Ni et al. (2013) found a significant improvement in upper limb motor function in those receiving standard acupuncture with Shixuan & Xiaohai acupoints, as opposed to standard acupuncture alone. Additionally, Han et al. (2015) found a significant improvement in upper limb motor function in those receiving Meridian sinew row needling combined with dermal needling in comparison to those receiving Cerebroprotein hydrolysate and piracetam injections.

All studies of high methodological quality investigating the improvement in level of independence and activities of daily living between those receiving acupuncture and those receiving a control found that there was no significant difference (Alexander et al., 2004; Bai et al., 2013; Gosman-Hedstrom et al., 1998; Hopwood et al., 2008; C. H. Liu et al., 2016; Wayne et al., 2005; Zhuangl et al., 2012).

Wayne et al. (2005) used a previously validated form of acupuncture that allows for successful patient blinding to treatment (Wayne et al., 2005). Although there were statistically significant results in favour of acupuncture treatment on a per protocol basis, a small sample size, ambiguous findings, and negative significance on ITT analysis effect the interpretation of results. The choice of outcome measure (Barthel Index) could be criticized as being unresponsive to subtle improvements in upper limb function.

The lack of an appropriate control treatment adds to the inconsistent effects of acupuncture. That is, does acupuncture itself provide therapeutic benefits or are its therapeutic benefits revealed only as an
additive benefit to physiotherapy? A high-quality RCT conducted by Bai et al. (2013) revealed no significant differences between acupuncture, physical therapy, and a combination of both after 28 days of therapy. However, at 56 days of therapy, Fugl-Meyer Assessment and Modified Barthel Index (MBI) scores were significantly higher in the physiotherapy group compared to the acupuncture group, but no differences were observed between both of these groups and the combined physiotherapy+acupuncture group. Although the authors highlight that all three groups improved over time, acupuncture may not be as efficacious as physiotherapy. A similar study conducted by Zhuangl et al. (2012) did not find any significant differences in FMA and MBI scores between all three groups after 14 and 28 days of therapy. The authors suggest that as physiotherapy did not result in significantly greater gains or improvements; acupuncture may be an equivalent alternative and could be a useful option for individuals who do not have access to a physiotherapist or the equipment required for physiotherapy. A combination of the two therapies did result in a favourable trend but this did not reach statistical significance. Zhuangl et al. (2012) suggest that future research should concentrate on longer follow-up times to assess for potential long-term benefits.

Credible sham treatments are required in order to effectively evaluate the benefits of acupuncture. For example, studies such as those by Chen et al. (2016) may find positive improvements in the group receiving acupuncture on measures of upper limb motor function, however, the therapy the control group received, if received, is not specified. Zhuangl et al. (2012) point out that sham acupuncture may or may not have a physiological effect with previous research suggesting no differences between “sham” and “real” acupuncture. Also, as reported by the literature, several different methods of acupuncture have been used including classical Chinese acupuncture (Kjendahl et al., 1997; Sallstrom et al., 1996), and electroacupuncture (R.L. Hsieh, L.Y. Wang, & W.C. Lee, 2007; Johansson et al., 2001; S.K. Moon et al., 2003; M. Mukherjee, L.K. McPeak, J.B. Redford, C. Sun, & W. Liu, 2007; Q.M. Si, G.C. Wu, & X.D. Cao, 1998; Wong, Su, Tang, Cheng, & Liaw, 1999). Furthermore, different acupoints may be influential as Ni et al. (2013) reported significantly greater improvements in finger-grip strength and FMA scores among patients who received additional acupuncture of the Shixuan and Xiaohai points, associated with blood flow, and the medial antebrachial cutaneous nerve and ulnar nerve stem respectively. A distinction between the different methods and their intended effects needs to be addressed. Third, Hu et al. (1993) have reported that patients with the most severe impairment showed the greatest improvements, the use of a homogenous sample and evaluation of patient characteristics that would most benefit from acupuncture is recommended. Again, the lack of consensus regarding what constitutes an appropriate control for acupuncture therapy makes interpreting these results difficult as subliminal stimulation and placement of electrodes may produce unspecific responses.

A systematic review conducted by Fu et al.(2012), has suggested that criteria for RCTs may not be suitable for evaluating studies of TCM and acupuncture. The authors reported issues such as: difficulty in recruitment, higher costs associated with these studies due to patients’ suspicions of placebo and unwillingness to take other CHM; lack of standardized terminology; difficulty creating CHM placebo packets that are similar in smell and appearance; efficacy of Chinese herbal medicines; interventions are often nonspecific and outcome measures are subjective (Fu et al., 2012). A computed search strategy conducted by Cai et al. (2012) showed that of 70% of all acupuncture RCTs are published in China, the number of Chinese RCTs ranking first in the Central Register of Controlled Trials (CENTRAL) and MEDLINE databases, while only 11% of Chinese RCTs are recognized in the Science Citation Index (SCI). The authors suggest that the quality of RCTs conducted in China may not be recognized by international standards, and the quality rather than quantity should be emphasized in future publications.

**Conclusions Regarding Acupuncture**
There is level 1a evidence from high-quality, high-powered studies that acupuncture does not improve upper extremity motor function or performance of activities of daily living.

There is conflicting level 1a evidence regarding the effect of acupuncture on spasticity.

Acupuncture likely does not improve upper limb motor function or level of independence.

### 10.11.2 Meridian Acupressure

Meridian acupressure is a form of treatment whereby finger pressure is applied to meridian points on the body. Meridians are either yin or yang, depending on the direction they flow on the body's surface. The yang meridians run from the fingers to the face or from the face to the feet. Yin meridians run from the feet to the torso or from the torso to the fingertips on the inside, yin side, of the arms. Theoretically, acupressure increases blood (qi) flow to the upper extremity, thus improving function. Although used in clinical practice in eastern parts of the world, only a few studies have examined its use on upper extremity recovery following stroke, the results of which are summarized in Table 10.11.2.1.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>PEDro Score</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yue et al. (2013)</strong></td>
<td>RCT (6)</td>
<td>E: Acupressure C: Routine care</td>
<td>• Barthel Index (+) • Fugl Meyer Scores (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N=78</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hua-feng et al. (2014)</strong></td>
<td>RCT (6)</td>
<td>E: Yin Yang manipulation C: Conventional needling manipulation</td>
<td>• Elbow spasm (+) • Clinical Spasticity Index (+) • Integral electric discharge of involved muscle (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N_{Start}=60 N_{End}=60</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Kang et al. (2009)</strong></td>
<td>RCT (5)</td>
<td>E: Meridian acupressure C: Standard care</td>
<td>• Grip power (+) • Pain (+) • Passive range of motion (+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N=56</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

### Discussion

The results of acupressure appear to be promising for improving upper-limb function and level of independence in activities of daily living. Yue et al (2013) reported significantly greater improvements in Barthel Index and Fugl-Meyer Assessment scores in the intervention group compared to a standard care control group at three months post intervention. However, there was no significant between group differences at 1 month post intervention, that acupressure requires greater time to demonstrate treatment efficacy (Yue et al., 2013). Kang et al. (2009) also reported significant gains in upper extremity range of motion, grip strength, and a reduction in pain following meridian acupressure compared to standard care. Hua-feng et al. (2014) investigated the therapeutic efficacy of balancing yin-yang manipulation with conventional needling manipulation, and reported significant between-group differences, favouring balancing yin-yang manipulation, on outcomes of upper extremity function, including spasticity and electromyography. The mechanisms as to why acupressure may be efficacious for the improvement of upper limb function remains unclear, Yue et al. (2013) suggest that the stimulation of acupoints may assist in the releasing of neurohormones and neurotransmitters, and could potentially generate electromagnetic signals. It has also been postulated that acupressure may stimulate
the release of endorphins, thereby reducing pain (Kang et al., 2009). Further research is required to assess the efficacy of acupressure and to investigate the potential hormonal reactions in order to bring clarity to the mechanisms underlying this intervention.

**Conclusions Regarding Meridian Acupressure**

*There is level 1a and limited level 2 evidence that meridian acupressure may improve spasticity, upper limb motor function, range of motion of the upper limb, and performance of activities of daily living.*

Limited evidence indicates a potential benefit of meridian acupressure on upper limb motor function, performance of activities of daily living, and pain post-stroke.

**10.11.3 Traditional Chinese Herbal Medicine (TCHM)**

Traditional Chinese Herbal Medicine (TCHM) has been used routinely in China for the past 30 years in the treatment of ischemic stroke, despite a lack of empirical evidence investigating its safety and effectiveness. Traditional medicines may help to promote stroke recovery by reducing cerebral edema, dilating cardiocerebral vessels, inhibiting the aggregation of platelets, improving circulation and enhancing ischemic reperfusion injury (Sze, Yeung, Wong, & Lau, 2005).

Wu et al. (2007) assessed the strength of the existing evidence regarding the 59 TCHMs used following stroke. Only 22 medicines have been evaluated by either a RCT or controlled trial. The most commonly evaluated medicines were: Milk vetch, Mailuoning, Ginko biloba, Danshen agents, Xuesetong, Puerarin and Acanthopanax. The use of TCHM was not associated with an improvement in the odds of death or dependency (OR=0.86, 95% CI, 0.35 to 2.11); however, there was an increase in the odds of neurological deficit improvement after treatment (OR= 3.93, 95% CI 3.14 to 3.65), although the methodological quality of the trials was generally poor. Only 3 RCTs were described as being definitively randomized, double-blind and placebo controlled.

Dan Shen is one of the most widely used forms of TCHM. It comes from the root of the plant *Salvia militorrhiza*. An updated Cochrane review identified six RCTs that compared Dan Shen to a placebo or open placebo control following ischemic stroke (B. Wu et al., 2007). After two weeks of therapy Dan Shen compounds were associated with significant neurological improvements (OR=3.02, 95% CI 1.73 to 5.26). No deaths were reported. However, the quality of the trials was poor and too few patients were included to provide reliable estimates of the treatment effect. The authors of the review recommended that additional high-quality RCTs need to be performed.

Pooled analysis of modified Edinburgh-Scandinavian Stroke Scale (MESSS) scores and TNA-α levels in a systematic review on *Qingkailing*, an acclaimed famous CHM to treat cerebrovascular conditions, suggested *Qingkailing* to be beneficial for patients with ischemic stroke when combined with conventional treatment (Cheng et al., 2012). However, no significant difference in terms of mortality between the two groups.

The results of RCTs evaluating CHM are summarized in Table 10.11.3.1.

**Table 10.11.3.1 Summary of RCTS Assessing Traditional Chinese Herbal Medicine for the Upper Extremity**
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>PEDro Score</th>
<th>Intervention</th>
<th>Main Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al. (2012)</td>
<td>RCT (9) N=68</td>
<td>E: Astalagus Membranaceus C: Placebo</td>
<td>• FIM (+)  • Barthel Index (-)  • Modified Rankin Scale (-)</td>
</tr>
<tr>
<td>Goto et al. (2009)</td>
<td>RCT (6) N=31</td>
<td>E: Tokishakuyakusan C: No treatment</td>
<td>• Stroke Impairment Assessment Scale (+)  • FIM (+)</td>
</tr>
<tr>
<td>Yu et al. (2015)</td>
<td>RCT (4) N_{Start}=100 \ N_{End}=87</td>
<td>E: Di Huang Yin Zi (DHYZ) Herbal Drug + physio/occupational therapy C: Placebo + physio/occupational therapy</td>
<td>• Barthel index (+)  • Fugl-Meyer Assessment (+)</td>
</tr>
</tbody>
</table>

\(-\) Indicates non-statistically significant differences between treatment groups  
\(+\) Indicates statistically significant differences between treatment groups

**Discussion**

Tokishakuyakusan was associated with prevention of worsening impairment and disability in the chronic phase of stroke among a small sample of elderly (> 80 years) stroke patients living in an institution (Goto et al., 2009). The mechanism through which benefit is conferred is not well-understood. Based on previous studies, Goto et al. (2009) suggest that the antioxdant, antiplatelet and muscle weakness amelioration properties of Tokishakuyakusan which may contribute towards potential positive outcomes. It is also believed to be neuroprotective and may enhance the synthesis and release of neurotransmitters including acetylcholine, dopamine and norepinephrine.

The Chinese herb *Astragalus membranaceus* (AM) has anti-inflammatory and antioxidative properties which are thought to help reduce brain edema if administered within the first few hours following stroke onset, thereby helping to improve functional recovery. The results from one small, but methodologically rigorous study indicate there is emerging evidence to support that this treatment may be effective following hemorrhagic stroke. Chen et al. (2012) reported significantly higher FIM gains among those taking AM which may have been the result of decreased inflammation; however, no differences in Barthel Index or Modified Rankin Scale were observed when compared with a placebo group.

Di Huang Yin Zi (DHYZ) is a herbal drug was shown in a study by Yu et al. (2015) to improve upper limb motor function and level of independence in comparison to a placebo.

**Conclusions Regarding Traditional Chinese Herbal Medicine**

There is level 1b conflicting evidence regarding the effectiveness of Astragalus Membranaceus for improving functional independence and performance in activities of daily living after hemorrhagic stroke.

There is level 1b evidence that Tokishakuyakusan improves functional independence and performance in activities of daily living in the chronic stage of stroke.

Limited evidence regarding the use of Traditional Chinese Herbal Medicine suggests potential benefits of improved functional independence after stroke.
10.11.4 Massage Therapy

“Massage is the practice of applying structured pressure, tension, motion or vibration — manually or with mechanical aids — to the soft tissues of the body, including muscles, connective tissue, tendons, ligaments, joints and lymphatic vessels, to achieve a beneficial response. As a form of therapy, massage can be applied to parts of the body or successively to the whole body, to heal injury, relieve psychological stress, manage pain, and improve circulation. Where massage is used for its physical and psychological benefits, it may be termed “therapeutic massage therapy” or manipulative therapy.”

Massage is among the most frequently used alternative nursing interventions and has been used as a complementary form of treatment following stroke (Holland & Pokorny, 2001). Several studies have evaluated the efficacy of massage therapy; the results of the controlled trials are summarized in Table 10.11.4.1.

Table 10.11.4.1 Summary of Controlled Trials Assessing Massage Therapy for the Upper Extremity

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>PEDro Score</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang et al. (2016)</td>
<td>RCT (8)</td>
<td>NStart=90 NEnd=79</td>
<td>E: Chinese massage therapy C: Placebo</td>
<td>• Fugl-Meyer Assessment (-) • Modified Barthel Index (-)</td>
</tr>
<tr>
<td>Thanakiatpinyo et al. (2014)</td>
<td>RCT (7)</td>
<td>NStart=50 NEnd=45</td>
<td>E: Thai massage C: Physical therapy</td>
<td>• Modified Ashworth Scale (-) • Barthel Index (-) • Anxiety and depression scores (-) • Quality of life (-)</td>
</tr>
<tr>
<td>Fox et al. (2006)</td>
<td>PCT</td>
<td>N=30</td>
<td>E: Marma therapy C: Standard care</td>
<td>• Motricity Index: 6wk (+), 12wk (+) • Nine Hole Peg Test: 12 wk (+ for control)</td>
</tr>
<tr>
<td>Van der Riet et al. (2015)</td>
<td>PCT</td>
<td>NStart=40 NEnd=40</td>
<td>E: Hot compression + thai massage + strength training C: Education</td>
<td>• Barthel Index (+) • Visual Analog Scale (-)</td>
</tr>
</tbody>
</table>

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Discussion

Yang et al. (2016) found that Chinese massage therapy did not improve upper limb motor function or performance on activities of daily living when compared to those receiving a placebo.

Thanakiatpinyo et al. (2014) investigated the use of traditional Thai massage compared with physical therapy and reported no differences between groups in regards to quality of life, spasticity, or level of independence. Although the findings are promising, it should be noted that both upper and lower extremity limbs were treated and evaluated without stratification, therefore future research should investigate Thai massage with a focus on upper extremity function.

Van der Riet et al. (2015) found that those receiving a hot compression, thai massage, and strength training had improved Barthel Index scores compared to those only receiving education alone. This suggests that hot compression with thai massage and strength training may improve performance of activities of daily living, although further studies are needed to confirm this observation.
Fox et al. (2006) was the only study that reported on the effectiveness of Marma therapy, a stroke-specific form of massage therapy. The Marma therapy group demonstrated significantly greater Motricity Index scores, indicating improvement in upper limb function. However, outcomes measuring hand dexterity using the 9-Hole Peg Test were found to be in favour of the control group. Further research regarding Marma therapy is warranted.

**Conclusions Regarding Massage Therapy**

*There is level 1a evidence that Chinese or Thai massage therapy does not improve functional independence or performance on activities of daily living.*

*There is level 1b evidence that Chinese or Thai massage therapy does not improve upper limb motor function, spasticity, or quality of life.*

**Massage Therapy likely does not improve functional independence, spasticity, hand dexterity, or quality of life after a stroke.**

### 10.11.5 Cupping

Cupping therapy is a technique which uses glass or plastic cups to create localized pressure by a vacuum. The vacuum inside the cups causes blood to form within the underlying area, which helps with healing in that area. Cupping is used most frequently for lower back pain. There are two types of cupping - wet and dry. In dry cupping, a vacuum is created which pulls the skin into the cup. In wet cupping, the skin is lacerated such that blood is drawn into the cup. Cupping is believed to help release harmful toxins by triggering the lymphatic system, and clearing the blood vessels.

A systematic review including the results from 5 studies (3 RCTs and 2 uncontrolled trials), all originating from China, examined the use of cupping in stroke rehabilitation (Lee, Choi, Shin, Han, & Ernst, 2010). Both wet and dry cupping were used as a treatment for painful shoulder, hand edema, upper limb myodynamia, aphasia, and hiccup following stroke, with acupuncture as the control condition in the RCTs. Although there was a benefit of treatment with respect to shoulder pain intensity and range of motion and reduction of myodynamia, the authors concluded that there was insufficient evidence to support the effectiveness of cupping treatment.

### 10.11 Treatment of Hand Edema

Hand edema following stroke with hemiparesis is associated with pain and stiffness, which can lead to a decrease in active motion and disuse. Hand edema may be an isolated problem or occur as a symptom of shoulder-hand syndrome. The etiology of the development of hand edema is unclear. The most widely accepted explanation is that of increased venous congestion related to prolonged dependency and loss of muscle pumping function in the paretic limb (Leibovitz et al., 2007).

Diagnosis is difficult and depends, in part, on the method of assessment. Estimates of the incidence of hand edema vary widely. Tepperman et al. (1984) reported that 83% of 85 acute stroke patients suffered from hand edema not associated with shoulder-hand syndrome. More recently, Post et al. (2003) reported that based on volumetric assessments, 33% of 96 stroke patients had hand edema, compared to 50% of patients assessed through clinical evaluation. Volumetric assessments of the hand...
appear to provide the best estimation; while the reliability of clinical evaluation through visual inspection is poor. A change of 12 mL or more is considered clinically significant (Post et al., 2003).

Using data from the same patient group as Post et al. (2003), Boomkamp-Koppen et al. (2005) reported a significant correlation between the presence of hand edema and measures of hand function (as measured by the Frenchay arm test). Patients without hand edema were more likely to have good hand function. Significant predictors of hand function following stroke included the degree of motor impairment, hypertonia, tactile inattention, and edema. In contrast, Gebruers et al. (2011) reported finding no relationship between activity limitations and the presence of edema in a cohort of 130 acute stroke patients followed over a period of 3 months. There were no statistically significant differences on a variety of clinical indications, including stroke severity and Fugl-Meyer Scale scores between the group of patients who developed edema and those who did not. The authors concluded that the theory suggesting that disuse in the paretic limb is the major cause of the development of hand edema is unlikely to be true. The incidence of edema was also lower in this study.

Leibovitz et al. (2007) compared the circumference of the hand in three places (mid-finger, hand and wrist) among subjects post stroke (m=188) and non-parietal institutionalized controls (n=70). Hand edema was detected in 37% of post stroke subjects compared with only 2% of control subjects.

Three different treatment approaches to aid in the reduction of hand edema following stroke have been studied, including passive range of motion exercises, neuromuscular stimulation and intermittent pneumatic compression. The results of a single RCT are presented in table 10.12.1.

<table>
<thead>
<tr>
<th>Author, Year PEDro Score Sample Size</th>
<th>Intervention</th>
<th>Main Outcome(s) Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Roper et al. (1999)</strong></td>
<td>E: Intermittent pneumatic compression + standard physiotherapy</td>
<td>• Motricity index (-)</td>
</tr>
<tr>
<td>N=37</td>
<td>C: Standard physiotherapy</td>
<td>• Hand volume (-)</td>
</tr>
</tbody>
</table>

+ Indicates a statistically significant difference between treatment groups
- Indicates a non-statistically significant difference between treatment groups

**Discussion**
Only one low-scoring RCT has been completed on the treatment of hand edema. Intermittent pneumatic compression combined with standard physiotherapy did not add any value when compared to standard physiotherapy alone according to hand volume and Motricity Index scores although greater improvements favoured the combined treatment group (Roper et al., 1999). One possible explanation was the working pressure of 50mmHg, 4 hours a day, was not sufficient for a treatment effect given that previous research used pressures of 80 to 130mmHg (Roper et al., 1999). However, the authors note that higher pressure can lead to discomfort. Further research is required to determine the efficacy of pneumatic compression but at the present, Roper et al. (1999) suggest this method not be recommendable in treating hand edema.

**Conclusions Regarding Intermittent Pneumatic Compression for Hand Edema**

*There is level 1b evidence that intermittent pneumatic compression does not reduce hand edema or strength in the upper extremity following stroke.*
Intermittent pneumatic compression does not appear to reduce hand edema or improve upper limb strength post stroke.
Summary

1. There is consensus opinion that in severely impaired upper extremities (less than stage 4) the focus of treatment should be on compensation.

2. For those upper extremities with signs of some recovery (stage 4 or better) there is consensus that attempts to restore function through therapy should be made.

3. There is level 1a evidence that neurodevelopmental techniques are not superior to other therapeutic approaches.

4. There is level 1b evidence that when compared to the Bobath treatment approach, Motor Relearning Programme may be associated with improvements in short-term motor functioning, shorter lengths of hospital stay and better movement quality.

5. There is level 1b evidence that Brunnstrom hand manipulation treatment is preferable over a motor relearning program.

6. There is level 1a evidence that bilateral training is not more effective than unilateral training for upper limb motor function outcomes.

7. There is level 1a evidence that bilateral training is not more effective than conventional therapies such as modified constraint induced movement therapy and cutaneous electrical stimulation.

8. There is level 1a evidence that bilateral arm training with rhythmic auditory cueing (BATRAC) is not more effective than unilateral arm training.

9. There is level 1a evidence that arm function training, task practice, and strength training provide significant functional improvements in the arm after stroke in comparison to similar leg training.

10. There is level 1a evidence that additional upper limb therapy is not superior to conventional therapy at improving upper extremity motor function or functional independence.

11. There is level 1b evidence that a therapist-supervised in-home program is not more effective than usual care at improving upper limb motor function.

12. There is level 1a evidence from a meta-analysis that strength training increases grip strength following stroke.

13. There is level 1a evidence that strength training improves upper limb motor function and shoulder range of motion.

14. There is level 1a evidence that task-related practice may be superior to conventional training at improving upper extremity motor function.

15. There is level 1b evidence that task-related training may not be superior to resistive training or bilateral arm training at improving general upper limb motor function; however, it may improve reaching arm movements.

16. There is level 1b evidence that combining task practice with active stimulation may improve manual dexterity and reaction time.
17. There is conflicting level 1a evidence regarding the efficacy of trunk restraint therapy on upper extremity function when combined with constraint induced movement therapy or delivered alone.

18. There is level 1a evidence that transcutaneous electrical nerve stimulation (TENS) improves upper limb motor function.

19. There is level 1a evidence that focal or whole-body vibration therapy improves upper limb motor function.

20. There is level 1a evidence that peripheral nerve/afferent stimulation does not significantly improve overall upper limb motor function.

21. There is level 1a evidence that mesh glove therapy improves motor function and dexterity based on the Box and Block test.

22. There is level 1b evidence that thermal stimulation is effective for upper limb motor function.

23. There is level 1a evidence that electroacupuncture is not more effective than an active control for improving upper limb motor function.

24. There is level 1a evidence that mental practice therapy is effective for improving upper extremity motor function; however, the evidence for its effect on activities of daily living is limited and conflicting.

25. There is level 1a evidence that motor imagery is not effective for improving upper extremity motor function.

26. There is level 1a that hand splinting/taping/orthoses do not improve upper extremity motor function.

27. There is level 1b and level 2 evidence that there is no benefit of CIMT in the early stage of stroke for improving upper limb motor function or dexterity.

28. There is level 1a evidence that CIMT in the chronic phase of stroke may help improve upper extremity motor function. The evidence regarding the ideal frequency of CIMT is currently unclear.

29. There is level 1a evidence that mCIMT in the early phase of stroke may improve adaptation strategies as it optimizes already preserved function. However, mCIMT does not improve neurological impairment in the early stage of stroke.

30. There is level 1a evidence that mCIMT in the chronic phase of stroke may improve upper limb function relative to conventional therapy.

31. There is level 1a evidence that mirror therapy improves upper limb motor function following stroke, especially for the wrist and hand.

32. There is level 1b evidence that Mirror therapy in combination with conventional therapy is not superior to the Bobath method for upper limb motor function.
33. There is conflicting level 1a evidence regarding the effect of mirror therapy on spasticity.

34. There is level 1a evidence that feedback is effective for improving upper limb motor function, and that it is ineffective for improving spasticity.

35. There is conflicting level 1a evidence regarding the effect of action observation on upper motor function.

36. There is level 1b evidence that action observation with brain-computer interface-based functional electrical stimulation is effective for improving upper limb motor function.

37. There is level 1a and level 1b evidence that music therapy can improve some aspects of upper extremity motor function but not muscle strength when compared to conventional rehabilitation.

38. There is level 1a evidence that telerehabilitation interventions are not effective for improving upper limb motor function.

39. There is conflicting evidence regarding the effectiveness of additional exercise therapy for improving upper limb motor function.

40. There is level 1a and 2 evidence in the acute phase and level 1a evidence in the chronic phase that MIT-Manus/InMotion therapies are no more effective than a control for improving upper limb motor function in the chronic phase.

41. There is level 2 evidence that Mirror-Image Motion Enabler Robots (MIME) are effective in the acute phase, level 2 evidence that (MIME) are not effective in the subacute phase, and level 1a conflicting evidence for the effectiveness in the chronic phase for improving upper limb motor function.

42. There is conflicting level 1b and 2 evidence for the use of ARMin during the chronic phase for improving upper limb motor function.

43. There is level 2 evidence that ARM Guide is not effective for improving upper limb motor function.

44. There is level 1b evidence during the acute phase that Bi-Manu-Track is not effective, level 1a conflicting evidence for the subacute phase, and level 1a evidence during the chronic phase that Bi-Manu-Track is effective for improving upper limb motor function.

45. There is conflicting level 2 evidence for the use of NeReBot during the acute phase, and level 1b evidence that NeReBot is not effective during the chronic phase for improving upper limb motor function.

46. There is level 2 evidence that Continuous Passive Motion (CPM) is not effective during the acute phase, and there is level 2 evidence that CPM is effective during the chronic phase for improving upper limb motor function.

47. There is level 1a evidence that the use of GENTLE during the chronic phase is not effective for improving upper limb motor function.
48. There is level 1b evidence that the use of Amadeo during the acute phase is effective, while there is level 1b evidence that the use of Amadeo during the chronic phase is not effective for improving upper limb motor function.

49. There is conflicting level 1a evidence regarding the effectiveness of MusicGlove during the chronic phase.

50. There is level 1a evidence that virtual reality does not improve upper limb motor function in the chronic stroke phase.

51. There is level 1a evidence that computer brain interface technology is not effective for improving upper limb motor function post-stroke.

52. There is level 1a evidence that splinting does not reduce the development of contracture nor reduce spasticity in the upper extremity.

53. There is level 1b evidence that a nurse-led stretching program may improve range of motion in the upper extremity and reduce pain in the chronic stage of stroke.

54. There is level 1b and 2 evidence that a hand stretching device may improve spasticity in the upper limb.

55. There is level 1a evidence that treatment with botulinum toxin significantly reduces spasticity in the upper extremity in stroke survivors.

56. There is level 1a evidence that treatment with botulinum toxin does not improve upper limb motor function.

57. There is level 1a evidence that electrical stimulation combined with botulinum toxin injection is associated with reductions in spasticity.

58. There is level 1b evidence that modified constraint induced movement therapy combined with botulinum toxin injection is associated with reductions in spasticity.

59. There is level 4 evidence that nerve blocks with ethyl alcohol improves elbow and finger passive range of motion and can decrease spasticity in the upper extremity in stroke survivors.

60. There is level 1a evidence that physical therapy may not improve motor function or contracture.

61. There is level 1a evidence that neuromuscular electrical stimulation does not reduce wrist or elbow spasticity.

62. There is level 1a evidence that extracorporeal shock wave therapy improves upper limb spasticity.

63. There is level 1b evidence that tolperisone can reduce spasticity following stroke.

64. There is level 1a evidence that EMG/biofeedback therapy does not improve upper extremity motor function or spasticity.

65. There is level 1a and level 2 evidence that FES/NMES may improve upper limb motor function, range of motion, and manual dexterity when offered in combination with conventional therapy or
delivered alone in subacute stroke. The evidence is also indicative of a beneficial effect on range of motion and manual dexterity when FES/NMES was offered to chronic stroke patients either alone or in combination with other therapies.

66. Despite improvements in both stages of stroke recovery, level 1b evidence indicates that delivering FES early (<6 months) may be more beneficial at recovering impaired motor function than delivering FES after 6 months post-stroke.

67. There is level 1b evidence that EMG-NMES in the subacute phase is not more effective than usual care for patients with an unfavourable prognosis based on voluntary finger extension.

68. There is level 1a evidence that high intensity NMES or FES exercise is no more effective for improving upper limb motor function than low intensity NMES or FES in the subacute phase.

69. There is level 1a and level 2 evidence that both EMG-triggered and cyclic approaches to NMES/electrical stimulation may improve upper limb motor function and range of motion in subacute and chronic stroke patients; however, evidence indicates no superior benefit of EMG-triggered NMES over cyclic or passive NMES at improving upper limb motor function in chronic (level 1a) and subacute (level 1b) stroke patients.

70. There is level 1b evidence that Contralaterally Controlled FES is not superior to cyclic NMES for improving upper limb motor function, although it may improve dexterity.

71. There is level 1b evidence that coupling continuous NMES with repetitive facilitative exercise may be beneficial at improving general upper extremity function and range of motion during elbow extension but not during shoulder or wrist flexion in subacute stroke patients.

72. There is level 1b evidence that high frequency NMEs may be superior to low frequency NMES at improving endurance of thumb adduction, lateral pinch strength and manual dexterity in chronic stroke individuals.

73. There is level 1a evidence that motor cortex stimulation does not improve upper limb motor function.

74. There is level 1b evidence that vagus nerve stimulation can improve overall upper limb motor function, but not dexterity or grip strength.

75. There is level 1a conflicting evidence regarding the effectiveness of low-frequency (1Hz) rTMS for the improvement of upper limb motor function and dexterity. There is also level 1a evidence that inhibiting rTMS does not improve upper limb spasticity when compared to sham stimulation.

76. There is level 1a evidence that high-frequency rTMS (≥5 Hz) improves upper limb motor function, dexterity, and grip strength when compared to sham stimulation.

77. There is level 1a evidence that there is no significant difference between inhibitory and excitatory rTMS for improving upper limb motor function or grip strength.

78. There is level 1b evidence that dual rTMS (the combination of both inhibitory and excitatory rTMS) improves upper limb motor function, but not grip strength when compared to sham stimulation.
79. There is level 1b and level 2 evidence that iTBS improves upper limb motor function, but not dexterity, in the acute or subacute period after stroke.

80. There is conflicting level 1a evidence that iTBS improves upper limb motor function and dexterity in the chronic phase after stroke. There is level 1b and level 2 evidence that iTBS improves spasticity in the chronic phase after stroke.

81. There is level 1a evidence that cTBS does not improve upper extremity motor function or dexterity following stroke.

82. There is level 1a evidence that anodal tDCS does not improve upper limb motor function, spasticity, or grip strength. There is conflicting level 1a evidence regarding whether anodal tDCS improves dexterity.

83. There is level 1a conflicting evidence for the effectiveness of cathodal tDCS for improving upper limb motor function, dexterity grip strength, and activities of daily living.

84. There is level 1a evidence that anodal and cathodal tDCS do not significantly differ on measures of motor function, dexterity, or on measures of independence/daily living.

85. There is level 1a evidence that dual tDCS (both anodal and cathodal tDCS administered at the same time) is effective for improving dexterity. There is level 1a conflicting evidence regarding the effectiveness of dual tDCS for improving grip force.

86. There is level 1b evidence that coupling methylphenidate with tDCS may improve hand function relative to when tDCS or methylphenidate are delivered alone.

87. There is level 1b evidence that combining tDCS with computer brain interface training may not improve spasticity or upper extremity motor function.

88. There is level 1a evidence that delivering stimulants in combination with additional therapy may improve upper extremity function; however, level 1b evidence suggests that grip strength may not improve.

89. There is Level 1b evidence that stimulants may only be effective at improving impaired upper limb function in the short term.

90. There is level 1b evidence that Levodopa may not improve arm and hand function however, level 2 evidence suggests that reaction time may be improved.

91. There is level 1a evidence that fluoxetine and nortriptyline may improve overall disability and upper extremity motor function.

92. There is level 1a that citalopram, reboxetine and lithium carbonate may enhance impaired arm and hand function however, level 1b evidence indicates that citalopram may not be effective at improving hand grip strength.

93. There is level 1b evidence that intra-articular steroid injections may not improve pain or range of motion of the upper extremity; however, limited level 2 evidence provides conflicting findings.
94. There is level 1b evidence that d-cycloserine delivered in combination with constraint-induced movement therapy may not improve upper extremity motor function.

95. There is limited level 2 evidence that ozonated autohemotherapy may improve general motor disability.

96. There is level 1a evidence that Cerebrolysin improves upper limb motor function.

97. There is level 1b evidence that Cerebrolysin improves dexterity and measures of independence/daily living.

98. There is level 1b evidence that NeuroAid does not improve upper limb motor function.

99. There is level 1b evidence that phosphodiesterase-5 inhibitor does not improve dexterity, grip strength, or level of independence/daily living.

100. There is level 1b evidence that Atorvastatin improves level of independence / activities of daily living.

101. There is level 1a evidence from high-quality, high-powered studies that acupuncture does not improve upper extremity motor function or performance of activities of daily living.

102. There is conflicting level 1a evidence regarding the effect of acupuncture on spasticity.

103. There is level 1a and limited level 2 evidence that meridian acupressure may improve spasticity, upper limb motor function, range of motion of the upper limb, and performance of activities of daily living.

104. There is level 1b conflicting evidence regarding the effectiveness of Astralagus Membranaceus for improving functional independence and performance in activities of daily living after hemorrhagic stroke.

105. There is level 1b evidence that Tokishakuyakusan improves functional independence and performance in activities of daily living in the chronic stage of stroke.

106. There is level 1a evidence that Chinese or Thai massage therapy does not improve functional independence or performance on activities of daily living.

107. There is level 1b evidence that Chinese or Thai massage therapy does not improve upper limb motor function, spasticity, or quality of life.

108. There is level 1b evidence that intermittent pneumatic compression does not reduce hand edema or strength in the upper extremity following stroke.
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