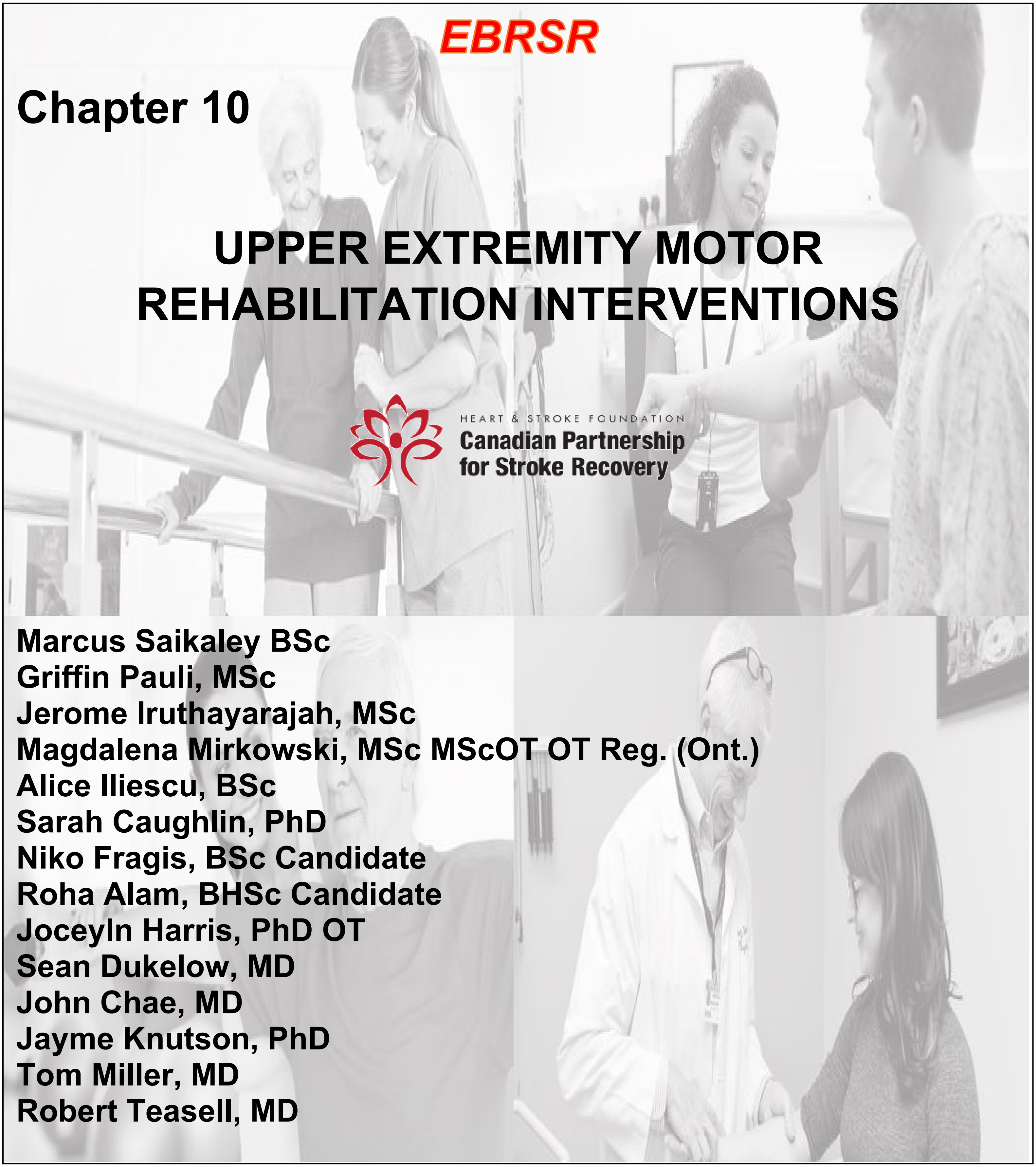

EBRSR

Chapter 10

UPPER EXTREMITY MOTOR REHABILITATION INTERVENTIONS

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Chapter 10: Upper Extremity Motor Rehabilitation Interventions Table of contents

Key Points

Bobath concept approaches and motor relearning programmes may not be beneficial for upper limb rehabilitation following stroke.

Brunnstrom movement therapy may be more beneficial than motor relearning programmes for upper limb function.

The literature is mixed regarding bilateral arm training for upper limb rehabilitation following stroke.

Bilateral arm training may not be beneficial compared to unilateral training for upper limb function.

Bilateral arm training in combination with other therapy approaches may not be beneficial for upper limb rehabilitation.

The literature is mixed regarding strength training and functional strength training for upper limb rehabilitation following stroke.

Task-specific training, alone or in combination with other therapy approaches, may be beneficial for some aspects of upper limb function following stroke.

Higher and lower intensity task-specific training may have similar effects on upper limb function.

Constraint-induced movement therapy may be beneficial for upper limb rehabilitation in the chronic phase following stroke.

The literature is mixed regarding constraint-induced movement therapy for upper limb rehabilitation in the subacute/acute phase following stroke.

Modified constraint-induced movement therapy may be beneficial for upper limb rehabilitation in the chronic phase following stroke.

Modified constraint-induced movement therapy may not be beneficial for upper limb rehabilitation in the subacute/acute phase following stroke.

Higher and lower intensity constraint-induced movement therapy may have similar effects on upper limb function in the chronic phase following stroke.

The literature is mixed regarding constraint-induced movement therapy in combination with other therapy approaches for upper limb rehabilitation following stoke.

Trunk restraint with reaching training or distributed constraint induced therapy may improve some aspects of upper limb function following stroke, but the effect of combining trunk restraint with constraint-induced movement therapy is less clear.

Stretching programs may improve some aspects of upper limb function following stroke.

Orthotics may not be beneficial for upper limb rehabilitation following stroke.

Mirror therapy on its own or in combination with other interventions can improve many aspects of upper limb function following stroke.

Mental practice, alone or in combination with constraint-induced movement therapy, may be beneficial for upper limb rehabilitation following stroke.

Mental practice in combination with virtual reality training may not be beneficial for upper limb function.

Action observation may be beneficial for some aspects of upper limb function following stroke.

The literature is mixed regarding music therapy for upper limb rehabilitation following stroke.

The literature is mixed regarding telerehabilitation for upper limb rehabilitation following stroke.

The evidence is mixed regarding arm/shoulder end-effector robotics, alone or in combination with other therapy approaches, for upper limb rehabilitation following stroke.

The evidence is mixed regarding arm/shoulder exoskeleton, hand exoskeleton, and hand end-effector robotics for upper limb rehabilitation.

Virtual therapy alone may not be more beneficial than conventional therapy for upper limb rehabilitation following stroke, however it may be beneficial for certain aspects of upper limb function when used in combination with conventional or other therapy approaches.

The literature is mixed regarding brain-computer interface technology for upper limb motor rehabilitation following stroke, either on its own or combined with other therapies, but it may not be beneficial alone for other aspects of upper limb function.

The literature is mixed regarding EMG biofeedback alone for upper limb rehabilitation following stroke, however it may not be beneficial when combined with other therapy approaches.

The literature is mixed regrading cyclic and EMG-triggered neuromuscular electrical stimulation types, as well as functional electrical stimulation, alone or combined with other therapy approaches, for upper limb rehabilitation following stroke.

The various types of neuromuscular electrical stimulation may not be more beneficial compared to one another.

Transcutaneous electrical nerve stimulation may be beneficial for some aspects of upper limb function following stroke.

Noxious thermal stimulation may not be beneficial for upper limb rehabilitation following stroke, whereas innocuous thermal stimulation may improve some aspects of upper limb function.

Muscle vibration may be beneficial for improving upper limb function following stroke.

The literature is mixed regarding additional afferent and peripheral stimulation for upper limb rehabilitation following stroke.

The literature is mixed regarding invasive cortical and nerve stimulation for upper limb rehabilitation following stroke.

The literature is mixed regarding low frequency repetitive transcranial magnetic stimulation, alone or in combination with other therapy approaches, for upper limb rehabilitation following stroke.

High frequency repetitive transcranial magnetic stimulation, alone or in combination with other therapy approaches, may be beneficial for upper limb rehabilitation.

The literature is mixed regarding bilateral repetitive transcranial magnetic stimulation for upper limb rehabilitation.

Theta burst stimulation alone may not be beneficial for upper limb function following stroke, however it may be beneficial for certain aspects of upper limb function when used in combination with repetitive transcranial magnetic stimulation.

The literature is mixed regarding anodal, cathodal, or dual transcranial direct current stimulation, alone or in combination with other therapy approaches, for upper limb rehabilitation following stroke.

Botulinum A likely improves spasticity in the upper limb following stroke, but not range of motion or activities of daily living. The effect on general upper limb motor function is conflicting and less clear.

Botulinum toxin A in combination with other types of therapeutic approaches may be beneficial for certain aspects of upper limb function.

Botulinum toxin B has been less well studied to date in comparison to botulinum toxin A.

Steroid injections may not be beneficial for upper limb rehabilitation following stroke.

Cerebrolysin may be beneficial for aspects of upper limb function following stroke.

The evidence is mixed regarding Levodopa for upper limb rehabilitation following stroke.

The evidence is mixed regarding atorvastatin for upper limb rehabilitation following stroke.

Antidepressants may be beneficial for aspects of upper limb function following stroke.

Dexamphetamine or methylphenidate may be beneficial for aspects of upper limb function following stroke.

Methylphenidate combined with dual transcranial direct current stimulation may be beneficial for upper limb rehabilitation following stroke.

The evidence is mixed regarding acupuncture alone for upper limb rehabilitation following stroke. Acupuncture combined with conventional or other therapy approaches may not be beneficial for upper limb function. Some forms of acupuncture may be more beneficial than others.

Electroacupuncture with neuronavigation-assisted aspiration may be beneficial for upper limb rehabilitation following stroke, however the evidence is mixed regarding electroacupuncture and transcutaneous electrical acupoint stimulation.

Both meridian acupressure and massage therapy may be beneficial for some aspects of upper limb function following stroke.

Modified Sackett Scale

Level of evidence	Study design	Description
Level 1a	Randomized controlled trial (RCT)	More than 1 higher quality RCT (PEDro score ≥6).
Level 1b	RCT	1 higher quality RCT (PEDro score ≥6).
Level 2	RCT	Lower quality RCT (PEDro score <6).
	Prospective controlled trial (PCT)	PCT (not randomized).
	Cohort	Prospective longitudinal study using at least 2 similar groups with one exposed to a particular condition.
Level 3	Case Control	A retrospective study comparing conditions, including historical cohorts.
Level 4	Pre-Post	A prospective trial with a baseline measure, intervention, and a post-test using a single group of subjects.
	Post-test	A prospective post-test with two or more groups (intervention followed by post-test and no re-test or baseline measurement) using a single group of subjects
	Case Series	A retrospective study usually collecting variables from a chart review.
Level 5	Observational	Study using cross-sectional analysis to interpret relations. Expert opinion without explicit critical appraisal, or based on physiology, biomechanics or "first principles".
	Case Report	Pre-post or case series involving one subject.

New to the 19th Edition of the Evidence-based Review of Stroke Rehabilitation

1) PICO conclusion statements

This edition of Chapter 10: Upper extremity motor rehabilitation interventions synthesizes study results from only randomized controlled trials (RCTs), all levels of evidence (LoE) and conclusion statements are now presented in the Population Intervention Comparator Outcome (PICO) format.

For example:

Population: Stroke survivors

Intervention **Comparator**

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Bilateral arm training** may not have a difference in efficacy when compared to **TENS** for improving spasticity.	1	Stinear et al. 2014

Outcome

New to these statements is also the use of colours where the levels of evidence are written.

Red statements like above, indicate that the majority of study results when grouped together show no significant differences between intervention and comparator groups.

Green statements indicate that the majority of study results when grouped together show a significant between group difference in favour of the intervention group.

For example:

Population: Stroke survivors

Intervention

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Bilateral arm training** may produce greater improvements in motor function than **conventional therapy**.	4	Meng et al. 2018; Lee et al. 2017; Stinear et al. 2008; Desrosiers et al. 2005

Outcome **Comparator**

Yellow statements indicate that the study results when grouped together are mixed or conflicting, some studies show benefit in favour of the intervention group, while others show no difference between groups.

For example:

Population: Stroke survivors

Outcome **Intervention**

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **CIMT** to improve dexterity when compared to **conventional therapy or motor relearning programmes** during the acute/subacute phase poststroke.	4	Shah et al. 2016; Yoon et al. 2014; Boake et al. 2007; Ro et al. 2006

Comparator

2) Upper extremity rehabilitation outcome measures

For the studies reviewed, upper extremity rehabilitation outcome measures were classified into the following broad categories to allow for synthesis of results and formulation of PICO conclusion statements:

Motor function: These outcome measures evaluated functional motor movements when using the upper extremities.

Dexterity: These outcome measures assessed fine motor and manual skills through a variety of tasks, particularly with the use of a stroke survivor's hand.

Activities of daily living: These outcome measures assessed performance and level of independence in various everyday tasks.

Spasticity: These outcome measures assessed changes in muscle tone, stiffness, and contractures.

Range of motion: These outcome measures assessed a patient's ability to freely move their upper extremity through flexion, abduction, and subluxation movements for instance, both passively and actively.

Proprioception: These outcome measures assessed sensory awareness about one's body and the location of limbs.

Stroke severity: These outcome measures assessed the severity of one's stroke through a global assessment of a multitude of deficits a stroke survivor may experience.

Muscle strength: These outcome measures assessed muscle power and strength during movements and tasks.

Outcome measures that fit these categories are described in the next few pages.

Outcome Measures Definitions

Motor Function

Action Research Arm Test (ARAT): Is a measure of activity limitation in the paretic arm that assesses a patient's ability to handle objects differing in size, weight and shape. The test evaluates 19 tests of arm motor function, both distally and proximally. Each test is given an ordinal score of 0, 1, 2, or 3, with higher values indicating better arm motor status. The total ARAT score is the sum of the 19 tests, and thus the maximum score is 57. This measure has been shown to have good test-retest reliability and internal validity when used to assess motor function in chronic stroke patients (Ward et al. 2019; Nomikos et al. 2018)

Brunnstrom Recovery Stages (BRS): Is a measure of motor function and muscle spasticity in stroke survivors. The measure contains 35 functional movements which are done with the guidance of a clinician (e.g. should abduction, shoulder adduction, leg flexion/extension). These movements are evenly divided into 2 sections: upper extremity and lower extremity. Each movement is then rated on a 6-point scale (1=Flaccidity is present, and no movements of the limbs can be initiated, 2=Movement occurs haltingly and spasticity begins to develop, 3=Movement is almost impossible and spasticity is severe, 4=Movement starts to be regained and spasticity begins to decline, 5=More difficult movement combinations are possible as spasticity declines further. 6=Spasticity disappears, and individual joint movements become possible). This measure has been shown to have good reliability and concurrent validity (Naghdi et al. 2010; Safaz et al. 2009).

Disabilities of the Arm, Shoulder and Hand (QuickDASH): Is a shortened version of DASH – a patient-reported outcome measure intended for upper extremity disorders. It consists of 11 items from the original 30-item DASH questionnaire, where each item has 5 response options, with scaled scores ranging from 0 (no disability) to 100 (most severe disability). The measure is shown to be valid and reliable in populations with upper extremity disorders (Gummesson et al. 2006; Salaffi et al. 2018).

Fugl-Meyer Assessment (FMA): Is an impairment measure used to assess locomotor function and control of the upper and lower extremities, including balance, sensation, and joint pain in patients poststroke. It consists of 155 items, with each item rated on a three-point ordinal scale. The maximum motor performance score is 66 points for the upper extremity section, 34 points for the lower extremity section, 14 points for the balance section, 24 points for sensation section, and 44 points each for passive joint motion and joint pain section, for a maximum of 266 points that can be attained. The upper extremity section consists of four categories (Shoulder/Elbow/Forearm, Wrist, Hand/Finger, and Coordination) and includes 23 different movements which evaluate 33 items. The items are scored on a 3-point rating scale: 0=unable to perform, 1=partial ability to perform and 2=near normal ability to perform. The measure is shown to have good reliability and construct validity (Okuyama et al. 2018; Villian-Villian et al. 2018; Nillson et al. 2001; Sanford et al. 1993).

Finger Oscillation Test (FOT): Measures motor control and speed and is used to help detect brain damage through motor dysfunction by assessing the speed of finger movement. It measures the maximal tapping speed of the index finger of each hand by requiring the patient to work the lever arm of a mechanical counter up and down as fast as he or she can. The average number of taps in a 10-second interval is determined, and the patient performs five trials. The measure is considered a reliable indicator of brain function (Prigatano et al. 2004; Eng et al. 2013).

Manual Function Test (MFT): Is an upper-limb function assessment measure used for evaluating proximal arm movements as well as fine and gross dexterity of hemiparetic patients after stroke. The test includes 8 subtests including forward and lateral elevation of arm, grasping, pinching, and pegboard manipulations, and ratings can range from 0 (severely impaired) to 32 (full function). The measure has been shown to have good reliability and validity (Miyamoto et al. 2009; Michimata et al. 2008).

Motor Club Assessment (MCA): Is a measure of functional movement that indicates balance and movement by assessing the range of active movement for shoulder shrugging, arm lifting, forearm supination, wrist cocking, and finger extension. Each movement is rated on a 3-point scale (where 0 = no movement, and 2 = full range of movement). (Sunderland et al. 1989)

Motor Evaluation Scale for Upper Extremity in Stroke Patients (MES-UE): Is a measure that assesses the quality of arm movement performance of the hemiparetic arm and hand in stroke patients. The scale encompasses 10 arm function items with six response categories (scores 0-5), nine hand function items with three response categories (scores 0-2), and three functional tasks with three response categories (scores 0-2). The measure is shown to be valid and reliable for measuring quality of arm movement in stroke patients (Van de Winckel et al. 2006).

Motor Status Scale (MSS): Is a measure of upper limb impairment and disability following stroke. It is divided into 4 sections and assesses shoulder, elbow/forearm, wrist and hand movements on a 6-point scale (maximum score = 82 points). This clinical scale is thought to provide a more complete measurement of upper-limb motor function than the FMA, as it evaluates the complete range of motor function of the upper limb by employing a finer grading of isolated movements. The scale has been shown to have good validity and reliability (Ferraro et al. 2002; Wei et al. 2011).

Rancho Los Amigos Functional Test for the Hemiparetic Upper Extremity (RLAFT-UE): Is a measure used to quantify functional movement ability of the hemiparetic arm in stroke patients. The test consists of a series 17 timed activities of daily living that focus on completion of everyday tasks involving the impaired limb (e.g., zipping a jacket, placing a pillow in a pillowcase). The tasks are arranged in seven levels by degree of difficulty ranging from simple single joint movements at the shoulder to complex multi-joint movements involving the hand and arm. The test has been shown to have high inter- and intra-rater reliability (Kahn et al. 2006; Wilson et al. 1984).

Rivermead Motor Assessment (RMA): Is a multi-faced measure that assesses gross motor function, leg and trunk movements and arm movements in post-stroke patients. The arm movements section consists of 15 items ranging from specific isolated movements (e.g. protracting shoulder girdle in supine position) to complex tasks (e.g. placing a string around the head and tying a bow at the back). Patients perform all movements actively, and dichotomous scores indicate either success (score 1) or failure (score 0). The measure is shown to have good test-retest reliability, content validity, and construct validity (Dong et al. 2018, Van de Winckel et al. 2007).

Sodring Motor Evaluation Scale (SMES): Is a measure of motor function and activities in patients with stroke. It is comprised of 3 subscales that evaluate the motor function of the upper and lower limb, and gross motor function. The first 2 subscales assess simple voluntary movements, while the third evaluates functional tasks including trunk movements, balance, and gait. The scale is comprised of 32 different items scored using a 5-point scale. The measure is shown to have good concurrent and construct validity, as well as good inter-rater reliability (Gor-Garcia_Fogeda et al. 2014).

Stroke Impairment Assessment Set (SIAS): Is a measure of overall motor function and visuospatial ability in stroke survivors. The measure consists of 20 functional tasks (e.g. walking, combing hair, bending, tying shoes). These tasks are then subdivided into 2 areas: tasks specific for the lower extremity and tasks specific for the upper extremity. Each task is then scored on a 6-point scale (0=cannot complete task, 5=completes task as well as the unaffected side). This measure has been shown to have good reliability and validity (Panarese et al. 2016; Seki et al. 2014).

Stroke Rehabilitation Assessment of Movement (STREAM): Is a measure of overall gross motor function in stroke survivors. The measure consists of 30 functional tasks (e.g. filling up and drinking from a cup, walking, getting into and out of the bathtub, buttoning a shirt). These tasks are then subdivided into 3 areas: upper limb, lower limb and basic mobility. Each task is then scored on a 3-point scale (0=cannot complete task, 2=completes task as well as the unaffected side). This measure has been shown to have good reliability and validity (Mateen et al. 2018).

Sollerman Hand Function Test (SHFT): Is a measure of general hand function and dexterity in stroke survivors. The measure consists of 20 functional tasks (e.g. stirring liquid, tying shoes, drinking from a cup, opening/shutting doors). Each task is then scored on a 6-point scale (0=cannot complete task, 5=completes task as well as the unaffected side). This measure has been shown to have good inter/intra reliability and validity (Singh et al. 2015; Brogardh et al. 2007).

Stroke Upper Limb Capacity Scale (SULCS): Is a measure of basic arm capacities and overall arm strength in stroke survivors. The measure consists of 10 functional tasks (e.g. carrying a briefcase, typing on a computer, writing on a notepad). These tasks are then subdivided into 3 areas: upper limb capacity with no control from wrist and fingers, upper limb capacity with basic control from wrist and fingers, and upper limb capacity with advanced control from wrist and fingers. Each task is then scored on a 3-point scale (0=cannot complete task, 2=completes task as well as the unaffected side). This measure has been shown to have good reliability and concurrent validity (Houwink et al. 2011; Roorda et al. 2011).

Upper Extremity Function Test (UEFT): Is a measure of total upper extremity dexterity and function in stroke survivors. The measure consists of 15 functional tasks (e.g. moving a jar around, stacking coins, reaching and grabbing a cup). There are 3 subsections of the UEFT: (speed of execution, functional rating, task analysis). Each task is then measured on a 6-point scale (-3=cannot complete task, +3=completes task as well as the unaffected side). This measure has good test/re-test reliability and validity (Platz et al. 2009; Feys et al. 2002).

Wolf Motor Function Test (WMFT): Is a measure that quantifies upper extremity motor ability in stroke survivors. The measure consists of 17 tasks (e.g. lifting arm up using only shoulder abduction, picking up a pencil, picking up a paperclip). These tasks are then subdivided into 3 areas: functional tasks, measures of strength, and quality of movement. Patients are scored on a 6-point scale (1=cannot complete task, 6=completes task as well as the unaffected side. This measure has been shown to have good reliability and validity (Wolf et al. 2005; Wolf et al. 2001).

Dexterity

Box and Block Test (BBT): Is a measure of gross unilateral manual dexterity in stroke survivors. This measure consists of 1 functional task. This task involves a patient moving as many wooden blocks as possible from one end of a partitioned box to the other, in a span of 60 seconds. Patients are scored based on the number of blocks they transfer (the higher the blocks transferred, the better the outcome). The measure has been shown to have good reliability and validity. (Higgins et al. 2005; Platz et al. 2005).

Finger to Nose Test (FNT): Is a measure of overall manual dexterity in stroke survivors. This measure consists of 1 functional task. This task involves the patient touching their index finger to their nose as 10 times as fast as possible. This task is then repeated 1 additional time. Patients are scored based on the number of times they touch their nose (the faster the time the better the outcome). The measure has been shown to have good reliability and construct plus concurrent validity (Rodrigues et al. 2017)

Grating Orientation Task (GOT): Is a measure of overall tactile spatial acuity in stroke survivors. This measure consisted of 1 functional task. Patients were asked to differentiate between a smooth and grooved surface that was placed both proximally and then distally from the patient. This process is repeated 10 different times. Patients are scored based on the number of times they successfully identify the type of surface (the higher the rate of identification, the better the outcome). This measure has been shown to have good reliability and validity (Craig 1999).

Grooved Pegboard Test (GPT): Is a measure of fine motor control in stroke survivors. This measure consists of 1 functional task. Patients are asked to place 25 pegs into the grooved pegboard and are typically given 5-10 minutes to do so. The patients are then scored based on the number of pegs inserted and the time it took them to do so (the higher the insertion rate and the lower the time, the better the outcome). This measure has been shown to have good reliability and validity (Lee et al. 2016; Thompson-Butel et al. 2014).

Jebsen-Taylor Hand Function Test (JTHFT): Is a measure used to evaluate fine motor skills with weighted and non-weighted hand functions. The test is derived from hand functions required for activities of daily living and is scored as the time taken (in seconds) to complete each subtest, with a maximum of 120 seconds permitted for each subtest. The test is shown to have good test-retest reliability (Allgower et al. 2017; Stern 1992)

Minnesota Manual Dexterity Test (MMDT): Is a measure of fine motor control and general dexterity in stroke survivors. The measure consists of 2 functional tasks. Patients are asked to place wooden discs instead of a cylindrical object for the first task. Then, they are asked to turn the discs clockwise 180 degrees and told to shut the lid on the cylinder. Patients are scored on the amount discs inserted and on the screwing of the lid. The higher the number of discs put in the cylinder and the faster/tighter the lid is screwed on, the better the outcome. This measure has been shown to have good reliability and validity (Wang et al. 2018; Surrey et al. 2003).

Nine Hole Peg Test (9HPT): Is a measure of overall manual dexterity in stroke survivors. The measure consists of 1 functional task. Patients are asked to take 9 pegs out of a container and insert them into the pegboard. Once all 9 pegs are inserted they are then taken out of the pegs as quickly as possible and placed back in the container. Patients are scored on how quickly they can insert and take out the pins, so the faster the time, the better the outcome. This measure has been shown to have good reliability and concurrent validity (da Silva et al. 2017).

Purdue Pegboard Test (PPT): Is a measure of precision grip strength and speed in stroke survivors. The measure consists of 1 functional task. Patients are asked to place as many pins as they can onto the pegboard in 30 secs, and then repeat this exercise for their other hand. Patients are scored on the number of pins they can place onto the pegboard in the given amount of time. This measure has been shown to have good reliability and validity (Gonzalez et al. 2017, Wittich & Nadon, 2017).

University of Maryland Arm Questionnaire (UMAQ): Is a measure of gross functional dexterity in the upper arm for stroke survivors. The measure consists of 10 functional tasks (e.g. opening/closing jars, opening/closing doors, reaching and grabbing common household items). Each task is then scored on a 6-point scale (0=cannot complete task, 5=completes task as well as the unaffected side). This measure has been shown to have good reliability and validity (Beebe et al. 2009, Bovend' Eerdt et al. 2002).

Activities of Daily Living

ABILHAND: Is a measure of how well a stroke survivor utilizes their hands to complete various manual tasks. The measure consists of 23 common bimanual activities (e.g. hammering a nail, wrapping gifts, cutting meat, buttoning a shirt, opening mail). Each task is then scored on a 3-point scale (0=impossible, 1=difficult, 2=easy) assessing overall ability. This measure has been shown to have good reliability and validity in its full form (Ashford et al. 2008; Penta et al. 2001).

Arm Motor Ability Test (AMAT): Is a measure of upper extremity limitation for stroke survivors in performing activities of daily living. The measure consists of 13 common unilateral and bilateral tasks (e.g. manipulating objects such as utensil and telephones; donning/doffing a piece of clothing). Each task is scored on two, 6-point ordinal scales assessing functional ability and the quality of the movement performed. The measure has been shown to have good reliability and construct validity, in its full form and in abbreviated versions for stroke survivors (Fulk et al. 2017; O'Dell 2013; O'Dell 2011).

Assessment of Motor and Process Skills (AMPS): Is a measure of processing skills and overall independence for stroke survivors in performing activities of daily living (ADL) (Ahn et al. 2016). The measure consists of 16 motor tasks (e.g. picking up/setting down a mug, donning/doffing a piece of clothing, turning doorknobs) and 20 process tasks (e.g.memory testing, matching shapes, word recall) (Ahn et al. 2016) Each task is scored on 10 item tool assessing functional ability and the accuracy/speed at which the skill(s) are completed (Lam et al. 2018). This measure has been shown to have good reliability and validity in both its full and abbreviated form (Lam et al. 2018; Ahn et al. 2016).

Barthel Index (BI): Is a measure of how well a stroke survivor can function independently and how well they can perform activities of daily living (ADL). The measure consists of a 10-item scale (e.g. feeding, grooming, dressing, bowel control). Possible total scores range from 0 to 100. This measure has been shown to have good reliability and validity in its full form (Gonzalez et al. 2018; Park et al. 2018).

Canadian Occupational Performance Measure (COPM): Is a measure of how well a stroke survivor engages in self-care, productivity and leisure. The measure consists of 25 functional items/tasks (e.g. bathing, ability to work at least part-time, activities involved in). Each task is then scored on a single 10-point rating scale primarily measuring proficiency in each of the 3 sub-categories (self-care, productivity and leisure). This measure has been shown to have good reliability and validity in its full form. (Yang et al. 2017).

Chedoke Arm and Hand Activity Inventory (CAHAI): Is an upper limb measure that uses a 13-point quantitative scale in order to assess recovery of the arm and hand in performing activities of daily living after a stroke. It is a performance test using 13 bimanually performed real-life items, designed to encourage bilateral upper limb use.

Scores represent the patient’s relative ability to independently perform stabilisation or manipulation in ADL with the impaired upper limb. The measure is shown to have good test-retest and interrater reliability, as well as good construct and concurrent validity (Ward et al. 2019; Schuster-Amft et al. 2018; Barteca et al. 2004).

Duruoz Hand Index (DHI): Is a measure used to assess hand-related activity limitation based on questions concerning activities in a person’s daily life. It contains 18 activities commonly performed by the hand in the kitchen, during dressing, while performing personal hygiene, while performing office tasks, and other general items. The measure is shown to have good construct validity, test-retest reliability, and internal consistency in patients with stroke (Sezer et al. 2007).

Frenchay Arm Test (FAT): Is a measure of upper extremity motor control that a stroke survivor possesses. The measure consists of 5 common tasks that require use of the upper extremity (e.g. stabilize a ruler/draw a line with a pencil, comb hair, clip a clothespin onto the edge of a table, grasp a cylinder, drink from a glass of water and then set it down). Each task is then scored on a 2-point scale wherein each task receives either a 0 (unsuccessful completion) or a 1 (successful completion). This measure has been shown to have good reliability and validity in its full form. (Heller et al. 1987; Parker et al. 1986)

Frenchay Activities Index (FAI): Is a measure of activities that stroke survivors have participated in recently. The measure consists of 15 items that are in turn split up into 3 subscales (domestic chores, leisure/work and outdoor activities). These items include: preparing meals, washing clothes, light/heavy housework, social outings etc. Each task is then scored on a 4-point scale with 1 being the lowest score. This measure has been shown to have good reliability and concurrent validity in its full form (Schuling et al. 1993)

Functional Activity Scale (FAS): Is a measure of functional everyday activities that stroke survivors participate in daily. The measure consists of 15 functional activities (e.g. cooking, cleaning, zipping up a coat). Each activity is then scored on a 5-point scale (0=cannot complete activity, 4=completes activity as well as the unaffected side). This measure has been shown to have good reliability and validity (Pang et al. 2006).

Functional Independence Measure (FIM): Is an 18-item outcome measure composed of both cognitive (5-items) and motor (13-items) subscales. Each item assesses the level of assistance required to complete an activity of daily living on a 7-point scale. The summation of all the item scores ranges from 18 to 126, with higher scores being indicative of greater functional independence. This measure has been shown to have excellent reliability and concurrent validity in its full form (Granger et al. 1998, Linacre et al. 1994; Granger et al. 1993).

Goal Attainment Scale (GAS): Is a measure that quantifies the progress made towards obtaining personalized rehabilitation goals. The measure consists of 5 levels of goal achievement. The items in these levels consist of various goals individual patients would like to achieve (e.g. bathing independently, being able to do housework, walking unaided). The patient is then rated on a 4-point scale on their ability to carry out said goals (-2=far behind schedule, +2=far ahead of schedule). This measure has been found to have good reliability and validity in its full form (Hanlan et al. 2017; Krasny-Pacini et al. 2016)

Modified Barthel Index (MBI): Is a measure of how well a stroke survivor can function independently and how well they can perform activities of daily living (ADL). The measure consists of a 10-item scale (e.g. feeding, grooming, dressing, bowel control). Possible scores range from 0 to 20. This measure has been shown to have good reliability and validity in its full form. (MacIsaac et al. 2017; Ohura et al. 2017).

Motor Activity Log (MAL): Is a patient-reported measure of the use and quality of movement of the impaired arm. The measure consists of 30 functional tasks (e.g. handling utensils, buttoning a shirt, combing hair). Each task is then measured on a 6-point scale (0=complete inability to use affected arm). This measure has been shown to have good reliability and validity (Chuang et al. 2017).

Motor Assessment Scale (MAS): Is a performance-based measure that assesses everyday motor function. The measure consists of 8 motor-function based tasks (e.g. supine lying, balanced sitting, walking). Each task is then measured on a 7-point scale (0=suboptimal motor performance, 6=optimal motor performance). This measure has been shown to have good reliability and concurrent validity (Simondson et al. 2003).

Nottingham Extended Activities of Daily Life (NEADL): Is a measure of a stroke survivor's independence with regards to their performance on various activities of daily living. The measure consists of 22 functional tasks (e.g. walking, cooking, cleaning, participation in active hobbies). These tasks are then further divided into 4 distinct subscales (mobility, kitchen, domestic, and leisure activities). In turn, each task is measured on a 5-point (0=not at all, 4=on my own with no difficulty). This measure has been shown to have good reliability and validity (das Nair et al. 2011; Sahin et al. 2008).

Nottingham Stroke Dressing Assessment (NSDA): Is a measure of a stroke survivor's ability to successfully dress themselves. The measure consists of 25 functional dressing tasks (e.g. buttoning up a shirt, buckling a belt/watch, putting on pants). These tasks are then measured on a 4-point scale (0=cannot complete task, 3=completes task as well as the unaffected side). This measure has been shown to have good reliability and validity (Walker et al. 2011).

Stroke Impact Scale (SIS): Is a patient-reported measure of multi-dimensional stroke outcomes. The measure consists of 59 functional tasks (e.g. dynamometer, reach and grab, walking, reading out loud, rating emotional regulation, word recall, number of tasks completed, and shoe tying). These tasks are then divided into 8 distinct subscales which include: strength, hand function, mobility, communication, emotion, memory, participation and activities of daily living (ADL). Each task is measured on a 5-point scale (1=an inability to complete the task, 5=not difficult at all). The measure has been shown to have good reliability and validity (Mulder et al. 2016; Richardson et al. 2016).

STAIS Stroke Questionnaire (SSQ): Is a measure of activities and participation in the physical environment for stroke survivors. The measure consists of 36 functional tasks (e.g. taking a bath or shower, ability to handle your finances, opening and closing doors). Each task is measured on a 4-point scale (1=no ability, 4=complete ability). The measure has been shown to have good reliability and concurrent validity (Bouffioulx et al. 2010 Bouffioulx et al. 2008)

Upper Limb Self-Efficacy Test (UPSET): Is a measure of a stroke survivor's confidence in their ability to carry out upper limb specific tasks with their affected side. The measure consists of 20 functional tasks (e.g. shaking hands, flipping a coin, opening/shutting doors). Each task is then measured on a 5-point scale (0=cannot complete task, 4=completes task as well as the unaffected side). The measure has been shown to have good test/retest reliability and validity (Abdullahi, 2016; Pang et al. 2007).

Spasticity

Ashworth Scale (AS): Is a measure of resistance to passive movement in stroke survivors. The measure contains 15 functional m'ovements which are done with the guidance of a trained clinician. These movements are evenly divided into 2 sections: upper extremity and lower extremity. Each movement is then rated on a 5-point scale (0=no increase in muscle tone, 1=barely discernible increase in muscle tone, 2=moderate increase in muscle tone 3=profound increase in muscle tone (movement of affected limb is difficult) 4=complete limb flexion/rigidity (nearly impossible to move affected limb)). This measure has been shown to have good reliability and validity (Merholz et al. 2005; Watkins et al. 2002).

Bhakta Finger Flexion Scale (BFFS): Is a measure of the overall finger flexion experienced by stroke survivors when completing functional tasks. This measure consists of 27 functional tasks (e.g. writing with a pen, typing, squeezing a ball). Each task is then rated on a 3-point scale (0=cannot complete task; fingers too rigid, 2=easily completes task; flexes and extends fingers). This measure has been shown to have good reliability and validity (Christina et al. 2015).

Disability Assessment Scale (DAS): Is a measure of resistance to passive movement in the upper extremity for stroke survivors. The measure consists of 20 functional tasks (e.g. brushing teeth, buttoning a shirt, gait technique & general pain). These tasks are then divided into 4 sections: hygiene, dressing, limb position and pain. Each task is then rated from: 0=no disability, 1=mild disability 2=moderate disability, 3=severe disability. This measure has been shown to have good reliability and validity (Thibaut et al. 2013; Brashear et al. 2002)

Modified Ashworth Scale (MAS): Is a measure of muscle spasticity for stroke survivors. The measure contains 20 functional movements which are done with the guidance of a trained clinician. These movements are evenly divided into 2 sections: upper extremity and lower extremity. Each movement is then rated on a 6-point scale (0=no increase in muscle tone, 1=barely discernible increase in muscle tone 1+=slight increase in muscle tone, 2=moderate increase in muscle tone 3=profound increase in muscle tone (movement of affected limb is difficult) 4=complete limb flexion/rigidity (nearly impossible to move affected limb)). This measure has been shown to have good reliability and validity (Merholz et al. 2005; Blackburn et al. 2002).

Modified Tardieu Scale (MTS): Assesses spasticity through measuring the quality and angle of muscle movements in response to stretches of different velocities. The velocities of muscle movement are as slow as possible (V1), speed of the limb falling from gravity (V2), and when the joint is moved as fast as possible (V3). The quality and angle of muscle reactions are recorded during these velocities. The quality of muscle reactions are scored as: 0 (no resistance throughout the duration of the stretch), 1 (slight resistance), 2 (clear catch occurring at a precise angle, followed by a release), 3 (fatigable clonus), 4 (infatigable clonus), 5 (joint is immovable) (Li et al. 2014b).

Resistance to Passive Movement Scale (REPAS): Is a measure of general muscle spasticity for stroke survivors. The measure contains 52 functional movements which are done with the guidance of a trained clinician. These movements are evenly divided into 2 sections: upper extremity and lower extremity. Each movement is then rated on a 5-point scale (0=no increase in muscle tone, 1=barely discernible increase in muscle tone, 2=moderate increase in muscle tone 3=profound increase in muscle tone (movement of affected limb is difficult) 4=complete limb flexion/rigidity (nearly impossible to move affected limb)). This measure has been shown to have good test/retest reliability and concurrent validity (Platz et al. 2008).

Spasm Frequency Scale (SFS): Is a measure of the amount of spasms experienced by stroke survivors in a day. The measure is only concerned with measuring the amount of spasms in a single day. The amount of spasms per day are rated based on a 5-point scale (0=No spasms. 1= One or fewer spasms per day 2=Between 1 and 5 spasms per day 3=Five to less than 10 spasms per day 4=Ten or more spasms per day, or continuous contraction). This measure has been shown to have good reliability and validity (Santamato et al. 2013; Snow et al. 1990).

Range of Motion

Active Range of Motion (AROM): Is a measure of the range of motion stroke survivors possess without receiving assistance. The measure consists of 20 functional movements for both the upper and lower extremity. The movements are evenly divided into 2 sections: upper extremity and lower extremity. These movements are then rated on a 4-point ordinal scale (0=cannot complete movement, 3=completes movement as well as the unaffected side). This measure has been shown to have good reliability and validity (Beebe & Lang 2009, Dickstein et al. 1986)

Maximal Elbow Extension Angle During Reach (MEEAR): Is a measure of the amount of elbow extension undergone by a stroke survivor while they are reaching for an object. The measure consists of 1 functional movement which is when a patient reaches for an object and their rate of elbow extension is measured (the higher the rate of extension, the better the outcome). This measure has been shown to have good inter/intra reliability and concurrent validity (Murphy et al. 2011; Cristea et al. 2003).

Passive Range of Motion (PROM): Is a measure of the range of motion stroke survivors possess while receiving assistance. The measure consists of 30 functional movements for both the upper and lower extremity. The movements are evenly divided into 2 sections: upper extremity and lower extremity. These movements are then rated on a 5-point ordinal scale (0=cannot complete movement, 4=completes movement as well as the unaffected side). This measure has been shown to have good test/retest reliability and validity (Lynch et al. 2005).

Proprioception

Joint Position Sense Test (JPST): Is a measure of how well stroke survivors can perceive the position of their joints in motion and standing still. The measure consists of 1 functional task repeated several times. This task involves the patient holding 2 different shaped objects that also weigh different from each other and then told to identify which one weighs more and which one has a stranger shape. The more times the patient (s) identifies which shape is heavier/unique, then the better the outcome. This measure has been shown to have good reliability and validity (Kattenstroth et al. 2013).

Kinesthetic Visual Imagery Questionnaire (KVIQ): Is the measure of the visual acuity and muscle movement that stroke survivors possess. The measure consists of 20 functional tasks (e.g. tying shoes, reading out loud, reaching for an object, peripheral vision testing). Each task is then measured on 3-point scale (0=cannot complete task, 2=completes task as well as the unaffected side). This measure has been shown to have good reliability and validity (Salles et al. 2017; Demanboro et al. 2018).

Revised Nottingham Sensory Assessment (RNSA): Is a measure of somatosensory perception in stroke survivors. The measure consists of 1 functional task repeated with 11 different objects. The task involves patients identifying 11 different objects with their eyes closed. The higher the rate of objects identified leads to a better overall outcome. This measure is shown to have good reliability and validity (Boccuni et al. 2018; Gorst et al. 2018).

Stroke Severity

Modified Rankin Scale (MRS): Is a measure of functional independence for stroke survivors. The measure contains 1 item. This item is an interview that lasts approximately 30-45 minutes and is done by a trained clinician. The clinician asks the patient questions about their overall health, their ease in carrying out ADLs (cooking, eating, dressing) and other factors about their life. At the end of the interview the patient is assessed on a 6-point scale (0=bedridden, needs assistance with basic ADLs, 5=functioning at the same level as prior to stroke). This measure has been shown to have good reliability and validity (Quinn et al. 2009; Wilson et al. 2002).

National Institutes of Health Stroke Scale (NIHSS): Is a measure of somatosensory function in stroke survivors during the acute phase of stroke. This measure contains 11 items and 2 of the 11 items are passive range of motion (PROM) assessments delivered by a clinician to the upper and lower extremity of the patient. The other 9 items are visual exams conducted by the clinician (e.g. gaze, facial palsy dysarthria, level of consciousness). Each item is then scored on a 3-point scale (0=normal, 2=minimal function/awareness). This measure has been shown to have good reliability and validity (Heldner et al. 2013; Weimar et al. 2004).

Neurological Function Deficit Scale (NFDS): Is a measure of neurological deficits experienced by stroke survivors in both the upper and lower extremities. This measure contains 40 functional movements done with the guidance of a clinician (e.g. should abduction, shoulder adduction, leg flexion/extension). These movements are evenly divided into 2 sections: upper extremity and lower extremity. Each movement is then measured on a 6-point scale (0=normal function, 5=severe stroke). This measure has been shown to have good test/retest reliability and validity (Yao & Ouyang. 2014).

Muscle Strength

Hand Grip Strength (HGS): Is a measure of the overall hand grip strength in stroke survivors. The measure consists of 1 functional task. This task involves a patient squeezing the dynamometer and then receiving a hand grip strength measurement. This action is then repeated 1 additional time and the best of the two readings is used as a score. This measure has been shown to have good test/retest reliability and validity (Bertrand et al. 2015).

Isokinetic Peak Torque (IPT): Is a measure of the work capacity of specific muscle groups of a stroke survivor. The measure consists of 1 functional task. The patient performs elbow flexion/extension while attached to a machine that measures force output. The process is then repeated for the leg. The output is then compared to healthy patients that are approximately the same age and build. This measure has been shown to have good test/retest reliability (Horvat et al. 1997).

Manual Muscle Strength Test (MMST): Is a measure of how well a stroke survivor can complete various upper extremity movements while resistance is applied by a trained clinician. The measure consists of 3 functional tasks: muscle contraction, total range of motion and resistance to applied pressure. Patients are scored on a 12-point scale (0=no movement, T=trace/barely discernable movement, 10=movement carried out as well as the unaffected side). This measure has been shown to have good reliability and validity (Kristensen et al. 2017; Ada et al. 2016)

Medical Research Council Scale (MRCS): Is a measure of overall muscle strength a stroke survivor possesses. The measure consists of 33 functional tasks (e.g. opening/shutting cupboards, screwing and unscrewing lids, lifting of light objects). Each task is then rated on a 4-point scale (0=cannot complete task, 3=completes task as well as the unaffected side). This measure has been shown to have good reliability and validity (Hsieh et al. 2011; Fasoli et al. 2004).

Motricity index: Is a measure of motor function involving strength testing of six muscle actions. The muscle actions are graded and assigned weighted scores based on movement present and resistance taken. Weighted scores for each action are then added to obtain scores for each of the three subscales of the measure (arm, leg, and trunk). Each section is scored from 0 to 100, where 0 indicates complete motor function loss. The measure is found to be reliable and valid for use with stroke patients (Safaz et al. 2009; Cameron & Bohannon 2000).

Therapy based interventions

Neurodevelopmental Techniques

Adopted from: http://www.bobathconcept.eu/en/main-site/

There are several approaches that are considered to be neurodevelopmental techniques (NDT). These include the Bobath concept, Brunnstrom movement therapy and motor relearning programmes.

The Bobath concept is a comprehensive, problem-solving treatment approach that focuses on motor recovery (e.g. function, movement and tone) of an individual's affected side after a lesion in the central nervous system (Michielsen et al. 2017). Prior to its introduction in the 1950's, stroke rehabilitation largely assumed a compensatory approach towards the unaffected side for rehabilitation (Kollen et al. 2009). The Bobath concept like other neurodevelopmental techniques relies on the tenets of neuroplasticity, in that motor recovery of the affected side is possible through individualised treatment plans that focus on how tasks are completed, facilitation of movements through therapeutic handling, movement analysis, modification of the environment and appropriate use of verbal cues from therapists (Michielsen et al. 2017).

Brunnstrom movement therapy focuses on retraining motor movements through emphasis of the synergistic and reflexive muscle movements that develop during recovery from hemiplegia. The approach encourages the use of abnormal or spastic muscle movements of the flexors and extensors during early recovery to regain muscle synergies, contrary to the Bobath concept which inhibits these movements (Pandian 2012; Brunnstrom 1970).

The motor relearning programme employs practice of task-specific activities to remediate specific motor skills needed to perform that task. Motor tasks are practiced in context relevant environments to enhance sensory input and modulate performance (Pandian 2012).

A total of 11 RCTs were found that evaluated neurodevelopmental techniques for upper extremity motor rehabilitation, interventions categories are listed below.

Two RCTs compared the Bobath concept to conventional therapy (van der Lee et al. 1999; Gelber et al. 1995). Two RCTs compared motor relearning programmes to conventional therapy (Walker et al. 2012; Platz et al. 2009). Four RCTs compared motor relearning programmes to Bobath concept approaches (El-Bahwary et al. 2012; Langhammer and Stanghelle, 2011; Platz et al. 2005; van Vliet et al. 2005). One RCT compared motor relearning programs to mirror therapy (Jan et al. 2019. One RCT compared Brunnstrom movement therapy to a motor relearning programme (Pandian et al. 2012). One RCT compared Bobath Concept Approaches to physical and behavioural therapy with EMG (Basmajian et al. 1987).

The methodological details and results of all 11 RCTs are presented in Table 1.

Table 1. RCTs Evaluating Neurodevelopmental Techniques for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Bobath concept approach compared to conventional therapy		
van der Lee et al. (1999) RCT (7) N_{start}=66 N_{end}=57 TPS=Chronic	E: Bobath concept C: Forced-use therapy Duration: 6h, 5d/wk for 2wk Data analysis: ANCOVA	• Action Research Arm Test (+con)
Gelber et al. (1995) RCT (5) N_{start}=20 N_{end}=20 TPS=Acute	E: Bobath concept C: Traditional techniques Duration: *Not reported*	• Functional Independence Measure (-) • Box and Block Test (-) • Nine Hole Peg Test (-)
Motor relearning programmes compared to conventional therapy		
Walker et al. (2012) RCT (7) N_{Start}=70 N_{End}=64 TPS=Acute	E: Motor relearning programme C: Dressing without a task-oriented approach Duration: 3d/wk for 6wk	• Nottingham Stroke Dressing Assessment (-) • 10-hole peg transfer test (-)
Platz et al. (2009) RCT (8) N_{start}=148 N_{end}=135 TPS=Not reported	E: Motor relearning programme E2: Passive therapy (with splints) C: Conventional therapy Duration: 45min, 5d/wk for 4wk	• Fugl-Meyer Assessment (-) • Upper Extremity Performance Test for the Elderly (-)
Motor relearning programme compared to Bobath concept approaches		
El-Bahrawy et al. (2012) RCT (8) N_{start}= 40 N_{end}= 40 TPS= Chronic	E: Motor relearning program (+electrical stimulation) C: Bobath (+electrical stimulation) Duration: 45min, 3x/wk, 6wks int - 1:15 on top of conventional rehab + stimulation	• Hand Grip Strength: (+exp) • Resting Angle of Ulnar Deviation: (+exp) • Purdue Pegboard Test: (-) • Modified Ashworth Scale: (-)
Langhammer & Stanghelle (2011). RCT (8) N_{start}=61 N_{end}=53 TPS=Not reported	E: Motor relearning programme E2: Bobath concept Duration: 40min, 5d/wk for 2wk	• Motor Assessment Scale (+exp) • Sodring Motor Evaluation Scale (+exp)
Platz et al. 2005 RCT (8) N_{start}=62 N_{end}=62 TPS=Subacute	E: Motor relearning programme (Arm BASIS) E2: Bobath concept C: No augmented exercise therapy time	• Fugl-Meyer Assessment (-)

	Duration: 4wk	
van Vliet et al. (2005) RCT (7) N_{start}=120 N_{end}=105 TPS=Acute	E: Motor Relearning Programme E2: Bobath concept Duration: 23min, 5d/wk for 4wk	• Motor Assessment Scale (-) • Barthel index (-) • Extended activities of daily living scale (-) • 10-hole peg test (-)
Motor Relearning vs Mirror Therapy		

Jan et al. (2019)
RCT (5)
N_{start}= 66
N_{end}= 66
TPS= Not reported
	E: Motor relearning program
	C: Mirror therapy
	Duration: 2hrs, 3x/wk, 6wks
		• Motor Assessment Scale
		  • Upper limb: (+exp)
		  • Hand: (+exp)
		  • Advance Hand: (+exp)

Brunnstrom movement therapy vs Motor relearning programme		
Pandian et al. (2012) RCT (6) N_{start}=30 N_{end}=30 TPS=Chronic	E: Brunnstrom hand manipulation treatment C: Motor relearning programme Duration: 1h, 3d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Brunnstrom recovery stages-hand (-)
Boboath concept vs Physical Therapy with EMG		
Basmajian et al. (1987) RCT (6) N_{start}=29 N_{end}=23 TPS=Sub-acute	E: Bobath concept C: Physical and behavioural therapy using EMG Duration: 45min, 3d/wk for 5wk	• Upper Extremity Performance Test for the Elderly (-) • Finger Oscillation Test (-)

Abbreviations and table notes: ANCOVA= analysis of covariance; C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions About Neurodevelopmental Techniques

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Bobath concept approaches** may not have a difference in efficacy when compared to **conventional therapy** for improving motor function.	1	Van der lee et al. 1999;
1b	**Motor relearning programmes** may not have a difference in efficacy when compared to **conventional therapy** for improving motor function.	1	Platz et al. 2009
1a	There is conflicting evidence about the effect of **motor relearning programmes** to improve motor function when compared to **Bobath concept approaches**.	2	Langhammer Stanghelle et al. 2011; Platz et al. 2005
1b	**Brunnstrom movement therapy** may produce greater improvements in motor function than **motor relearning programmes**.	1	Pandian et al. 2012
1b	**Bobath concept approaches** may not have a difference in efficacy when compared to **physical and behavioural therapy with EMG** for improving motor function.	1	Basmajian et al. 1987

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	**Motor relearning programs** may produce greater improvements in muscle strength than **Bobath concept approaches.**	1	Jan et al. 2019

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
2	**Bobath concept approaches** may not have a difference in efficacy when compared to **conventional therapy** for improving performance of activities of daily living.	1	Gelber et al. 1995
1b	**Motor relearning programmes** may not have a difference in efficacy when compared to **conventional therapy** for improving performance of activities of daily living.	1	Walker et al. 2012
1a	There is conflicting evidence about the effect of **motor relearning programmes** to improve performance of activities of daily living when compared to **Bobath concept approaches**.	2	Langhammer Stanghelle et al. 2011; Van Vliet et al. 2005
2	**Motor relearning programmes** may produce greater improvements in activities of daily living than **mirror therapy.**	1	Jan et al. 2019

DEXTERITY

LoE	Conclusion Statement	RCTs	References
2	**Bobath concept approaches** may not have a difference in efficacy when compared to **conventional therapy** for improving dexterity.	1	Gelber et al. 1995
1b	**Motor relearning programmes** may not have a difference in efficacy when compared to **conventional therapy** for improving dexterity.	1	Walker et al. 2012
1a	**Motor relearning programmes** may not have a difference in efficacy when compared to **Bobath concept approaches** for improving dexterity.	1	El-Bahrawy et al. 2012

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1a	**Motor relearning programmes** may not have a difference in efficacy when compared to **Bobath concept approaches** for improving spasticity.	1	El-Bahrawy et al. 2012

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References

1b	**Brunnstrom movement therapy** may produce greater improvements in stroke severity than **motor relearning programmes**.	1	Pandian et al. 2012

Key points

Bobath concept approaches and motor relearning programmes may not be beneficial for upper limb rehabilitation following stroke.

Brunnstrom movement therapy may be more beneficial than motor relearning programmes for upper limb function.

Bilateral Arm Training

Adopted from: https://www.newswise.com/articles/stroke-survivors-rehab-arms-with-in-home-device

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

Interventions for bilateral arm training included: 12 RCTs evaluating bilateral arm training compared to unilateral arm training (Renner et al. 2020; Han and Kim, 2016; Shim et al. 2015; McCombe et al. 2014; Kim et al. 2013; Wu et al. 2013; Morris and van Wijck, 2012; Yang et al. 2012; Lin et al. 2010; Stoykov et al. 2009; Morris et al. 2008; Summers et al. 2007). Seven RCTs evaluating bilateral arm training compared to conventional rehabilitation (Arya et al, 2020; Easow et al. 2019; Meng et al. 2018; Lee et al. 2017; Lee et al. 2013; Stinear et al. 2008; Desrosiers et al. 2005). Four RCTs evaluating bilateral arm training with rhythmic auditory cueing compared to unilateral arm training or conventional rehabilitation (Dispa et al. 2013; Whitall et al. 2011; McCombe Waller et al. 2008; Luft et al. 2004), and task-oriented bilateral arm training (Song et al. 2015). One RCT looked at occupation-based compared to task-based training (Kim et al. 2019). A single RCT looked at bilateral arm training compared to TENS (Stinear et al. 2014); while two RCTs looked at EMG-triggered NMES bilateral arm training (Singer et al. 2013; Cauraugh and Kim, 2002). One study looke at long term compared to short term bilateral arm training with NMES (Cauraugh et al. 2011). Two RCTs looked at bilateral arm training compared to CIMT (Brunner et al. 2012; Wu et al. 2011), and another two compared bilateral arm training with rhythmic auditory cueing to modified CIMT (van Delden et al. 2015; van Delden et al. 2013).

The methodological details and results of all 33 RCTs evaluating bilateral arm training for the upper extremity motor rehabilitation are presented in Table 2.

Table 2. RCTs Evaluating BAT Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Bilateral arm training compared to unilateral arm training		

Renner et al. (2020)
RCT (5)
N_{start}=69
N_{end}=51
TPS=Subacute
	E: Bilateral arm training
	C: Unilateral arm training
	Duration: 1hr, 5x/wk, 6wks
		• Fugl Meyer Assessment Upper Extremity total: (-)
		  • Proximal: (-)
		  • Distal: (-)
		• Grip force: (-)
		• Rate of rise of tension: (-)
		• Dorsal hand extension: (-)
		• Isometric force and rate of rise of tension:
		  • Rate of Rise of Tension DE: (-)
		  • Elbow flex: (-)
		  • Elbow extension: (-)
		• Modified Ashworth Scale: (+con)

Han & Kim (2016) RCT (5) N_{Start}=25 N_{End}=25 TPS=Not reported	E: Bilateral arm training C: Unilateral arm training Duration: 5x/wk for 6wk	• Box and Block Test (-) • Elbow Amplitude (-) • Shoulder Amplitude (+exp)
Shim et al. (2015) RCT (6) N_{Start}=20 N_{End}=20 TPS=Chronic	E: Bilateral training C: Unilateral training Duration: 30min, 5x/wk for 6wk	• Manual Function Test (+exp) • Functional Independence Measure (+exp) • Affected hand amount of sedentary and moderate activity (+exp)
McCombe et al. (2014) RCT (7) N_{Start}=30 N_{End}=26 TPS=Subacute	E: Bilateral + Unilateral training C: Unilateral training Duration: 1h, 3d/wk for 12wk	• Wolf Motor Function Test (+exp) • University of Maryland Arm Questionnaire (+exp) • Fugl-Meyer Assessment (-) • Box and Block Test (-) • Modified Ashworth Scale (-)
Kim et al. (2013) RCT (3) N_{start}=15 N_{end}=15 TPS=Subacute	E1: Bilateral robotic training E2: Unilateral robotic training C: Usual Care Duration: 90min, 2d/wk for 6wk	• Fugl-Meyer Assessment (-)
Wu et al. (2013) RCT (7) N_{Start}=53 N_{End}=53 TPS=Chronic	E1: Bilateral robotic training E2: Unilateral robotic training C: Conventional therapy Duration: 90 to 105min, 1d/wk for 4wk	E1 Vs E2 Vs C • Motor Activity Log (-) • Wolf Motor Function Test (-) • ABILHAND Scale (-)
Morris & van Wijck (2012) RCT (7) N_{start}=106 N_{end}=85 TPS=Not reported	E: Bilateral training C: Unilateral training Duration: 20min, 5d/wk for 6wk	• 9 Hole Peg Test (+exp) • Action Research Arm Test (-)
Yang et al. (2012) RCT (7)	E1: Unilateral robot assisted training E2: Bilateral robot assisted training	E1 Vs E2 Vs C • Fugl-Meyer Assessment (-)

N_{start}=21 N_{end}=21 TPS=Chronic	C: Standard training group Duration: 90min, 5d/wk for 4wk	• Medical Research Council Scale (-) • Modified Ashworth Scale (-) • Grip Strength (-)
Lin et al. (2010) RCT (6) N_{start}=33 N_{end}=33 TPS=Chronic	E: Bilateral training C: Unilateral training Duration: 2h, 5d/wk for 3wk	• Fugl Meyer Assessment (+exp) • Functional Independence Measure (-) • Motor Activityt Log (-)
Stoykov et al. (2009) RCT (5) N_{start}=21 N_{end}=21 TPS=Chronic	E: Bilateral training C: Unilateral training Duration: 1h, 3d/wk for 8wk	• Motor Assessment Scale (-) • Motor Status Scale (-)
Morris et al. (2008) RCT (7) N_{start}=106 N_{end}=85 TPS=Chronic	E: Bilateral training C: Unilateral training Duration: 20min, 5d/wk for 6wk	• Arm Research Arm Test (-) • Rivermead Motor Assessment (-) • 9 Hole Peg Test (+exp) • Modified Barthel Index (-)
Summers et al. (2007) RCT (5) N_{start}=12 N_{end}=10 TPS=Chronic	E: Bilateral training C: Unilateral training Duration: *Not reported*	• Modified Motor Assessment Scale (+exp)
Bilateral arm training compared to conventional rehabilitation		
Arya et al. 2020 RCT (8) N_{start}= 50 N_{end}=50 TPS= Chronic	E: Bilateral arm training C: Conventional Care Duration: 1hr. 3x/wk for 8wks	• Fugl-Meyers Upper Extremity: (+exp) • Modified Rankin Scale: (-)
Easow et al. (2019) RCT (7) N_{start}= 30 N_{end}= 30 TPS=Not reported	E: Bilateral arm training C: Conventional therapy Duration: 20min, 6d/wk, 1 wk + (30min/d of conventional therapy)	• Action Research Arm Test: (-) • Functional Independence Measure: (+exp) • Nine Hole Peg Test: (-)
Meng et al. (2018) RCT (7) N_{start}=128 N_{end}=123 TPS=Acute	E: Hand-Arm Bimanual Intensive Therapy C: Conventional Rehabilitation Program Duration: 1h (twice per d), 5d/wk for 2wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (+exp)
Lee et al. (2017) RCT (6) N_{Start}=30 N_{End}=30 TPS=Chronic	E: Bilateral Arm Training C: Upper Extremity Training Duration: 1h, 5d/wk for 8wk	• Fugl-Meyer Assessment (+exp) • Box and Block Test (+exp) • Modified Barthel Index (+exp)
Lee et al. (2013) RCT (6) N_{Start}=26 N_{End}=26 TPS=Chronic	E: Bilateral training + conventional rehabilitation C: Conventional rehabilitation Duration: 30min, 3d/wk for 4wk	• Functional Independence Measure (+exp)
Stinear et al. (2008) RCT (6) N_{start}=32 N_{end}=27 TPS= Chronic	E: Bilateral training C: Self-directed motor practice Duration: 10min (three times per day), 7d/wk for 4wk	• Fugl Meyer Assessment (+exp) • Grip strength (-)
Desrosiers et al. (2005) RCT (7) N_{start}=41 N_{end}=33 TPS=Subacute	E: Bilateral training C: Conventional therapy Duration: 45min, 15-20 sessions	• Fugl Meyer Assessment (-) • Grip strength (-) • Box and Block Test (-) • Purdue Pegboard Test (-) • Finger-to-Nose Test (-)

		• Upper Extremity Performance test for the Elderly (-) • Functional Independence Measure (-) • The Assessment of Motor and Process Skills (-)
Bilateral arm training with rhythmic auditory cueing compared to unilateral arm training or conventional rehabilitation		
Dispa et al. (2013) RCT (7) N_{Start}=10 N_{End}=10 TPS=Not given	E: Bilateral therapy + Rhythmic Auditor Cueing (BATRAC) C: Unilateral therapy Duration: 1h, 3d/wk for 4wk	• Purdue pegboard Test (-) • ABILHAND scale (-) • STAIS-stroke questionnaire (-)
McCombe Waller et al. (2008) RCT (4) N_{start}= 18 N_{end}= 18 TPS= Chronic	E: Bilateral Arm Training + Rhythmic Auditory Cueing (BATRAC) C: Does matched conventional therapy Duration: 1hrs, 3x/wk, 6wks	• Reach Task Kinematics: (+exp)
Whitall et al. (2011) RCT (6) N_{Start}=111 N_{End}=92 TPS=Chronic	E: Bilateral arm training with rhythmic auditory cueing C: Dose matched unilateral therapeutic exercises Duration: 20min, 3d/wk for 6wk	• Fugl Meyer Assessment (-) • Wolf Motor Function Test (-) • Stroke Impact Scale (-) • Elbow extension (-) • Shoulder extension (-) • Wrist extension (+exp) • Elbow flexion (-)
Luft et al. (2004) RCT (7) N_{start}=26 N_{end}=21 TPS=Chronic	E: Bilateral arm training + rhythmic auditory cueing C: Therapeutic exercises. Duration: 1 h, 3d/wk for 6wk	• Fugl Meyer (-) • Wolf Motor Arm Test (-) • University of Maryland Arm Questionnaire for Stroke (-) • Elbow Strength (-) • Shoulder Strength (-)
Bilateral arm training with rhythmic auditory cueing compared to task orientated unilateral arm training		
Song et al. (2015) RCT (5) N_{Start}=40 N_{End}=40 TPS=Chronic	E: Bilateral arm training with rhythmic auditory cueing C: Task-oriented bilateral arm training Duration: 30min, 5d/wk for 12wk	• Box and Block Test (+con) • Jebsen Taylor Hand Function Test (+con) • Modified Barthel Index (+con)
Occupation-based bilateral arm training versus Task-based bilateral arm training		

Kim et al. (2019)
RCT (7)
N_{start}= 20
N_{end}= 20
TPS= Chronic
	E: Occupation-based bilateral upper
	extremity training
	C: Task-based bilateral upper extremit
	training
	Duration: 30min, 5x/wk for 4wks
		• Canadian Occupational Performance Measure
		  • Performance: (+exp)
		  • Satisfaction: (+exp)
		• Stroke Impact Scale:
		  • Strength: (+exp)
		  • Activities of Daily Living and Instrumental Activities of Dai
		  Living: (+exp)
		  • Mobility: (-)
		  • Hand Function: (-)
		  • Memory: (-)
		  • Communication: (-)
		  • Emotion: (+exp)
		  • Participant: (+exp)
		• Action Research Arm Test:
		  • Grasp: (-)
		  • Grip: (-)
		  • Pinch: (-)
		  • Gross Movement: (-)
		• Yonsei-Bilateral Activity Test
		  • Quality of performance: (-)
		  • Satisfaction: (+exp)
		• Accelerometer
		  • Use of unaffected side: (-)
		  • Use of affected side: (+exp)

Bilateral arm training compared to TENS		
Stinear et al. (2014) RCT (6)	E: Bilateral training C: TENS	• Modified Ashworth Scale (-) • Stroke Impact Scale (-)

N_{Start}=57 N_{End}=51 TPS=Not given	Duration: 45min, 5d/wk for 4wk	
EMG-triggered NMES with bilateral arm training compared to EMG-triggered NMES with unilateral training		
Singer et al. (2013) RCT (4) N_{Start}=24 N_{End}=21 TPS=Chronic	E: Bilateral training + EMG-triggered NMES C: Unilateral training + EMG-triggered NMES Duration: 30min, 7d/wk for 6wk	• Fugl-Meyer Assessment (-) • Arm Motor Ability Test (-)
Cauraugh & Kim (2002) RCT (5) N_{start}=25 N_{end}=25 TPS=Chronic	E: EMG-triggered NMES + bilateral training E2: EMG-triggered NMES + unilateral training C: Control Duration: 90min, 4d/wk for 2wk	E1 vs E2/C • Box and Block Test: (+exp) E2 vs C • Box and Block Test (+exp_2)
Long term NMES with bilateral arm training compared to short term NMES with bilateral arm training		
Cauraugh et al. (2011) RCT (6) N_{start}= 18 N_{end}= 18 TPS= Chronic	E: Long term care (BAT +NMES) (10mo) C: Short term care (BAT +NMES) (4wks) Duration: 90min, 1x/wk, (16mo follow-u retention test)	• Box and Block Test: (+exp) • Reaction time: (+exp) • Force produced: (+exp)
Bilateral arm training compared to CIMT		
Brunner et al. (2012) RCT (7) N_{start}=30 N_{end}=30 TPS=Not given	E: Bilateral training C: mCIMT Duration: 4h, 7d/wk for 4wk	• Action Research Arm Test (-) • 9 Hole Peg Test (-) • Motor Activity Log (-)
Wu et al. (2011) RCT (5) N_{start}=66 N_{end}=58 TPS=Chronic	E: dCIT E2: Bilateral training C: Control Duration: 2h, 5d/wk for 3wk	E/E2 vs C • Normalized Movement Unit for unilateral and bilateral tasks (+exp, exp_2) E2 vs C • Peak Velocity for unilateral and bilateral tasks (exp_2) E vs C • Wolf Motor Function Test (+exp) E vs E2/C • Motor Activity Log (+exp) • Wolf Motor Function Test (-) • Peak Velocity for unilateral and bilateral tasks (-) • Normalized Movement Unit for unilateral and bilateral tasks (-)
Modified CIMT with unilateral training compared to rhythmic auditory cueing with bilateral arm training		
van Delden et al. (2015) RCT (6) N_{Start}=60 N_{End}=52 TPS=Subacute	E: Modified CIMT + unilateral training E2: Rhythmic auditory cueing + bilatera training C: Dose-matched Control Duration: 1h, 3d/wk for 6wk	E2 vs C • Bimanual coordination task: (+exp_2) E vs C • Unimanual reference task (+con) E vs E2 • Unimanual reference task (+exp_2)
van Delden et al. (2013) RCT (6) N_{Start}=60 N_{End}=55 TPS=Subacute	E1: Modified CIMT + unilateral training E2: Rhythmic auditory cueing + bilateral training C: Dose-matched control group Duration: 1h, 3d/wk for 6wk	• Action Research Arm Test (-) • Nine Hole Peg Test (-) • Motricity Index (-) • Fugl-Meyer Assessment (-) • Motor Activity Log (-) • Stroke Impact Scale (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Bilateral Arm Training

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Bilateral arm training** may not have a difference in efficacy when compared to **unilateral arm training** for improving motor function.	12	Renner et al. 2020; Hung et al. 2019; Hung et al. 209; Shim et al. 2015; McCombe et al. 2014; Kim et al. 2013; Wu et al. 2013; Morris and van Wijck, 2012; Yang et al. 2012; Lin et al. 2010; Stoykov et al. 2009; Morris et al. 2008
1a	There is conflicting evidence about the effect of **Bilateral arm training** to produce greater improvements in motor function than **conventional therapy**.	4	Arya et al. 2020; Easow et al. 2019; Meng et al. 2018; Lee et al. 2017; Stinear et al. 2008; Desrosiers et al. 2005
1a	**Bilateral arm training with rhythmic auditory cueing** may not have a difference in efficacy when compared to **unilateral arm training or conventional therapy** for improving motor function.	4	Dispa et al. 2013; Whiteall et al. 2011; Luft et al. 2004; McCombe Waller et al. 2004
2	**Bilateral arm training with rhythmic auditory cueing** may no have a difference in efficacy compared to **task orientated unilateral arm training** for improving motor function.	1	Song et al. 2015
1b	**Occupation-based bilateral arm training** may not have a difference in efficacy when compared to **task-based bilateral arm training** for improving motor function.	1	Kim et al. 2019
2	**EMG-triggered NMES with bilateral arm training** may not have a difference in efficacy when compared to **EMG-triggered NMES with unilateral arm training** for improving motor function.	1	Singer et al. 2013
1b	**Bilateral arm training** may not have a difference in efficacy when compared to **CIMT** for improving motor function.	2	Brunner et al. 2012; Wu et al. 2011
1a	There is conflicting evidence about the effect of **bilateral arm training with rhythmic auditory cueing** to improve motor function when compared to **mCIMT**.	2	Van Delden et al. 2015; Van Delden et al. 2013

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Bilateral arm training** may not have a difference in efficacy when compared to **unilateral arm training** for improving spasticity.	3	Renner et al. 2020; McCombe et al. 2014; Yang et al. 2012

1b	**Bilateral arm training** may not have a difference in efficacy when compared to **TENS** for improving spasticity.	1	Stinear et al. 2014

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Bilateral arm training** may not produce greater improvements in stoke severity than **conventional therapy**.	1	Arya et al. 2020

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **bilateral arm training** on improving dexterity when compared to **unilateral arm training.**	4	Han and Kim, 2016; McCombe et al. 2014; Morris and van Wijck, 2012; Morris et al. 2008
1a	**Bilateral arm training** may not improve dexterity when compared to **conventional therapy**.	3	Easow et al. 2019; Lee et al. 2017; Desrosiers et al. 2005
2	**Bilateral arm training with rhythmic auditory cueing** may no have a difference in efficacy compared to **task orientated unilateral arm training** for improving dexterity.	1	Song et al. 2015
2	**EMG-triggered NMES with bilateral arm training** may produce greater improvements in dexterity than **EMG-triggered NMES with unilateral arm training or conventional therapy**.	1	Cauraugh and Kim, 2002
1b	**Long term EMG-triggered NMES with bilateral arm training** may produce greater improvements in dexterity than **short-term EMG-triggered NMES with bilateral arm training**.	1	Cauraugh et al. 2011
1b	**Bilateral arm training** may not have a difference in efficacy when compared to **CIMT** for improving dexterity.	1	Brunner et al. 2012
1b	**Bilateral arm training with rhythmic auditory cueing** may not have a difference in efficacy when compared to **unilateral training** for improving dexterity.	1	Dispa et al. 2103
1b	**Bilateral arm training with rhythmic auditory cueing** may not have a difference in efficacy when compared to **mCIMT** for improving dexterity.	1	Van Delden et al. 2013

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Bilateral arm training** may not have a difference in efficacy when compared to **unilateral arm training** for improving muscle strength.	3	Renner et al. 2020; McCombe et al. 2014; Yang et al. 2012

1a	**Bilateral arm training** may not have a difference in efficacy when compared to **conventional therapy** for improving muscle strength.	2	Stinear et al. 2008; Desrosiers et al. 2005
1a	**Bilateral arm training with rhythmic auditory cueing** may not have a difference in efficacy when compared to **unilateral arm training or conventional therapy** for improving muscle strength.	2	Whiteall et al. 2011; Luft et al. 2004
1b	**Occupation-based bilateral arm training** when compared to **task-based bilateral arm training** may produce greater improvements in muscle strength.	1	Kim et al. 2019
1b	**Long term bilateral arm training with EMG-NMES** may produce greater improvements in muscle strength compared to **short-term bilateral arm training with EMG-NMES**	1	Cauruagh et al. 2011

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
2	**Bilateral arm training** may not have a difference in efficacy compared to **unilateral arm training** for improving range of motion.	1	Renner et al. 2020

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
1a	**Bilateral arm training** may not have a difference in efficacy compared to **unilateral arm training** for improving performance of activities of daily living.	8	Hung et al. 2019; Hung et al. 2019; Shim et al. 2015; Wu et al. 2013; Lin et al. 2010; Stoykov et al. 2009; Morris et al. 2008; Summers et al. 2007
1a	There is conflicting evidence about the effect of **bilateral arm training** to improve performance of activities of daily living when compared to **conventional therapy**.	4	Easow et al. 2019; Lee et al. 2017; Lee et al. 2013; Desrosiers et al. 2005
1a	**Bilateral arm training with rhythmic auditory cueing** may not have a difference in efficacy when compared to **unilateral arm training** for improving performance of activities of daily living.	2	Dispa et al. 2013; Whiteall et al. 2011
2	**Bilateral arm training with rhythmic auditory cueing** may no have a difference in efficacy compared to **task orientated unilateral arm training** for improving performance in activities of daily living.	1	Song et al. 2015
1b	**Occupation-based bilateral arm training** when compared to **task-based bilateral arm training** may produce greater improvements in performance of activities of daily living.	1	Kim et al. 2019
1b	**Bilateral arm training** may not have a difference in efficacy when compared to **TENS** for improving performance of activities of daily living.	1	Stinear et al. 2014

2	**EMG-triggered NMES with bilateral arm training** may not have a difference in efficacy when compared to **EMG-triggered NMES with unilateral arm training** for improving performance of activities of daily living.	1	Singer et al. 2013
1b	There is conflicting evidence about the effect of **bilateral arm training** to improve performance of activities of daily living when compared to **CIMT**.	2	Brunner et al. 2012; Wu et al. 2011
1b	**Bilateral arm training with rhythmic auditory cueing** may not have a difference in efficacy when compared to **mCIMT** for improving performance of activities of daily living.	1	Van Delden et al. 2013

Key points

The literature is mixed regarding bilateral arm training for upper limb rehabilitation following stroke.

Bilateral arm training may not be beneficial compared to unilateral training for upper limb function.

Bilateral arm training in combination with other therapy approaches may not be beneficial for upper limb rehabilitation.

Exercise and Strength Training

Adopted from: https://www.flintrehab.com/2018/arm-exercises-for-stroke-patients/

Exercise can be broadly divided into two categories; anaerobic and aerobic activities both of which may be important to post-stroke recovery (Marzolini et al 2018). Anaerobic training often involves small numbers of repetition and/or a short time period during exercise that does not activate aerobic respiration systems. One common type of anaerobic exercise is strength training which is defined as an intervention involving repetitive and effortful muscle contractions with the goal of increasing motor unit activity (Ada et al. 2006). The strength training interventions analyzed were classified as either traditional strength training or functional strength training. Traditional strength training involves resistance training in which individual muscles are often isolated and stabilized through protocols involving free weights or machines (Tomljenovic et al. 2011). Functional strength training is based on the principle of specific adaptations to imposed demands (SAID) in which training programs involve tasks that are modeled after common daily activities (Tomljenovic et al. 2011). These tasks often involve multiple muscle groups and require functional movements that are more applicable and may produce gains in strength in performing everyday tasks (Tomljenovic et al. 2011).

Aerobic training encompasses exercises involve higher amounts of repetition and/or longer durations of exercise aimed at promoting positive adaptations of the cardiorespiratory system. These adaptions are believed to modulate neurotrophins; growth-promoting factors that stimulate synaptogenesis, dendritic branching, and long-term potentiation (Abraha et al. 2018, da Silva et al. 2016). Interventions such as high intensity interval training and circuit classes aim to seek the possible benefits of activating the cardiorespiratory system for improving stroke-associated motor deficiencie.

33 RCTs were found evaluating strength training for upper extremity motor rehabilitation. Ten RCTs compared strength training to conventional rehabilitation, simple joint mobilization or scapular exercises (Coroian et al. 2018; Dell'Uomo et al. 2017; Kim et al. 2017; Kim and Yim, 2017; Jeon et al. 2016; Da Silva et al. 2015; Lin et al. 2015; Wang et al. 2007; Winstein et al.

2004; Trombly et al. 1986). Four RCTs looked at strength training compared to task-specific training (Folkerts et al. 2017; Awad et al. 2015; Thielman et al. 2013; Corti et al. 2012). Three RCTs compared functional strength training to conventional therapy, non-functional strength training or movement performance therapy (Hunter et al. 2018; Park et al. 2017; Graef et al. 2016; Donaldson et al. 2009). Two RCTs looked at functional strength training compared to task-specific training (Agni and Kulkarni, 2017; Pattern et al. 2013). One RCT looked at aerobic exercise compared to stretching (Quaney et al. 2009). Four RCTs evaluated the effect of high intensity interval/circuit training compared to moderate intensity or conventional therapy (Abraha et al. 2018; Nepveu et al. 2017; English et al. 2015; Hesse et al. 2011). Three RCTS examined the effect of high intensity therapy vompared to low intensity therapy (Hogg et al. 2020; Han et al. 2013; Rodgers et al. 2003). One RCT evaluated bilateral isometric handgrip force training with visual feedback vs routine Therapy (Lin et al. 2015). Three RCTs examined the effect of exercise training with feedback versus exercside training without feedback (Cristea et al. 2006; Gilmore and Spaulding 2007; Platz et al. 2001). One RCT examined the effect of motor tasks with 3D characterization intrinsic feedback amplification versus 3D characterization alone (Cruz et al. 2014).

The methodological details and results of all 33 RCTs are presented in Table 3.

Table 3. RCTs Evaluating Strength Training Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Strength training versus conventional rehabilitation, simple joint mobilization or scapular exercises		
Coroian et al. (2018) RCT (7) N_{Start}=20 N_{End}=16 TPS=Chronic	E: Isokinetic Strengthening C: Passive Joint Mobilization Duration: 45min/d, 3d/wk for 6wk	• Fugl-Meyer Assessment (+con) • Isokinetic Peak Torque (-) • Box and Block Test (-) • Modified Ashworth Scale (-)
Dell'Uomo et al. (2017) RCT (5) N_{Start}=28 N_{End}=28 TPS=Subacute	E: Scapulohumeral Rehabilitation C: Conventional Arm/Trunk Rehabilitation Duration: 20min/d, 5d/wk for 6wk	• Barthel Index (-) • Fugl-Meyer Assessment (-) • Modified Ashworth Scale (-)
Kim et al. (2017) RCT (5) N_{Start}=24 N_{End}=17 TPS=Chronic	E: Scapular Stabilization Exercise C: Simple Scapular Exercise Duration: 30min/d, 3d/wk for 8wk	• Manual Function Test (+exp)
Kim & Yim (2017) RCT (5) N_{Start}=30 N_{End}=29 TPS=Chronic	E: Hand Training and Treadmill Weight Bearing Training C: Conventional Therapy Duration: 30min/d, 3d/wk for 6wk	• Handgrip Strength (-)
Jeon et al. (2016) RCT (5) N_{Start}=12 N_{End}=12 TPS=Chronic	E: Repetitive bilateral and unilateral movements with strength exercises C: Conventional rehabilitation Duration: 30min/d, 3d/wk for 12wk	• Flexion and abduction range of motion (+exp)
Da Silva et al. (2015) RCT (8)	E: Strength training C: Standard care	• TEMPA (+exp) • Glumerohumeral flexion strength (+exp)

N_{Start}=20 N_{End}=20 TPS=Chronic	Duration: 30min/d, 2d/wk for 6wk	• Active shoulder Range of Motion (+exp) • Fugl-Meyer Assessment (+exp)
Lin et al. (2015) RCT (7) N_{Start}=33 N_{End}=33 TPS=Chronic	E: Bilateral Isometric Handgrip Force Training with Visual Feedback C: Routine Therapy Duration: 30min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp) • Motor Assessment Scale (+exp) • Barthel Index (+exp)
Wang et al. (2007) RCT (4) N_{start}=44 N_{end}=44 TPS=Subacute	E: Resistance training C: Conventional physical therapy Duration: 5d/wk, 4wks + (con 60min, 5x/wk 4wks)	• Blood pressure: (-) • Heart rate: (-) • Brunnstrom stage: (+exp) • Barthel Index: (-)
Winstein et al. (2004) RCT (6) N_{start}=64 N_{end}=44 TPS=Acute	E1: Strength training E2: Functional task practice C: Standard care Duration: 1h/d, 5d/wk for 4wk	E1/E2 vs. C • Fugl Meyer Assessment: (+exp & +exp_2) • Functional test of the hemiparetic upper extremity (+exp & +exp_2) • Isometric torque (+exp & +exp_2)
Trombly et al. (1986) RCT (4) N_{start}=20 N_{end}=20 TPS=Chronic	E1: Resisted Grasp E2: Resisted Extension C: Ballistic Extension Duration: 7d/wk for 3wk	• Finger Extension Range of Motion (-) • Speed and ability to rapidly reverse movement (-)
Strength training versus task-specific training		
Folkerts et al (2017) RCT Crossover (4) N_{Start}=11 N_{End}=10 TPS=Chronic	E1: Eccentric Strength Training followed by Task-Oriented Strength Training E2: Task-Oriented Strength Training followed by Eccentric Strength Training Duration: 3d/wk for 4wk	• Action Research Arm Test (-) • Shoulder, Elbow and Wrist Strength (-)
Awad et al. (2015) RCT (4) N_{Start}=30 N_{End}=23 TPS=Chronic	E: Shoulder Strength Training, Trunk Control Training, and Additional Strengthening Exercises. C: Shoulder Strength Training and Trunk Control Training. Duration: 3d/wk for 6wk	• Shoulder Abduction Peak Torque (+exp) • Shoulder External Rotator Peak Torque (+exp) • Supraspinatus Peak Force (+exp) • Upper Trapezius Peak Force (+exp) • Serratus Anterior Peak Force (+exp) • Scapular Upward Rotation Angle (+exp) • Spinal Lateral Deviation Angle (+exp)
Thielman et al. (2013) RCT (6) N_{Start}=16 N_{End}=16 TPS=Chronic	E: Progressive resistive strength training C: Task-related training Duration: *Not reported*	• Activate range of motion for shoulder and elbow (+exp) • Wolf Motor Function Test (+exp) • Reaching (+exp)
Corti et al. (2012) RCT Crossover (7) N_{start}=14 N_{end}=14 TPS=Chronic	E1: Power Training E2: Functional Task Practice Duration: 90min/d, 3d/wk for 10wk	• Shoulder Flexion and Elbow Extension (+exp)
Functional strength training versus conventional therapy, strength training or movement performance therapy		
Hunter et al. (2018) RCT (6) N_{Start}=288 N_{End}=240 TPS=Acute	E: Functional Strength Training C: Movement Performance Therapy Duration: 90min/d, 5d/wk for 6wk	• Action Research Arm Test (-) • Wolf Motor Function Test (-) • Grip and Pinch Force (-)
Park et al. (2017) RCT (5) N_{Start}=30 N_{End}=26	E: Boxing C: Conventional Therapy Duration: 30min/d, 3d/wk for 6wk	• Manual Function Test (+exp) • Unaffected Side Hand Grip Strength (+exp)

TPS=Subacute		
Graef et al. (2016) RCT (8) N_{Start}=28 N_{End}=27 TPS=Chronic	E: Strength training with a functional goal C: Strength training with non-functional movements Duration: 30min/d, 3d/wk for 5wk	• Upper-Extremity Performance Test (+exp) • Shoulder Strength (-) • Grip Strength (-) • Shoulder Active Range of Motion (-) • Fugl-Meyer Assessment (-) • Modified Ashworth Scale (-)
Donaldson et al. (2009) RCT (8) N_{start}= 30 N_{end}= 19 TPS= Acute	E1: Conventional therapy + functional strength E2: Conventional therapy (time matched) C: Conventional therapy Duration: 1hr, 4d/wk for 6wks	E1 Vs C • Active Range of Motion: (-) • 9 Hole Peg Test: (-) • Grip Force: (-) • Pinch Force: (-) • Elbow Force (Flexion, Extension): (-) E2 Vs C • Active Range of Motion: (-) • 9 Hole Peg Test: (-) • Grip Force: (-) • Pinch Force: (-) • Elbow Force (Flexion, Extension): (-) E1 Vs E2 • Active Range of Motion: (-) • 9 Hole Peg Test: (-) • Grip Force: (-) • Pinch Force: (-) • Elbow Force (Flexion, Extension): (-)
Functional strength training versus task-specific training		
Agni and Kulkarni (2017) RCT (5) N_{start}=45 N_{end}=37 TPS=Chronic	E1: Strength Training E2: Functional Task-Related Training E3: Functional Task-Related Training with Strength Training Duration: 70min/d, 3d/wk for 6wk	E1 vs. E2: • Chedoke Arm and Hand Inventory (exp_2) • Manual Muscle Strength (+exp) • Fugl-Meyer Assessment (-) E1 vs E3: • Chedoke Arm and Hand Inventory (+exp_3) • Manual Muscle Strength (+exp_3) • Fugl-Meyer Assessment (-) E2 vs E3: • Chedoke Arm and Hand Inventory (-) • Manual Muscle Strength (+exp_3) • Fugl-Meyer Assessment (-)
Patten et al. (2013) RCT (7) N_{start}=19 N_{end}=17 TPS=Chronic	E: Functional Task Practice and Power Training C: Functional Task Practice Duration: 75min/d, 3d/wk for 4wk	• Wolf Motor Function Test (-) • Ashworth Scale (-) • Functional Independence Measure (+exp)
Aerobic Exercises Vs Stretching		

Quaney et al. (2009)
RCT (6)
N_{start}=40
N_{end}=38
TPS=Chronic
	E: Aerobic exercise
	C: Stretching
	Duration: 45min, 3x/wk, 8wks
		• VO2 max: (+exp)
		• Wisconsin Card Sorting Task: (-)
		• Stroop task: (-)
		• Trail-making B-A: (-)
		• Serial reaction time task:
		  • Repeat: (+exp)
		  • Random: (-)
		• Predictive grip force modulation: (+exp)
		• Fugl Meyer total: (-)

Interval and Circuit Training Vs Moderate Exercise or Conventional Therapy		
Abraha et al. (2018) RCT (4) N_{start}= 12 N_{end}= 10	E: High intensity interval training C: Moderate Intesity Exercise Duration: 5 cycles of 20min	• Box and Block Test: (-) • Grip strength: (-)

TPS= Chronic		
Nepveu et al. (2017) RCT (5) N_{start}= 22 N_{end}= 21 TPS= Chronic	E: High-Intensity Interval Training C: Rest control Duration: 1x, 15min	• Skill retention: (+exp)
English et al. 2015 RCT (4) N_{start}=281 N_{end}=261 TPS=acute/subacute Int code 39 Chap 11	E: Circuit Class physiotherapy (90min/day 2x/day 37hr/week) E2: 7 days/week physiotherapy 18hr/week C: Conventional physiotherapy (5 days/week 15hr/week) Duration: 4 weeks	• Wolf Motor Function Test (-) • Functional Independence Measure (-) • Stroke Impact Scale (-)
Hesse et al. (2011) RCT (8) N_{start}= 50 N_{end}= 48 TPS= Subacute	E: High intensity training C: Conventional care Duration: 4x/wk, 30-45min, 2 months at a time, (1-2, 5-6, 9-10) for 12 mos	• Rivermead Mobility Index: (-) • Rivermead Arm: (-) • Box and Block Test: (-) • Modified Ashworth Scale: (-)
High Intensity Therapy Versus Low Intensity Therapy or Conventional Care		
Högg et al. (2020) RCT (8) N_{start}= 43 N_{end}= 32 TPS= Acute	E: High intensity arm training therapy C: Low intensity arm training therapy Duration: 60min, 3x/wk, 3wks	• Grip Strength: (-) • Motricity Index: (-) • Fugle-Meyers Assessment Upper Extremity: (+exp) • Box and Block Test: (-)
Han et al. (2013) RCT (8) N_{start}= 32 N_{end}= 30 TPS= Subacute	E1: 3hr/d arm training E2: 2hrs/d arm training C: 1hr/d arm training Duration: 5d/wk, 6wks	E1 Vs C • Fugle-Meyers Assessment Upper Extremity: (+exp1) • Action Research Arm Test: (+exp1) • Barthel's Index: (-) E2 Vs C • Fugle-Meyers Assessment Upper Extremity: (+exp2) • Action Research Arm Test: (+exp2) • Barthel's Index: (-) E1 Vs E2 • Fugle-Meyers Assessment Upper Extremity: (-) • Action Research Arm Test: (-) • Barthel's Index: (-)
Rodgers et al. (2003) RCT (8) N_{start}= 123 N_{end}= 96 TPS= Acute	E: High intensity interdisciplinary upper limb therapy (physiotherapist and occupational therapist) C: Usual care Duration: 30minutes, 5x/week for 6 weeks	• Action research Arm Test (-) • Motricity Index (-) • Frenchay Arm test (-) • Barthel Activities of Daily Living Index (-) • Nottingham EADL (-)
Bilateral isometric handgrip force training with visual feedback vs Routine Therapy		
Lin et al. (2015) RCT (7) N_{start}= 33 N_{end}= 33 TPS= Chronic	E: Bilateral isometric handgrip force training with visual feedback C: Routine therapy Duration: 30 min, 3 days/ week for 4 weeks, total of 12 sessions	• Fugl-Meyers Upper Extremity (+exp) • Wolf Motor Function Test (+exp) • Modified Ashworth Scale (+exp) • Barthel Index (+exp)
Exercise training with feedback versus training with out feedback		
Chang-Yong et al. (2015) RCT (7) N_{Start}=44 N_{End}=40 TPS=Chronic	E: Target reaching training with biofeedback + routine therapy C: Routine therapy Duration: *Not Specified*	• Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp) • Reach speed (+exp) • Reaching angle (+exp) • Maximum reach distance (-)

Gilmore and Spaulding (2007) RCT (5) N_{start}= 10 N_{end}= 10 TPS= Subacute	E: Occupational therapy with video feedback C: Occupational therapy Duration: 10 sessions	• Klein-Bell Activities of Daily Living Scale (-) • Canadian Occupational Performance Measure (-)
Cristea et al. (2006) RCT (6) N_{start}= 37 N_{end}= 37 TPS= Chronic	E1: Reaching task with knowledge of results E2: Reaching task with knowledge of performance C: Non-reaching practice Duration: 1 hr, 5x/week for 2 weeks (10 sessions total)	• Movement Time and Variability (+exp2) • Precision of Movement (-) • Fugle-Meyers Assessment (-) • TEMPA (Performance Test for the Elderly) (-) • Spasticity Index of Elbow (-)
Platz et al. (2001) RCT (4) N_{start}= 45 N_{end}= 45 TPS= Subacute Mixed pop (75% stroke)	E: Daily arm ability training with knowledge of results feedback E2: Arm ability training no feedback C: Usual care Duration:	E Vs C • Test Evaluant les Membres superieurs des Personnes Agees (+exp) E2 VS C • Test Evaluant les Membres superieurs des Personnes Agees (+exp) E1 Vs E2 • Test Evaluant les Membres superieurs des Personnes Agees (-)
Motor tasks 3D characterization with intrinsic feedback amplification versus 3D characterization alone		
Cruz et al. (2014) RCT (5) N_{start}= 44 N_{end}= 42 TPS= Acute Crossover	E: Repetitive motor task under vibratory feedback and 3D motor characterization C: 3D motor characterization only Duration: Not reported	• Correct movements and movements per minute (+exp) • Range of Motion (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Strength Training

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Strength training** may produce greater improvements in **motor function** than **conventional therapy, simple joint mobilization or scapular exercises**.	7	Coroian et al. 2018; Dell'Uomo et al. 2017; Kim et al. 2017; Da Silva et al. 2015; Lin et al. 2015; Wang et al. 2007; Winstein et al. 2004
1b	There is conflicting evidence about the effect of **strength training** to improve **motor function** when compared to **task-specific training**.	3	Agni and Kulkarni, 2017; Folkerts et al. 2017; Thielman et al. 2013
1a	**Functional strength training** may not have a difference in efficacy when compared to **conventional therapy, strength training or movement performance therapy** for improving **motor function**.	5	Hunter et al. 2018; Agni and Kulkarni, 2017; Park et al. 2017; Graef et al. 2016 Donaldson et al. 2009

1b	**Functional strength training** may not have a difference in efficacy when compared to **task-specific training** for improving **motor function**.	3	Agni and Kulkarni, 2017; Pattern et al. 2013;
1b	**Aerobic exercise** may not have a difference in efficacy when compared **stretching** for improving **motor function**.	1	Quaney et al. 2009
1b	**High intensity interval training or circuit training** may not have a difference in efficacy when compared to **conventional therapy or rest** control for improving motor function.	2	English et al. 2015; Hesse et al. 2011
1b	There is conflicting evidence about the effect of high **internsity arm training** to improve motor function when compared to **low intensity arm training.**	3	Hogg et al. 2020; Han et al. 2013; Rogers et al. 2003
1b	**Bilateral isometric handgrip force training with visual feedback** may produce greater improvements in motor function than **routine therapy**.	1	Lin et al. 2015
1b	There is conflicingt evidence about the effct **of arm training with feedback** when compared to **arm training with out feedback** for improving motor function.	1	Chang-Yong et al. 2015; Cristea et al. 2006
2	**Motor tasks with 3D characterization and intrinsic feedback amplification** may produce greater improvements in motor function when compared to **3D characterization alone.**	1	Cruz et al. 2014

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1b	**Strength training** may not have a difference in efficacy when compared to **conventional therapy, simple joint mobilization or scapular exercises** for improving dexterity.	2	Corian et al. 2018; Trombly et al. 1986
1a	**Functional Strength training** may not have a difference in efficacy when compared to **conventional therapy, simple joint mobilization or scapular exercises** for improving dexterity.	1	Donaldson et al. 2009
1b	**High intensity interval training or circuit training** may not have a difference in efficacy when compared to **conventional therapy or rest** control for improving dexterity.	2	Abraha et al. 2018; Hesse et al. 2011
1b	**High internsity arm training** may not have a difference in efficacy when compared to **low intensity or conventional arm training** for increasing dexterity.	1	Hogg et al. 2020

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1b	**Strength training** may not have a difference in efficacy when compared to **conventional therapy, simple joint mobilization or scapular exercises** for improving spasticity.	2	Coroian et al. 2018; Dell'Uomo et al. 2017

1b	**Functional strength training** may not have a difference in efficacy when compared to **strength training** for improving spasticity.	1	Graef et al. 2016
1b	**Functional strength training** may not have a difference in efficacy when compared to **task-specific training** for improving spasticity.	1	Pattern et al. 2013
1b	**High intensity interval training or circuit training** may not have a difference in efficacy when compared to **conventional therapy or rest** control for improving spasticity.	1	Hesse et al. 2011
1b	**Bilateral isometric handgrip force training with visual feedback** may produce greater improvements in spasticity than **routine therapy**.	1	Lin et al. 2015
1b	**Arm training with feedback** may not have a difference in efficacy for improving spasticity when compared to **arm training with out feedback.**	1	Cristea et al. 2006

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
1a	**Strength training** may produce greater improvements in range of motion than **conventional therapy, simple joint mobilization or scapular exercises**.	4	Jeon et al. 2016; Da Silva et al. 2015; Winstein et al. 2004; Trombly et al. 1986
1a	**Strength training** may produce greater improvements in range of motion than **task-specific training**.	2	Thielman et al. 2013; Corti et al. 2012
1b	**Functional strength training** may not have a difference in efficacy when compared to **strength training** for improving range of motion.	2	Graef et al. 2016; Donaldson et al. 2009
2	**Motor tasks with 3D characterization and intrinsic feedback amplification** may not have a difference in efficacy when compared to **3D characterization alone** for improving range of motion.	1	Cruz et al. 2014

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
1b	There is conflicting evidence about the effect of **strength training** to improve performance of activities of daily living when compared to **conventional therapy, simple joint mobilization or scapular exercises**.	3	Dell'Uomo et al. 2017; Lin et al. 2015; Wang et al. 2007
2	**Functional strength training** may produce greater improvements in performance of activities of daily living than **strength training**.	1	Agni and Kulkarni, 2017
1b	There is conflicting evidence about the effect of **functional strength training** to improve performance of activities of daily living when compared to **task-specific training**.	2	Agni and Kulkarni, 2017; Pattern et al. 2013

1b	**High internsity arm training** may not have a difference in efficacy when compared to **low intensity or conventional arm training** for increasing performance on acitivites of daily living.	2	Han et al. 2013; Rogers et al. 2003
1b	**Bilateral isometric handgrip force training with visual feedback** may produce greater improvements in performance on activities of daily living than **routine therapy**.	1	Lin et al. 2015

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **strength training** to improve muscle strength when compared to **conventional therapy, simple joint mobilization or scapular exercises**.	3	Coroian et al. 2018; Kim and Yim, 2017; Da Silva et al. 2015;
2	**Strength training** may produce greater improvements in muscle strength than **task-specific training**.	3	Agni and Kulkarni, 2017; Folkerts et al. 2017; Awad et al. 2015
1a	**Functional strength training** may not have a difference in efficacy when compared to **conventional therapy, strength training or movement performance therapy** for improving muscle strength.	5	Hunter et al. 2018; Agni and Kulkarni, 2017; Park et al. 2017; Graef et al. 2016; Donaldson et al. 2009
2	**Functional strength training** may produce greater improvements in muscle strength than **task-specific training**.	1	Agni and Kulkarni, 2017
1b	**Aerobic exercise** may produce greater improvements in muscle strength when compared to **stretching**.	1	Quaney et al. 2009
1b	**High intensity interval training or circuit training** may not have a difference in efficacy when compared to **conventional therapy or rest** control for improving dexterity.	1	Hesse et al. 2011
1b	**High internsity arm training** may not have a difference in efficacy when compared to **low intensity or conventional arm training** for increasing muscle strength.	1	Hogg et al. 2020
1b	**Arm training with feedback** may not have a difference in efficacy for improving performance on activities of daily living when compared to **arm training with out feedback.**	3	Gilmore and Spaulding 2007; Cristea et al. 2006; Platz et al. 2001

Key points

Strength training may be more beneficial for upper limb function than conventional therpay.

The literature is mixed regarding strength training when compared to functional strength training

Task-Specific Training

Adopted from: https://www.stltoday.com/lifestyles/health-med-fit/custom-made-rehab-helps-victims-of-stroke/article_06eb5759-3291-5730-930f-725c0d436450.html

Task-specific training involves integrating tasks that are relevant to daily life (e.g. pouring a drink into a cup) into rehabilitation programs, while repetitive task training involves repeated practice of these tasks (Van Peppen et al. 2004; McCombe Waller et al. 2008; Stewart et al. 2006). Usually these consist of motor tasks that are focused on improvement of performance and function through goal-directed practice and repetition (Hubbard et al. 2009). It is well established that task-specific practice is required for motor learning to occur (Schmidt, 1991). 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 (Classen et al.1998). 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 et al.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; Winstein et al. 2001).

A total of 25 RCTs were found that looked task-specific training for upper extremity motor rehabilitation. 16 RCTs looked at task-specific training compared to conventional rehabilitation

(Song et al. 2020; Moon et al. 2018; Khallaf et al. 2017; Marryam et al. 2017; Skubik-Peplaski et al. 2017; Brkic et al. 2016; Winstein et al. 2016; Kim et al. 2015; Hubbard et al. 2015; Zondervan et al. 2014; Shimodozono et al. 2013; Thielman et al. 2013; Arya et al. 2012; Boyd et al. 2010; Ross et al. 2009; Thielman et al. 2004). Two RCTs looked at the intensity of task-specific training delivered (Waddell et al. 2017; Lang et al. 2016). Two RCTs looked at robotic training with task-specific training compared to robotic training (Page et al. 2020; Hung et al. 2016), and another RCT looked at EMG-triggered NMES with task-specific training compared to EMG-triggered NMES (Kim et al. 2016). One RCT looked at task-specifc training with functional electrical stimulation and (Alon et al. 2009). One RCT looked at immediate versus delayed task-specific training (Almhdawi et al. 2016). One study evaluated task-specific training combined with bilateral arm training versus task-specific training alone (Hsieh et al. 2016) and one RCT evaluated task-specific training with external feedback versus task-specific training with internal feedback (Durham et al. 2014).

The methodological details and results of all 25 RCTs are presented in Table 4.

Table 4. RCTs Evaluating Task-Specific Training for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Task-specific training compared to conventional rehabilitation		
Song et al. (2020) RCT (5) N_{start}= 32 N_{end}= 32 TPS= Chronic	E: Task Specific Training C: Non-Task Specific Training Duration: 30min, 5d/wk for 4wks	• Fugl-Meyers Upper Extremity: (-) • Modified Barthel Index: (-)

Moon et al. (2018)
RCT (5)
N_{start}= 18
N_{end}= 18
TPS= Acute
	E: Task oriented circuit training
	C: Conventional therapy
	Duration: 30min, 5-6x/wk for 4wks
		• Fugl-Meyers Upper Extremity: (-)
		  • Shoulder/elbow: (-)
		  • Wrist: (-)
		  • Hand: (-)
		  • Coordination: (-)
		• Motor Activity Log
		  • Amount of Use: (+exp)
		  • Quality of Movement: (-)
		• Stroke Impact Scale: (-)
		  • Arm Strength: (+exp)
		  • Hand Grip Strength: (+exp)
		  • Using Spoon: (+exp)
		  • Dress Top Up: (-)
		  • Wash: (-)
		  • Toenail: (-)
		  • Doorknob: (-)
		  • Can or Jar: (-)
		  • Shoe Lace: (-)
		  • Coin Grip: (-)
		  • Recovery: (-)

Khallaf et al. (2017)
RCT (8)
N_{start}= 24
N_{end}= 24
TPS= Chronic
	E: Received task specific exercises
	C: Traditional passive stretch and range of motion exercises
	Duration: 16 wks, 5x/wk, 60 min and study group wore splint for 2h each 3h
		• Nine Hole Peg Test: +(exp)
		• Fugl-Meyers Assessment:
		  • Upper Extremity: (-)
		  • Hand: (-)
		• Wrist Extension: (+exp)
		• Metacarpophalangeal Extension: (+exp)
		• Thumb Carpometacarpal Extension: (+exp)

Marryam et al. (2017) RCT (4)	E: Task oriented training	• Motor Assessment Scale: (+exp) • Upper Arm Function: (+exp)

N_{start}= 43 N_{end}= 38 TPS= Subacute (*Not reported*)	C: Conventional therapy Duration: 2hrs/d for 4wks	• Hand Item: (+exp) • Advanced Hand Activity: (+exp)
Skubik-Peplaski et al. (2017) RCT (7) N_{Start}=16 N_{End}=16 TPS=Chronic	E: Repetitive Task Practice C: Occupation-Based Intervention Duration: 55min/d, 2d/wk for 4wk	• Fugl-Meyer Assessment (-) • Stroke Impact Scale (-) • Canadian Occupational Performance Measure (-)
Brkic et al. (2016) RCT (5) N_{Start}=24 N_{End}=22 TPS=Acute	E: Repetitive upper limb functional task practice C: Conventional rehabilitation Duration: 7d/wk for 4wk	• Action Research Arm Test (+exp) • Grip Strength (+exp)
Winstein et al. (2016) ICARE Trial RCT (7) N_{Start}=361 N_{End}=361 TPS=Subacute	E1: Structured, task-oriented upper extremity training E2: Dose-equivalent occupational therapy C: Monitoring-only occupational therapy Duration: 1h/d, 3d/wk for 10wk	E1/E2 vs C; E1 vs E2 • Wolf Motor Function Test: (-) E1/E2 vs C; E1 vs E2 • Stroke Impact Scale: (-)
Kim et al. (2015) RCT (8) N_{Start}=44 N_{End}=40 TPS=Chronic	E: Target reach training with visual biofeedback, routine occupational and physical therapy C: Routine occupational and physical therapy Duration: 1h/d, 3d/wk for 4wk	• Fugl-Meyer Upper Extremity (+exp) • Wolf Motor Function Test (+exp) • Range of Motion of the shoulder (+exp)
Hubbard et al. (2015) RCT (6) N_{Start}=23 N_{End}=23 TPS=Acute	E: Task-specific training and standard care C: Standard Care Duration: 2h/d, 5d/wk for 3wk	• Upper Limb Motor Assessment Scale (-) • Modified Rankin Scale (-)
Zondervan et al. (2014) RCT (6) N_{Start}=17 N_{End}=16 TPS=Chronic	E: Self-guided, high-repetition home therapy with mechanical arm exerciser C: Conventional therapy Duration: 1h/d, 3d/wk for 3wk	• Fugl-Meyer Assessment (-) • Motor Activity Log (-) • Ashworth Scale (-)
Shimodozono et al. (2013) RCT (7) N_{Start}=52 N_{End}=49 TPS=Subacute	E: Repetitive functional exercise C: Conventional rehabilitation Duration: 40min/d, 5d/wk for 4wk	• Action Research Arm Test (+exp) • Grasp and pinch (+exp) • Fugl Meyer (+exp)
Thielman et al. (2013) RCT (6) N_{start}=37 N_{end}=37 TPS=Chronic	E1: Task-Related Training (TRT) E2: Progressive Resistive Exercises (PRE) Duration: *Not reported*	• Motor Activity Log (+exp) • Wolf Motor Function Test (+exp) • Reaching Performance Scale (+exp) • Fugl-Meyer Assessment (+exp)
Arya et al. (2012) MTST Trial RCT (9) N_{Start}=103 N_{End}=102 TPS=Subacute	E: Task-specific training C: Standard training using the Bobath approach Duration: 1h/d, 4-5d/wk for 4wk	• Fugl Meyer Score (+exp) • Action Research Arm Test (+exp)
Boyd et al. (2010) RCT (5) N_{start}=18 N_{end}=18 TPS=Chronic	E: Task-specific training C: General arm training Duration: 3 sessions	• Change in reaction and movement time (+exp)
Ross et al. (2009) RCT (5)	E: Task-specific therapy directed at the hand C: Usual care	• Action Research Arm Test (-) • Manual Muscle Test (-)

N_{start}=39 N_{end}=37 TPS= Acute/subacute Stroke 90%) TBI (10%)	Duration: TST 1hr/week + 10 mins/week, 3x/week for 6 weeks	
Thielman et al. (2004) RCT (4) N_{start}=12 N_{end}=12 TPS=Chronic	E: Progressive resistive exercises C: Task-related training Duration: 35min/d, 3d/wk for 4wk	• Modified Ashworth Scale (-) • Rivermead Motor Assessment (-)
Intensity of task-specific training		
Waddell et al. (2017) RCT (5) N_{Start}=85 N_{End}=78 TPS=Chronic	E1: 13.6 hours of task-specific training (100 repetitions/session) E2: 20 hours of task-specific training (200 repetitions/session) E3: 26.3 hours of task-specific training dose group (300 repetitions/session) Duration: 25-50min/d, 4d/wk for 8wk	• Action Research Arm Test (-)
Lang et al. (2016) RCT (5) N_{Start}=85 N_{End}=82 TPS=Chronic	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 Duration: 1h/d, 4d/wk for 8wk	• Action Research Arm Test (-) • Stroke Impact Scale (-) • Canadian Occupational Performance Measure (-)
Robotic training with task-specific training		
Page et al. (2020) RCT (7) N_{start}= 35 N_{end}= 31 TPS= Chronic	E1: Myomo electromyography (EMG) powered orthosis with repetitive task practice (RTP) E2: Myomo EMG powered orthosis C: RTP Duration: 1hr, 3x/wk, 8wk	• Fugl-Meyers Upper Extremity: (-) • Action Research Arm Test: (-)
Hung et al. (2016) RCT (8) N_{Start}=21 N_{End}=21 TPS=Chronic	E: Robotic training + task-specific training C: Robotic training + impairment-oriented training Duration: 20min/d, 3d/wk for 6wk	• Fugl-Meyer Assessment (+exp) • Stroke Impairment Scale (+exp)
EMG-triggered NMES with task-specific training		
Kim et al. (2016) RCT (6) N_{Start}=20 N_{End}=20 TPS=Chronic	E: EMG-triggered NMES with task-oriented training on paretic arm C: EMG-triggered NMES Duration: 30min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Box and Block Test (+exp) • Jebsen-Taylor Hand Function Test (+exp)
Task Specific Training combined with Functional Electrical Stimulation		
Alon (2009) RCT (5) N_{start}= 46 N_{end}= 46 TPS= Not reported	E: Task specific training (TST) + functional electrical stimulation C: Task specific training Duration: 30min 2x/wk for 12wks	• Box and Block Test: (+exp) • Jebsen Taylor Hand Function Test: (-) • Modified Fugl-Meyer (11 to 33 range): (+exp)
Immediate vs Delayed Task Specific Training		

Almhdawi et al. (2016)
RCT (7)
N_{start}= 21
N_{end}=20
TPS= Chronic
	E: Immediate task specific training (TST)
	C: Delayed TST
	Duration: 3hr 1x/wk for 6wks
		• Canadian Occupational Performance Measure: (+exp)
		• Motor Activity Log
		  • Amount of Use: (+exp)
		  • Quality of Movement: (+exp)
		• Wolf Motor Function Test: (-)
		• Shoulder Flexion: (-)
		• Active Range of Motion: (-)

Task-Specific Training Combined with Bilateral Arm Training		
Hsieh et al. (2016) RCT (6) N_{Start}=31 N_{End}=31 TPS=Subacute	E: Bilateral arm priming + task-oriente training C: Task-oriented training alone Duration: 90min, 5d/wk for 4wk	• Fugl-Meyer Assessment (-) • Box and Block Test (-) • Grip Strength (-) • Modified Rankin Scale (-) • Functional Independence Measure (-) • Activities of Daily Living (-) • Stroke Impact Scale (+exp)
Task-Specific Training with External Feedback Vs Task-Specific Training with Internal Feedback		
Durham et al. (2014) RCT (6) N_{start}= 42 N_{end}= 42 TPS= Chronic Cross over	E: Task specific training with external feedback C: Task specific training with internal feedback Duration: 96 reaches performed in tot	• Raise object task (-) • Reach to grasp: peak velocity, push object: peak deceleration and movement duration (+exp) • Push object peak velocity, raising object (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Task-Specific Training

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **Task-specific training** on producing greater improvements in motor function than **conventional therapy**.	12	Moon et al. 2018; Khallaf et al. 2017; Skubik-Peplaski et al. 2017; Brkic et al. 2016; Winstein et al. 2016; Kim et al. 2015; Zondervan et al. 2014; Shimodozono et al. 2013; Thielman et al. 2013; Arya et al. 2012; Boyd et al. 2010; Thielman et al. 2004
2	**Higher intensity task-specific training** may not have a difference in efficacy when compared to **lower intensity task-specific training** for improving motor function.	2	Waddell et al. 2017; Lang et al. 2016
1b	**Robotic training with task-specific training** may produce greater improvements in motor function than **robotic training with impairment-oriented training**.	1	Hung et al. 2016
1b	**EMG-triggered NMES with task-specific training** may produce greater improvements in motor function than **EMG-triggered NMES alone**.	1	Kim et al. 2016
2	**Task-specific training with functional electrical stimulation** may produce greater improvements in motor function than **Task-specific training alone.**	1	Alon et al. 2009
1b	**Immediate Task-specific training** may not produce greater improvements in motor function than **delayed Task-specific training.**	1	Almhdawi et al. 2016
1b	**Task-specific training with external feedback** may not have a difference in efficacy when compared to **task-specific training with internal feedback** for improving motor function.	1	Durham et al. 2014

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1b	**Task-specific training** may produce greater improvements in dexterity than **conventional therapy.**	1	Khallaf et al. 2017
1b	**EMG-triggered NMES with task-specific training** may produce greater improvements in dexterity than **EMG-triggered NMES alone**.	1	Kim et al. 2016
2	There is conflicting evidence about the effect of **Task-specific training with functional electrical stimulation** on producing greater improvements in dexterity than **Task-specific training alone.**	1	Alon 2009

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1a	**Task-specific training** may produce greater improvements in spasticity than **conventional therapy**.	2	Zondervan et al. 2014; Thielman et al. 2004

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
1b	**Task-specific training** may produce greater improvements in range of motion than **conventional therapy**.	2	Khallaf et al. 2017; Kim et al. 2016
1b	**Immediate Task-specific training** may not produce greater improvements in motor function than **delayed Task-specific training.**	1	Almhdawi et al. 2016

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References
1b	**Task-specific training** may not have a difference in efficacy when compared to **conventional therapy** for improvements on measures of stroke severity.	1	Hubbard et al. 2015

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
1a	**Task-specific training** may not have a difference in efficacy when compared to **conventional therapy** for improving performance of activities of daily living.	9	Song et al. 2020; Moon et al. 2018; Marryam et al. 2017; Skubik-Peplaski et al. 2017; Hung et al 2016; Winstein et al. 2016; Hubbard et al. 2015; Zondervan et al. 2014; Thielman et al. 2013
2	**Task-specific training** may produce greater improvements in performance of activities of daily living than **strength training**.	1	Agni and Kulkarni, 2017

2	**Higher intensity task-specific training** may not have a difference in efficacy when compared to **lower intensity task-specific training** for improving performance of activities of daily living.	1	Lang et al. 2016
1b	**Robotic training with task-specific training** may produce greater improvements in performance of activities of daily living than **robotic training with impairment-oriented training**.	1	Hung et al. 2016
1b	**Immediate Task-specific training** may produce greater improvements in motor function than **delayed Task-specific training.**	1	Almhdawi et al. 2016

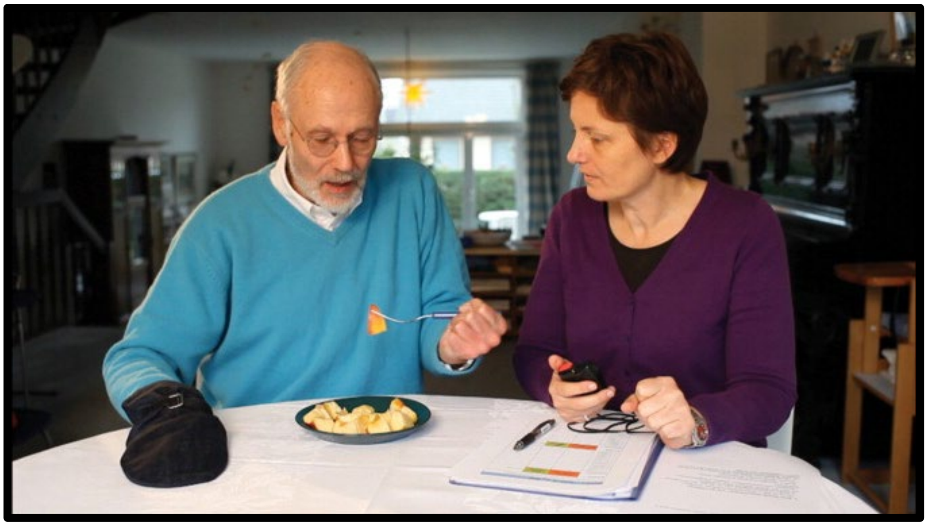
MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Task-specific training** may produce greater improvements in muscle strength than **conventional therapy**.	2	Brkic et al. 2016; Shimodozono et al. 2013

Key points

Task-specific training, alone or in combination with other therapy approaches, may be beneficial for some aspects of upper limb function following stroke.

Both the timing of, and higher and lower intensity, task-specific training may have similar effects on upper limb function.

Constraint-Induced Movement Therapy (CIMT)



Adopted from: https://neenahsatellite.com/15429/student-life/creative-writing/magazines/effectiveness-of-cimt/

Roughly 80% of all stroke survivors are left with motor impairments of the upper limb which affects their ability to perform activities of daily living (ADLs) (Kwakkel et al. 2016; Langhorne et al. 2009). Constraint-Induced Movement Therapy (CIMT) is a neurorehabilitation technique originally designed in the 1970s for the purpose of improving upper extremity function post-stroke (Christie et al. 2019; Morris et al. 2006). Traditional CIMT involves three key components: 1) immobilization of the non-paretic hand/arm using a mitt for 90% of waking hours, 2) high intensity task-oriented training with the paretic hand/arm, and 3) behavioural strategies to encourage use of the paretic upper limb after the patient leaves therapy, also known as a transfer package (Etoom et al. 2016).

CIMT is designed to overcome the tendency among hemiparetic patients to avoid the use of their paretic limb, a process termed "learned non-use". By constraining the non-paretic upper limb, the patient is forced to activate the muscles and neural pathways of their paretic limb, promoting neuroplasticity and use-dependent cortical reorganization (Taub et al. 1999). This form of treatment has shown promise, especially among stroke survivors with moderate upper limb disability. Modified versions of CIMT (mCIMT) have since been developed with varied dosage, timing, and composition of therapy but generally include less intense training of the paretic limb over a longer period of time (Kwakkel et al. 2016). CIMT is often compared to "forced use", or constraint only treatments, which are conceptually simpler versions of CIMT that do not apply operant training techniques.

Here we provide a review of 63 published RCTs related to CIMT for upper extremity motor rehabilitation. In order to better contextualize this body of evidence, studies were separated and classified according to the type of treatment (CIMT or mCIMT) as well as the time poststroke (acute/subacute phase (<6 months) or chronic stage (>6 months)), leading to 4 groups of RCTs. The authors' own declaration of the type of therapy (i.e. mCIMT or CIMT) was used for classification purposes.

Tables 5 list the summary of 12 examining CIMT in the acute/subacute phase poststroke (Shah et al. 2016; Song et al. 2016; Batool et al. 2015; Thrane et al. 2015; Yoon et al. 2014; Dromerick et al. 2009; Boake et al. 2007; Ro et al. 2006; Page et al. 2005; Albets et al. 2004; Plougman and Corbett 2004; Dromerick et al. 2000).

Table 6 lists 26 RCTs evaluating CIMT in the chronic phase (Doussoulin et al. 2018; Souza et al. 2015; Nadeau et al. 2014; Takebayshi et al. 2013; Huseyinsinoglu et al. 2012; Khan et al. 2011; Wu et al. 2011; Lin et al. 2010; Tariah et al. 2010; Wolf et al. 2010; Lin et al. 2009; Dahl et al. 2008; Gauthier et al. 2008; Lin et al. 2008; Sawaki et al. 2008; Wolf et al. 2008; Lin et al. 2007; Wu et al. 2007; Brogardh and Bengt, 2006; Richards et al. 2006; Underwood et al. 2006; Wolf et al. 2006; Alberts et al. 2004; Suputtitada et al. 2004; Wittenberg et al. 2003)

Tables 7 lists the summary of 10 mCIMT in the acute phase postroke (Yu et al. 2017; Kwakkel et al. 2016; Liu et al. 2016; El-Helow et al. 2014; Treger et al. 2012; Brogardh et al. 2009; Hammer and Lindmark, 2009; Myint et al. 2007.

Table 8 lists 15 RCTs examining the use of mCIMT in the chronic phase (Doussoulin et al. 2017; Hsieh et al. 2016; Yadav et al. 2016; Barzel et al. 2015; Bellay et al. 2015; Smania et al. 2012; Wang et al. 2011; Hayner et al. 2010; Page et al. 2008; Lin et al. 2007; Wu et al. 2007b; Wu et al. 2007c; Yen et al. 2005; Page et al. 2004; Page et al. 2002.)

Table 5. Summary of RCTs Evaluating CIMT in the Acute/Subacute (<6months) Phase for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Shah et al. (2016) RCT (5) N_{Start}=45 N_{End}=40 TPS=Subacute	E: CIMT C: Motor Relearning Program Duration: 80% of working hours	• Motor Activity Log (+exp) • Nine Hole Peg Test (-) • Fugl-Meyer Assessment (-)
Batool et al. (2015) RCT (5) N_{Start}=42 N_{End}=42 TPS=Subacute	E: CIMT C: Motor Relearning Programme Duration: 2h, 6d/wk for 3wk	• Modified Ashworth Scale (+exp) • Functional Independence Measure (+exp)
Thrane et al. (2015) RCT (7) N_{Start}=47 N_{End}=47 TPS=Acute	E: CIMT C: Usual Care Duration: 3h, 1/d for 10d	• Wolf Motor Function Test (-) • Stroke Impact Scale (-) • Fugl-Meyer Assessment (-)
Boake et al. (2007) RCT (5) N_{start}=23 N_{end}=16 TPS=Acute	E: CIMT C: Traditional rehabilitation Duration: 3h, 6d/wk for 2wk	• Fugl Meyer Motor recovery (-) • Grooved Pegboard test (-) • Motor Activity Log: Quality of Movement (+exp)
Ro et al. (2006) RCT (6) N_{start}=8 N_{end}=8 TPS=Acute	E: CIMT C: Traditional rehabilitation Duration: 3h, 6d/wk for 2wk	• Grooved Pegboard test (+exp) • Fugl-Meyer Assessment (+exp) • Motor Activity Log (-)
Page et al. (2005) RCT (5) N_{start}=10 N_{end}=10 TPS=Subacute	E: CIMT C: Regular rehabilitation Duration: 30min, 3d/wk for 10wk	• Action Research Arm Test (-) • Fugl-Meyer Assessment (-) • Motor Activity Log (-)

Alberts et al. (2004) RCT (5) N_{start}=10 N_{end}=10 TPS=Subacute	E: CIMT C: Conventional rehabilitation Duration: 6h, 5d/wk for 2wk	• Maximum precision grip (+exp) • Wolf Motor Function Test (+exp)
Ploughman & Corbett (2004) RCT (5) N_{start}=23 N_{end}=23 TPS=Subacute	E: Forced Use Therapy (Constraint without Shaping) C: Conventional Therapy Duration: 1-6h (incremental increase), 5d/wk for 2wk	• Chedoke McMaster Impairment Inventory (+exp) • Action Research Arm Test (-) • Functional Independence Measure (-)
Dromerick et al. (2000) RCT (6) N_{start}=23 N_{end}=20 TPS=Acute	E: CIMT C: Traditional upper extremity therapy Duration: 2h, 5d/wk for 2wk	• Action Research Arm Test (+exp) • Functional Independence Measure (-) • Barthel Index (-)
High Intensity CIMT compared to CIMT		
VECTORS (Study Acronym) Dromerick et al. (2009) RCT (6) N_{start}=52 N_{end}=52 TPS=Subacute	E1: High-intensity CIMT E2: Standard CIMT C: ADL and UE bilateral training Exercises Duration: 2-3h, 5d/wk for 2wk	E2/C vs E1 • Action Research Arm Test: (+exp_2, +con) • Functional Independence Measure (-) • Stroke Impact Scale (-)
CIMT combined with another intervention		
Seok et al. (2016) RCT (5) N_{Start}=32 N_{End}=30 TPS=Subacute	E1: CIMT with Visual Biofeedback E2: Visual Biofeedback C: Conventional Occupational Therapy Duration: 1h, 5d/wk for 2wk	E1 vs C • Grasp Strength (+exp) • Pinch Strength (+exp) • Wolf Motor Function Test (+exp) • Fugl-Meyer Assessment (+exp) E2 vs C • Grasp Strength (-) • Pinch Strength (-) • Wolf Motor Function Test (+exp_2) • Fugl-Meyer Assessment (+exp_2)
Yoon et al. (2014) RCT (7) N_{Start}=26 N_{End}=26 TPS=Subacute	E1: CIMT combined with mirror therapy E2: CIMT C: Conventional therapy Duration: 6h, 5d/wk for 2wk	E1 v E2 • Box and block test (+exp) • Nine-hole pegboard test (+exp) • Grip strength (+exp) • Brunnstrom Recovery Stages (-) • Wolf motor function test (-) • Fugl-Meyer Assessment (-) • Korean Modified Barthel Index (-) E1 v C • Box and block test (+exp) • Nine-hole pegboard test (+exp) • Grip strength (+exp) • Brunnstrom Recovery Stages (-) • Wolf motor function test (+exp) • Fugl-Meyer Assessment (-) • Korean Modified Barthel Index (+exp) E2 vs C • Box and block test (+exp_2) • Nine-hole pegboard test (-) • Grip strength (+exp_2) • Brunnstrom Recovery Stages (-) • Wolf motor function test (+exp_2) • Fugl-Meyer Assessment (-) • Korean Modified Barthel Index (+exp_2)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.

+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Table 6. Summary of RCTs Evaluating CIMT in the Chronic (>6months) Phase Poststroke for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Huseyinsinoglu et al. (2012) RCT (6) N$_{start}$=24 N$_{end}$=21 TPS=Chronic	E: CIMT C: Bobath Duration: 3h/d for 10d	• Motor Activity Log (+exp) • Wolf Motor Function Test (-) • Functional Independence Measure (-)
Khan et al. (2011) RCT (6) N$_{start}$=44 N$_{end}$=39 TPS=Chronic	E1: CIMT E2: Therapeutic Climbing C: Conventional Neurological Therapy Duration: 15-20h/wk for 4wk	E1 vs E2 • Wolf Motor Function Test (+exp) • Motor Activity Log (-) • Isometric Strength (-) • Active Range of Motion (-) E1 vs C • Wolf Motor Function Test (-) • Motor Activity Log (-) • Isometric Strength (-) • Active Range of Motion (-)
Wu et al. (2011) RCT (5) N$_{start}$=66 N$_{end}$=65 TPS=Chronic	E1: Distributed CIMT E2: Bilateral Arm Training C: Routine Therapy Duration: 2h, 5d/wk for 3wk	E1/E2 vs C • Unilateral and Bilateral Smoothness while Reaching: (+exp, +exp2) E1 vs E2/C • Motor Activity Log: (+exp) E1 vs E2/C • Wolf Motor Function Test: (+exp)
Lin et al. (2010) RCT (5) N$_{start}$=13 N$_{end}$=13 TPS=Chronic	E: Distributed CIMT C: Routine Therapy Duration: 2h, 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp)

Tariah et al. (2010)
RCT (6)
N$_{start}$=20
N$_{end}$=18
TPS=Chronic
	E: CIMT
	C: Neuro-developmental Treatment (NDT)
	Duration: 2hrs/d, 2mo
		• Wolf Motor Function Test:
		  • Time: (-)
		  • Score: (-)
		• Motor Activity Log:
		  • Amount of use: (-)
		  • Quality of use: (-)
		• Fugl Meyer Assessment:
		  • Joint motion: (-)
		  • Pain score: (-)
		  • Sensation: (-)
		  • Motor function: (-)

Lin et al. (2009) RCT (5) N$_{start}$=32 N$_{end}$=32 TPS=Chronic	E: CIMT C: Dose Matched Control Intervention Duration: 2h, 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Stroke Impact Scale (+exp) • Nottingham Extended Activities of Daily Living (+exp) • Motor Activity Log (+exp)
Dahl et al. (2008) RCT (8) N$_{start}$=30	E: CIMT C: Community-based rehabilitation Duration: 6h, 5d/wk for 2wk	• Wolf Motor Function Test: post (+exp), 6mo (-) • Motor Activity Log (-)

N_{end}=30 TPS=Chronic		• Functional Independence Measure (-) • Stroke Impact Scale (-)
Lin et al. (2008) RCT (5) N_{start}=22 N_{end}=22 TPS=Chronic	E: CIMT C: Traditional Intervention Duration: 2h, 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Functional Independence Measure (+exp) • Motor Activity Log (-) • Nottingham Extended Activities of Daily Living Scale (-), mobility subsection (+exp)
Lin et al. (2007) RCT (5) N_{start}=35 N_{end}=32 TPS=Chronic	E: CIMT C: Neurodevelopmental techniques Duration: 2h, 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Functional Independence Measure (+exp) • Motor Activity Log (-)
Wu et al. (2007a) RCT (6) N_{start}=47 N_{end}=47 TPS=Chronic	E: CIMT C: Regular interdisciplinary rehab Duration: 2h, 5d/wk for 3wk	• Motor Activity Log (+exp) • Fugl-Meyer Assessment (-)
Underwood et al. (2006) RCT (8) N_{start}=41 N_{end}=32 TPS=Chronic	E: CIMT + shaping procedure C: Usual care Duration: 6h, 5d/wk for 2wk	• Fugl-Meyer Assessment (-) • Wolf Motor Function Test (-)
Wolf et al. (2006) RCT (8) EXCITE N_{start}=222 N_{end}=201 TPS=Chronic	E: CIMT + shaping procedure C: Usual care Duration: 6h, 5d/wk for 2wk	• Wolf Motor Function Test (+exp) • Motor Activity Log (+exp)
Suputtitada et al. (2004) RCT (6) N_{start}=69 N_{end}=69 TPS=Chronic	E: CIMT C: Bimanual-upper-extremity training based on NDT approach Duration: 6h, 5d/wk for 2wk	• Action Research Arm Test (+exp) • Pinch test (+exp)
High compared to low intensity CIMT		
Souza et al. (2015) RCT (5) N_{start}=24 N_{end}=19 TPS=Chronic	E1: CIMT high intensity (3h) E2: CIMT low intensity (1h) Duration: 1/3h, 3-4d/wk for 4wk	• Fugl-Meyer Assessment (-) • Motor Activity Log (-)
Brogårdh & Bengt (2006) RCT (7) N_{start}=16 N_{end}=16 TPS=Chronic	E: CIMT and using mitt at home for another 3 months every other day C: CIMT Duration: 6h, 5d/wk for 2wk	• Modified Motor Assessment Scale (-) • Sollerman Hand Function Test (-) • Motor Activity Log (-)
Wittenberg et al. (2003) RCT (5) N_{start}=16 N_{end}=16 TPS=Chronic	E: Intense CIMT (6h) C: Less intense CIMT (3h) Duration: 3/6h/d for 10d	• Motor Activity Log (+exp) • Wolf Motor Function Test (-) • Assessment of Motor and Process Skills (-)
High intensity CIMT compared to low intensity CIMT combined with cyloserine (antibiotic)		
Nadeau et al. (2014) RCT (7) N_{Start}=24 N_{End}=22 TPS=Chronic	E1: CIMT-6hr + cycloserine C1: CIMT-6hr + placebo E2: CIMT-2hr + cycloserine C2: CIMT-2hr + placebo Duration: 2/6h, 3-5d/wk for 10wk	• Fugl-Meyer Assessment (-) • Wolf Motor Function Test (-) • Motor Activity Log (-)
Early compared to delayed CIMT		
Wolf et al. (2010) RCT (8) N_{start}=226	E1: CIMT early (3-9 months' post stroke) E2: CIMT delayed (15 to 21 months post stroke)	• Wolf Motor Function Test (+exp) • Motor Activity Log (+exp) • Stroke Impact Scale (+exp)

N_{end}=192 TPS=Chronic	Duration: 90% of waking time for 2wk	
Sawaki et al. (2008) RCT (8) N_{start}=30 N_{end}=30 TPS=Chronic	E: Early CIMT C: Delayed CIMT (4mo after randomization) Duration: 90% of d for 2wk	• Grip strength (+exp) • Wolf Motor Function Test (-)
Wolf et al. (2008) RCT (8) N_{start}=98 N_{end}=70 TPS=Chronic	E1: CIMT early (3-9 months' post stroke) E2: CIMT delayed (15 to 21 months post stroke) Duration: 90% of waking time for 2wk	• Wolf Motor Function Test (+exp) • Motor Activity Log (+exp) • Functional Independence Measure (+exp) • Stroke Impact Scale (+exp)
CIMT with transfer package		
Takebayashi et al. (2013) RCT (5) N_{Start}=23 N_{End}=21 TPS=Chronic	E: CIMT + transfer package (train affected arm) C: CIMT Duration: 4.5h spread over 2wk	• Fugl-Meyer Assessment (-) • Motor Activity Log (+exp)
Taub et al. (2013) RCT (5) N_{Start}=45 N_{End}=40 TPS=Chronic	E1: Shaping training + CIMT transfer package (TP) E2: Repetitive task practice + TP E3: Repetitive task practice C: Shaping training	E1/E2 vs. E3/C • Motor Activity Log (+exp, +exp2) E1/E2 vs. E3/C • Wolf Motor Function Test (+exp, +exp2)
Gauthier et al. (2008) RCT (4) N_{start}= 49 N_{end}= 36 TPS= Chronic	E: CIMT with transfer package C: CIMT Duration: 3hrs/d, 5d/wk, 2wks (+30min transfer package)	• Motor Activity Log (Quality of Movement): (+exp) • Wolf Motor Function Test (Time): (-)
CIMT combined with rTMS or donepezil (cholinesterase inhibitor)		
Richards et al. (2006) Secondary analyses of two parallel RCTs (7) N_{start}=39 N_{end}=35 TPS=Chronic	E1: Traditional CIMT (6h) + donepezil C1: Traditional CIMT (6h) + placebo E2: Shortened CIMT (1h) + repetitive transcranial magnetic stimulation (rTMS) C2: Shortened CIMT (1h) + sham rTMS Duration:1/6h, 5d/wk for 2wk	E1 vs C1 • Motor Activity Log (+exp) • Wolf Motor Function Test: (-) E2 vs C2 • Motor Activity Log (-) • Wolf Motor Function Test: (-)

Nadeau et al. (2004)
RCT (5)
N_{start}= 24
N_{end}= 20
TPS= Chronic
	E: Donepezil + CIMT
	C: Placebo + CIMT
	Duration: 5mg/d, 2wks + 10mg/d 4wks
		• Wolf Motor Function Test: (-)
		  • Time: (-)
		• Motor Activity Log
		  • Amount of Use: (-)
		  • Quality of Movement: (-)
		  • Fugl-Meyers Upper Extremity: (-)
		• Stoke Impact Scale Item 8 (Participation): (-)
		• Geriatric Depression Scale: (-)
		• Actual Amount of Use Test: (-)
		  • Amount: (-)
		  • Quality: (-)
		• Stroke Impact Scale - Item 9: (-)
		• Caregiver Strain Index: (-)
		• Finger-Tapping: (-)

Individual compared to Group CIMT		
Doussoulin et al. (2018) RCT (4) N_{start}= 36 N_{end}= 36 TPS= Chronic	E: CIMT (group) C: CIMT (individual) Duration: 3hrs, 10 consecutive days	• Motor Activity Log (Amount of Use): (+exp) • Action Research Arm Test: (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Table 7. Summary of RCTs Evaluating Modified CIMT in the Acute/Subacute (<6 months) Phase for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)

Yu et al. (2017)
RCT (5)
N_{start}=29
N_{end}=29
TPS=Acute
	E: mCIMT
	C: Conventional therapy
	Duration: 3h/d for 10d
		• Wolf Motor Function Test: (+exp)
		  • Time: (-)
		• Motor Activity Log
		  • Amount of Usage: (+exp)
		  • Quality of Movement: (-)

Kwakkel et al. (2016) RCT (7) N_{Start}=159 N_{End}=159 TPS=Subacute	E1: Electromyographic Neuromuscular Stimulation on finger extensors E2: Modified Constraint Induced Movement Therapy C1: Unfavourable prognosis based on voluntary finger extension. Received usual care. C2: Favourable prognosis based on voluntary finger extension. Received usual care. Duration: 3h, 5d/wk for 3wk	E2 vs C2; E1 vs C1 • Action Research Arm Test: (+exp_2) • Fugl-Meyer Assessment: (-) • Wolf Motor Function Test (-) • Motricity Index (-) • Erasmus Modified Nottingham Sensory Assessment (-) • Nine-Hole Peg Test (-) • Frenchay Arm Test (-) • Motor Activity Log (-) • Stroke Impact Scale-Hand (+exp_2)
Liu et al. (2016) RCT (6) N_{Start}=90 N_{End}=86 TPS=Subacute	E1: Modified Constraint Induced Movement Therapy E2: Self-Regulated Modified Constraint Induced Movement Therapy C: Conventional Therapy Duration: 1h, 5d/wk for 2wk	E1 vs C • Action Research Arm Test (+exp) • Fugl-Meyer Assessment (+exp) • Lawton Instrumental Activities of Daily Living (+exp) • Motor Activity Log (+exp) E2 vs C • Action Research Arm Test (+exp_2) • Fugl-Meyer Assessment (+exp_2) • Lawton Instrumental Activities of Daily Living (-) • Motor Activity Log (+exp_2) E1 vs E2 • Action Research Arm Test (-) • Fugl-Meyer Assessment (+exp_2) • Lawton Instrumental Activities of Daily Living (+exp_2) • Motor Activity Log (+exp_2)
El-Helow et al. (2014) RCT (6) N_{start}=60 N_{end}=60 TPS=Acute	E: Modified Constraint Induced Movement Therapy C: Conventional Rehabilitation Duration: 6h/d for 2wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (+exp)
Treger et al. (2012) RCT (7) N_{start}=28	E: mCIMT C: Traditional rehabilitation Duration: 4h, 2d/wk for 2wk	• Functional Independence Measure (-) • Manual Function Test (-)

N_{end}=28 TPS=Subacute		
Brogårdh et al. (2009) RCT (5) N_{start}=24 N_{end}=24 TPS=Subacute	E: Shortened CIMT (mitt use) C: No mitt use Duration: 90% of waking time for 12d	• Motor Assessment Scale (-) • Sollerman Hand Function Tst (-) • 2-Point Discrimination Test (-) • Motor Activity Log Test (-)
Hammer & Lindmark (2009) RCT (6) N_{Start}=30 N_{End}=26 TPS=Subacute	E: Restraining sling and Standard Rehabilitation C: Standard Rehabilitation Duration: 6h, 5d/wk for 2wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Motor Assessment Scale (-) • 16-Hole Peg Test (-) • Grip strength ratio (-) • Modified Ashworth Scale (-)
Myint et al. (2007) RCT (7) N_{start}=43 N_{end}=43 TPS=Subacute	E: mCIMT C: Traditional rehabilitation Duration: 4h/d for 10d	• Action Research Arm Test (+exp) • Motor Activity Log (+exp)
mCIMT combined with audiotry feedback		

Bang. (2016)
RCT (7)
N_{start}= 20
N_{end}= 20
TPS= Subacute
	E: mCIMT combined with auditory feedback
	C: mCIMT
	Duration: 1 hour/day) intervention sessions (5 days/week for 4 weeks)
		• Action Research Arm Test: (+exp)
		• Fugl-Meyers upper extremity (+exp)
		• Modified Barthel Index (+exp)
		• Motor Activity log
		  • Amount of Use (+exp)
		  • Quality of Movement (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Table 8. Summary of RCTs Evaluating Modified CIMT in the Chronic (>6 months) Phase for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample $Size_{start}$ Sample $Size_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Hsieh et al. (2016) RCT (7) N_{start}=34 N_{end}=34 TPS=Chronic	E: mCIMT C: Regular Therapy Duration: 105min, 5d/wk for 4wk	• Wolf Motor Function Test (+exp) • Nottingham Extended Activities of Daily Living (+exp) • Functional Independence Measure (-)
Yadav et al. (2016) RCT (5) N_{start}=65 N_{end}=60 TPS=Chronic	E: mCIMT C: Conventional rehabilitation Duration: 3h, 3d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp)
Barzel et al. (2015) RCT (6) N_{start}=156 N_{end}=156 TPS=Chronic	E: Home CIMT C: Standard Therapy Duration: 5h/wk for 4wk	• Motor Activity Log (+exp) • Wolf Motor Function Test (-) • Nine Hole Peg Test (-) • Stroke Impact Scale (-) • Barthel Index (-) • Instrumental Activities of Daily Living (-)
Bellay et al. (2015) RCT (5) N_{start}= 40	E: mCIMT C: Hand-arm bimanual intensive training (HABIT) training	• Action Research Arm Test (+exp) • Fugl-Meyer Upper Extremity (+exp)

N_{end}= 40 TPS= NR	Duration: 30min/d, 6wks	
Smania et al. (2012) RCT (8) N_{start}=66 N_{end}=40 TPS=Chronic	E: mCIMT C: Dose-match task-specific therapy Duration: 2h, 5d/wk for 2wk	• Wolf Motor Function Test (+exp) • Motor Activity Log (+exp)
Wang et al. (2011) RCT (4) N_{start}=30 N_{end}=30 TPS=Chronic	E1: mCIMT E2: Intensive conventional therapy C: Conventional therapy Duration: 3h, 5d/wk for 4wk	• Wolf Motor Function Test (+exp)
Hayner et al. (2010) RCT (4) N_{start}=12 N_{end}=12 TPS=Chronic	E: mCIMT C: Bilateral training Duration: 6h/d for 10d	• Wolf Motor Function Test (-) • COPM (-)
Page et al. (2008) RCT (5) N_{start}=35 N_{end}=35 TPS=Chronic	E1: mCIMT + physical and occupational therapy E2: Traditional rehab C: No therapy Duration: 5h, 5d/wk for 10wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (+exp)
Lin et al. (2007) RCT (7) N_{start}=34 N_{end}=31 TPS=Chronic	E: mCIMT C: Traditional rehab Duration: 6h, 5d/wk for 3wk	• Motor Activity Log (+exp) • Functional Independence Measure (+exp)
Wu et al. (2007b) RCT (5) N_{start}=26 N_{end}=26 TPS=Chronic	E: mCIMT + a restraining mitt on the unaffected hand C: Traditional therapy Duration: 2h, 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Functional Independence Measure (+exp) • Motor Activity Log (+exp) • Stroke Impact Scale (+exp)
Wu et al. (2007c) RCT (6) N_{start}=30 N_{end}=30 TPS=Chronic	E: mCIMT C: Regular occupational therapy Duration: 2h, 5d/wk for 3wk	• Motor Activity Log (+exp) • Functional Independence Measure (+exp)

Yen et al. (2005)
RCT (6)
N_{start}=30
N_{end}=30
TPS=Chronic
	E: mCIMT
	C: Conventional therapy
	Duration: 6hrs/d for 2wks
		• Wolf Motor Function Test items:
		  • Extend elbow (weight): (+exp)
		  • Lift pencil: (+exp)
		  • Stack checkers: (+exp)
		  • Flip cards: (+exp)
		  • Turn key in lock: (+exp)
		  • Lift basket: (+exp)
		  • Forearm to table (side): (-)
		  • Forearm to box (side): (-)
		  • Extend elbow (side): (-)
		  • Hand to table (front): (-)
		  • Hand to box (front): (-)
		  • Reach and retrieve: (-)
		  • Lift can: (-)
		  • Lift paper clip: (-)
		  • Fold towel: (-)

Page et al. (2004) RCT (6) N_{start}=17 N_{end}=17 TPS=Chronic	E: mCIMT C1: Traditional Rehabilitation C2: No Therapy Duration: 5h, 5d/wk for 10wk	E vs C1: • Fugl-Meyer Assessment (+exp) • Action Research Arm Test (-) E1 vs C2: • Fugl-Meyer Assessment (+exp)

		• Action Research Arm Test (+exp) C1 vs C2: • Fugl-Meyer Assessment (-) • Action Research Arm Test (+con$_1$)
Page et al. (2002) RCT (5) N_{start}=14 N_{end}=14 TPS=Chronic	E1: mCIMT + physical and occupational therapy E2: Traditional rehab C: No therapy Duration: 30min, 3d/wk for 10wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (+exp)
mCIMT in group or individual setting		
Doussoulin et al. (2017) RCT (5) N_{Start}=36 N_{End}=36 TPS=Chronic	E1: mCIMT group therapy E2: mCIMT individual therapy Duration: 3h/d for 10d	• Motor Activity Log (+exp) • Action Research Arm Test (+exp) • Functional Independence Measure (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about CIMT and mCIMT

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**CIMT** may not have a difference in efficacy when compared to **conventional therapy or motor relearning programmes** for improving motor function during the acute/subacute phase poststroke.	9	Shah et al. 2016; Song et al. 2016; Thrane et al. 2015; Yoon et al. 2014; Dromerick et al. 2009; Boake et al. 2007; Page et al. 2005; Alberts et al. 2004; Plougman and Corbett 2004; Dromerick et al. 2000
1b	**High intensity CIMT** may not have a difference in efficacy when compared to **low intensity CIMT** on its own for improving motor function during the acute phase poststroke.	1	Dromerick et al. 2009
2	**CIMT combined with visual biofeedback** may produce greater improvements in motor function than **conventional therapy** on its own during the acute/subacute phase poststroke.	1	Seok et al. 2016
1b	**CIMT combined with mirror therapy** may not have a difference in efficacy when compared to **CIMT on its own** for improving motor function during the acute/subacute phase poststroke.	1	Yoon et al. 2014
1a	**CIMT** may produce greater improvements in motor function than **conventional therapy or neurodevelopmental techniques** during the chronic phase poststroke.	14	Huseyinsinoglu et al. 2012; Khan et al. 2011; Wu et al. 2011; Lin et al. 2010; Tariah et al. 2020; Lin et al. 2009; Dahl et al. 2008; Lin et al. 2008; Lin et al. 2007; Wu et al. 2007; Underwood et al. 2006; Wolf et al. 2006; Alberts et al. 2004; Suputtitada et al. 2004
1b	**High intensity CIMT** may not have a difference in efficacy when compared to **low intensity CIMT** on its own for improving motor function during the chronic phase poststroke.	3	Souza et al. 2015; Brogardh and Bengt, 2006; Wittenberg et al. 2003

1b	**High intensity CIMT with/without cycloserine** may not have a difference in efficacy when compared to **low intensity CIMT with/without cycloserine** for improving motor function during the chronic phase poststroke.	1	Nadeau et al. 2014
1a	**Early CIMT** may produce greater improvements in motor function than **delayed CIMT** during the chronic phase poststroke.	3	Wolf et al. 2010; Sawaki et al. 2008; Wolf et al. 2008
2	**CIMT with the transfer package protocol** may not have a difference in efficacy for improving motor function when compared to **traditional CIMT.**	3	Takebayashi et al. 2013; Taub et al. 2013; Gauthier et al. 2008
2	**CIMT with donepezil** may not have a difference in efficacy for improving motor function when compared to traditional **CIMT or placebo.**	2	Richards et al. 2006; Nadeau et al. 2004
2	**Group based CIMT** may produce greater improvements in motor function than **one on one CIMT sessions** during the chronic phase poststroke.	1	Doussoulin et al. 2018
1a	There is conflicting evidence about the effect of **mCIMT** to improve motor function when compared to **conventional therapy or bilateral arm training** during the acute/subacute phase poststroke.	9	Yu et al. 2017; Kwakkel et al. 2016; Liu et al. 2016; Bang et al. 2014; El-Helow et al. 2014; Treger et al. 2012; Brogardh et al. 2009; Hammer and Lindmark, 2009; Myint et al. 2007
1b	**mCIMT combined with auditory feedback** may produce greater improvements in motor function than **mCIMT alone** during the chronic phase poststroke.	1	Bang et al. 2016
1a	**mCIMT** may produce greater improvements in motor function than **conventional therapy or bilateral arm training** during the chronic phase poststroke.	12	Hsieh et al. 2016; Yadav et al. 2016; Barzel et al. 2015; Bellay 2015; Smania et al. 2012; Wang et al. 2011; Hayner et al. 2010; Page et al. 2008; Wu et al. 2007b; Yen 2005; Page et al. 2004; Page et al. 2002
2	**Group based mCIMT** may produce greater improvements in motor function than **one on one mCIMT sessions** during the chronic phase poststroke.	1	Doussoulin et al. 2017

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1b	**CIMT** may not have a difference in effiacy when compared to **conventional therapy or motor relearning programmes** to improve dexterity during the acute/subacute phase poststroke.	3	Shah et al. 2016; Boake et al. 2007; Ro et al. 2006
1b	**CIMT combined with mirror therapy** may produce greater improvements in dexterity than **CIMT on its own** during the acute/subacute phase poststroke.	1	Yoon et al. 2014
1b	**mCIMT** not have a difference in efficacy when compared to **conventional therapy or bilateral arm training** for improving dexterity during the acute/subacute phase poststroke.	1	Kwakkel et al. 2016
1b	**mCIMT** not have a difference in efficacy when compared to **conventional therapy or bilateral arm**	1	Barzel et al. 2015

	training for improving dexterity during the chronic phase poststroke.		

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**CIMT** may produce greater improvements in spasticity than **conventional therapy or motor relearning programmes** during the acute/subacute phase poststroke.	1	Batool et al. 2015
1b	**mCIMT** not have a difference in efficacy when compared to **conventional therapy or bilateral arm training** for improving spasticity during the acute/subacute phase poststroke.	1	Hammer and Lindmark, 2009

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**CIMT** not have a difference in efficacy when compared to **conventional therapy or neurodevelopmental techniques** for improving range of motion during the chronic phase poststroke.	1	Khan et al. 2011
1b	**mCIMT** may produce greater improvements in range of motion than **conventional therapy or motor relearning** programmes during the acute/subacute phase poststroke.	1	Bang et al. 2014

PROPRIOCEPTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**mCIMT** not have a difference in efficacy when compared to **conventional therapy or bilateral arm training** for improving proprioception during the acute/subacute phase poststroke.	2	Kwakkel et al. 2016; Brogardh et al. 2009

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**CIMT** may produce greater improvements in muscle strength than **conventional therapy or motor relearning programmes** during the acute/subacute phase poststroke.	1	Alberts et al. 2004
2	**CIMT combined with visual biofeedback** may produce greater improvements in muscle strength than **conventional therapy or motor relearning programmes** during the acute/subacute phase poststroke.	1	Seok et al. 2016
1b	**CIMT combined with mirror therapy** may produce greater improvements in muscle strength than **CIMT**	1	Yoon et al. 2014

	on its own during the acute/subacute phase poststroke.		
1a	**CIMT** may produce greater improvements in muscle strength than **conventional therapy or neurodevelopmental techniques** during the chronic phase poststroke.	2	Alberts et al. 2004; Suputtitada et al. 2004
1b	**Early CIMT** may produce greater improvements in muscle strength than **delayed CIMT** during the chronic phase poststroke.	1	Sawaki et al. 2008
1a	**mCIMT** not have a difference in efficacy when compared to **conventional therapy or bilateral arm training** for improving muscle strength during the acute/subacute phase poststroke.	2	Kwakkel et al. 2016; Hammer and Lindmark, 2009

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**CIMT** may not have a difference in efficacy when compared to **conventional therapy or motor relearning programmes** to improve performance of activities of daily living during the acute/subacute phase poststroke.	8	Shah et al. 2016; Batool et al. 2015; Thrane et al. 2015; Boake et al. 2007; Ro et al. 2006; Page et al. 2005; Ploughman and Corbett 2004; Dromerick et al. 2000
1b	**High intensity CIMT** may not have a difference in efficacy when compared to **low intensity CIMT** on its own for improving motor function during the acute phase poststroke.	1	Dromerick et al. 2009
1b	**CIMT combined with mirror therapy** may not have a difference in efficacy when compared to **CIMT on its own** for improving performance of activities of daily living during the acute/subacute phase poststroke.	1	Yoon et al. 2014
1a	**CIMT** may produce greater improvements in performance of activities of daily living than **conventional therapy or neurodevelopmental techniques** during the chronic phase poststroke.	10	Huseyinsinoglu et al. 2012; Khan et al. 2011; Wu et al. 2011; Lin et al. 2010; Lin et al. 2009; Dahl et al. 2008; Lin et al. 2008; Lin et al. 2007; Wu et al. 2007; Wolf et al. 2006
1b	**High intensity CIMT** may not have a difference in efficacy when compared to **low intensity CIMT** on its own for improving performance of activities of daily living during the chronic phase poststroke.	3	Souza et al. 2015; Brogardh and Bengt, 2006; Wittenberg et al. 2003
1b	**High intensity CIMT with/without cycloserine** may not have a difference in efficacy when compared to **low intensity CIMT with/without cycloserine** for improving performance of activities of daily living during the chronic phase poststroke.	1	Nadeau et al. 2014

1a	**Early CIMT** may produce greater improvements in performance of activities of daily living than **delayed CIMT** during the chronic phase poststroke.	2	Wolf et al. 2010; Wolf et al. 2008
2	**CIMT with the transfer package protocol** may produce greater improvements in performance of activities of daily living when compared to **traditional CIMT** during the chronic phase poststroke.	3	Takebayashi et al. 2013; Taub et al. 2013; Gauthier et al. 2008
2	**CIMT with donepezil** may not have a difference in efficacy when compared to traditional **CIMT or placebo** for improving activities of daily living.	2	Richards et al. 2006; Nadeau et al. 2004
2	**Group based CIMT** may produce greater improvements in performance of activities of daily living when compared to **one on one CIMT sessions** during the chronic phase poststroke.	1	Doussoulin et al. 2018
1a	**mCIMT** not have a difference in efficacy when compared to **conventional therapy or bilateral arm training** for improving performance of activities of daily living during the acute/subacute phase poststroke.	4	Yu et al. 2017; Liu et al. 2016; Treger et al. 2012; Myint et al. 2007
1b	**mCIMT combined with auditory feedback** may produce greater improvements in performance on activities of daily living than **mCIMT alone** during the chronic phase poststroke.	1	Bang et al. 2016
1a	**mCIMT** may produce greater improvements in performance of activities of daily living than **conventional therapy or bilateral arm training** during the chronic phase poststroke.	8	Hsieh et al. 2016; Yadav et al. 2016; Barzel et al. 2015; Smania et al. 2012; Hayner et al. 2010; Lin et al. 2007; Wu et al. 2007b; Wu et al. 2007c
2	**Group based mCIMT** may produce greater improvements in performance of activities of daily living than **one on one mCIMT sessions** during the chronic phase poststroke.	1	Doussoulin et al. 2017

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References
1b	**CIMT combined with mirror therapy** may not have a difference in efficacy when compared to **CIMT on its own** for stroke severity during the acute/subacute phase poststroke.	1	Yoon et al. 2014

Key points

Constraint-induced movement therapy may be beneficial for upper limb rehabilitation in the chronic phase following stroke.

The literature is mixed regarding constraint-induced movement therapy for upper limb rehabilitation in the subacute/acute phase following stroke.

Modified constraint-induced movement therapy may be beneficial for upper limb rehabilitation in the chronic phase following stroke.

Modified constraint-induced movement therapy may not be beneficial for upper limb rehabilitation in the subacute/acute phase following stroke.

Higher and lower intensity constraint-induced movement therapy may have similar effects on upper limb function in the chronic phase following stroke.

Constraint-induced movement therapy in combination with other therapeutic approaches may be beneficial for upper limb rehabilitation following stoke.

Trunk Restraint

Adopted from: https://www.ortopedia-almirall.com/en/producto/cinturon-sujecion-tronco-y-pelvis-cierre-magnetico/

Reaching movements performed with the affected arm poststroke are often accompanied by compensatory trunk or shoulder girdle movements, which overextend the reach of the arm (Michaelsen et al. 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 (Michaelsen & Levin, 2004). Ten RCTs (Baldwin et al. 2018; Bang et al. 2015; Lima et al. 2014; Wu et al. 2012a; Wu et al. 2012b; Thielman et al. 2010; Woodbury et al. 2009; Michaelsen et al. 2006; Michaelsen and Levin, 2004) have evaluated the effectiveness of trunk restraint combined with other training to improve the movement quality of reaching tasks.

Their methodological details and results are presented in Table 9.

Table 9. RCTs Evaluating Trunk Restraint Training for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	**Interventions Duration: Session length, frequency per week for total number of weeks**	**Outcome Measures Result (direction of effect)**
mCIMT + trunk restraint training		

Baldwin et al. (2018)
RCT (5)
N_{start}=19
N_{end}= 14
TPS= Chronic
	E: mCIMT + trunk restrainit
	C: mCIMT
	Duration: 60min 5x/wk for 4wks
		• Action Research Arm Test: (+exp)
		• Fugl-Meyer Upper Extremity: (+exp)
		• Modified Barthel Index: (+exp)
		• Motor Activity Log: (+exp)
		  • Amount of Use: (+exp)
		  • Quality of Movement: (+exp)

		• Maximal Elbow Extension Angle During Reaching: (+exp)
Bang et al. (2015) RCT (9) N_{Start}=18 N_{End}=18 TPS=Subacute	E: mCIMT + trunk resistant training C: mCIMT Duration: 30 min, 5 d/wk, for 4 wk	• Action Research Arm Test (+exp) • Fugl-Meyer Assessment (+exp) • Modified Barthel Index (+exp) • Motor Activity Log (+exp)

Bang et al. (2014)
RCT (8)
N_{start}= 18
N_{end}= 18
TPS= Subacute
	E: mCIMT + trunk restrainit
	C: mCIMT
	Duration: 60min 5x/wk for 4wks
		• Action Research Arm Test: (+exp)
		• Fugl-Meyer Upper Extremity: (+exp)
		• Modified Barthel Index: (+exp)
		• Motor Activity Log: (+exp)
		  • Amount of Use: (+exp)
		  • Quality of Movement: (+exp)
		• Maximal Elbow Extension Angle During Reaching: (+exp)

Lima et al. (2014) RCT (8) N_{Start}=22 N_{End}=15 TPS=Chronic	E: mCIMT + trunk resistant training C: mCIMT Duration: *Not Reported*	• Motor Activity Log (-) • Bilateral Activity Assessment Scale (-) • Wolf Motor Function Test (-) • Global strength (-)
Woodbury et al. (2009) RCT (5) N_{start}=11 N_{end}=11 TPS=Chronic	E: mCIMT + trunk restraint C: mCIMT Duration: 6 hr, 5d/wk for 2 wk	• Hand path trajectories (+exp)
Distributed CIT + trunk restraint training		
Wu et al. (2012a) RCT (5) N_{start}=57 N_{end}=57 TPS=Chronic	E1: Distributed constraint-induced therapy (dCIT) + trunk restraint E2: dCIT C: Usual care (neurodevelopmental treatment techniques) Duration: 2hr, 5d/wk for 3 wk	E1/E2 vs. C • Action Research Arm Test (+exp, exp_2) • Frenchay Activities Index (+exp, exp_2) • Motor Activity Log (+exp, exp_2) • Stroke Impact Scale (+exp, exp_2)
Wu et al. (2012b) RCT (5) N_{start}=45 N_{end}=45 TPS=Chronic	E1: Distributed constraint-induced therapy (dCIT) + trunk restraint E2: dCIT C: Dose-matched control intervention (neurodevelopmental treatment techniques) Duration: 2hr, 3d/wk for 3 wk	E1/E2 vs. C • Motor Activity Log (+exp, $+exp_2$) • Fugl-Meyer Assessment (+exp)
Auditory feedback		
Thielman (2010) RCT (4) N_{start}=16 N_{end}=16 TPS=Chronic	E: Auditory feedback about trunk position C: Trunk restraint with external device Duration: 45 min, 3d/wk for 4 wk	• Reaching Performance Scale Near Target (+exp) • Reaching Performance Scale Far Target (-)
Reach to grasp training with trunk restraint		
Michaelsen el al. (2006) RCT (7) N_{Start}=30 N_{End}=10 TPS=Chronic	E: Object-related reach-to-grasp training + trunk restraint C: Unrestrained reach-to-grasp training Duration: 40 min, 3d/wk for 5 wk	• Upper Extremity Performance Test (+exp) • Fugl-Meyer Assessment (+exp) • Box and Block Test (-)
Michaelsen & Levin (2004) RCT (5) N_{start}=28 N_{end}=28 TPS=Chronic	E: Reach-to-grasp training + trunk restraint C: Unrestrained reach-to-grasp training Duration: 60 sessions over 8 weeks	• Shoulder horizontal adduction (-) • Shoulder flexion (-) • Elbow Extension (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
$+exp_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group

+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Trunk Restraint Training

MOTOR FUNCTION			
LoE	Conclusion Statement	RCTs	References
1a	**Trunk restraint combined with mCIMT** may produce greater improvements in motor function than **mCIMT**.	4	Baldwin et al. 2018; Bang et al. 2015; Bang et al. 2014; Lima et al. 2014
2	**Trunk restraint combined with distributed CIT** may produce greater improvements in motor function than **conventional rehabilitation**.	2	Wu et al. 2012a; Wu et al. 2012b
2	There is conflicting evidence about the effect of **auditory feedback regarding trunk position** to improve motor function when compared to **trunk restraint training**.	1	Thielman 2010
1b	**Trunk restraint combined with reaching training** may produce greater improvements in motor function than **reaching training alone**.	2	Michaelsen & Levin 2004; Michaelsen et al. 2006

DEXTERITY			
LoE	Conclusion Statement	RCTs	References
1b	**Trunk restraint combined with reaching training** compared to **reaching training alone** may not have a difference in efficacy for dexterity.	1	Michaelsen et al. 2006

RANGE OF MOTION			
LoE	Conclusion Statement	RCTs	References
1a	**Trunk restraint combined with mCIMT** may produce greater improvements in range of motion than **mCIMT**.	4	Baldwin et al. 2018; Bang et al. 2015; Bang et al. 2014; Lima et al. 2014

MUSCLE STRENGTH			
LoE	Conclusion Statement	RCTs	References
1b	**Trunk restraint combined with mCIMT** may not have a difference in efficacy for producing greater improvements in muscle strength compared to **mCIMT**.	1	; Lima et al. 2014

ACTIVITIES OF DAILY LIVING			
LoE	Conclusion Statement	RCTs	References
1a	**Trunk restraint combined with mCIMT** may produce greater improvements in performace of activities of daily living than **mCIMT**.	4	Baldwin et al. 2018; Bang et al. 2015; Bang et al. 2014; Lima et al. 2014
2	**Trunk restraint combined with distributed CIMT** may produce greater improvements in performance of activities of daily living than **conventional rehabilitation**.	2	Wu et al. 2012a; Wu et al. 2012b

Key points

Trunk restraint with reaching training or modified and distributed constraint induced moement therapy may improve some aspects of upper limb function following stroke.

Stretching Programs

Adopted from: http://advrehabnj.com/2014/10/08/trigger-finger-occupational-therapy/

Spasticity following stroke relates to hypertonicity or increased active tension of the muscle. Contracture may also occur as a result of spasticity and 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, although the evidence base is extremely limited for this intervention.

The methodological details and results of three RCTs evaluated stretching compared to conventional therpay (You et al. 2014; Tseng et al. 2007; Turton et al. 2005). Two RCTs examined stretching combined with NMES (Dejong et al. 2013; Sahin et al. 2012) and one RCT examined stretching verus NMES (King et al. 1996)

The methodological data evaluating 6 RCTs implementating stretching for upper extremity motor rehabilitation are presented in Table 10.

Table 10. RCTs Evaluating Stretching Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
You et al. (2014) RCT (5) N_{Start}=45 N_{End}=41 TPS=Chronic	E1: Stretching program + joint stabilizing exercise (combo) E2: Stretching program C: Traditional exercise therapy Duration: 30min/d, 5d/wk for 8wk	E1 vs C • Muscle thickness (+exp) • Motor assessment scale (+exp) E2 vs C • Muscle thickness (+exp$_2$) Motor assessment scale (+exp$_2$) E1 vs E2 • Muscle thickness (-) • Motor assessment scale (-)
Tseng et al. (2007) RCT (7) N_{start}=59 N_{end}=59 TPS=Chronic	E1: Nurse assisted range of motion exercise program E2: Nurse supervised range of motion exercise program C: Usual care Duration: 20-40min/d, 6d/wk for 4wk	E1/E2 vs C • Joint angles (+exp, +exp$_2$) • FIM (+exp, +exp$_2$)
Turton et al. (2005) RCT (6) N_{start}=29 N_{end}=25 TPS=Acute Chap 11	E: Muscle stretching regime C: Conventional care Duration: 1hr/d up to 12wks post stroke	• Shoulder Rang of Motion: (-) • Wrist Range of Motion: (-) • Shoulder contracture (unaffected - affected side): (-) • Wrist contracture (unaffected - affected side): (-)
Stretching combined with NMES verusus NMEs or stretching alone		
De Jong et al. (2013) RCT (8) N_{start}=46 N_{end}=46 TPS=Subacute	E: Arm stretch positioning + NMES C: Sham stretch positioning + Sham NMES Duration: 45 min (2x/d), 5d/wk, for 8 wk	• Modified Ashworth Scale (-)
Sahin et al. (2012) RCT (5) N_{start}=42 N_{end}=38 TPS=Chronic	E: Stretching + NMES C: Stretching Duration: 5d/wk for 4wk	• Modified Ashworth Scale (+exp)
King et al. (1996) RCT (4) N_{start}=21 N_{end}=NR TPS=Chronic	E: Passive stretch C: NMES Duration: *Not reported*	• Tone reduction (+con)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Stretching Programs

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the efiacy of **Stretching programs** compared to **conventional therapy** for producing improvements in spasticity.	2	You et al. 2014; Turton et al. 2005

1b	There is conflicting evidence on **stretching combined with NMES** for improving spasticity when compared to **sham** or **stretching alone.**	2	De jong et al. 2013; Sahin et al. 2012
2	**Stretching** may not have a difference in efficacy when compared to **NMES** for improving spasticity**.**	1	King et al. 1996

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence on **Stretching programs** for producing greater improvements in range of motion than **conventional therapy**.	2	Tseng et al. 2007; Turton et al. 2005

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Stretching programs** may produce greater improvements in performance of activities of daily living than **conventional therapy**.	2	You et al. 2014; Tseng et al. 2007

Key points

The evidence surrounding stretching programs and stretching combined with NMES for improving upper limb function following stroke is mixed.

Orthotics

Adopted from: https://www.amazon.com/Soft-Resting-Hand-Splint-Left/dp/B007G4TVIK

Upper limb orthotic devices such as splints or kinesthetic tape are generally used to minimize or prevent contractures, reduce spasticity and pain, and prevent edema poststroke (Lannin & Herbert, 2003). Arm weighted support rehabilitation through orthic devices can facilitate recovery of hand movements through performing semiautonomous rehabilitation programs (Bartolo et al. 2014).

25 RCTs were found that used orthotic devices for upper extremity motor rehabilitation (Liu et al. 2020; Ooi et al. 2020; Zheng et al. 2020; Huang et al. 2019; Jung et al. 2019; Comley-White et al. 2018; D'allAngol et al. 2018; Willigenburg et al. 2017; Choi et al. 2016a; Choi et al. 2016b; Lannin et al. 2016; Appel et al. 2015; Kim et al. 2015; Bartolo et al. 2014; Page et al. 2013; Barry et al. 2012; Basaran et al. 2012; Jung et al. 2011; Suat et al. 2011; Housman et al. 2009; Lannin et al. 2007; Lannin et al. 2003; Langlois et al. 1991; Poole et al. 1990; Rose et al. 1987), the methodological details and results of these RCTs are presented in Table 11.

Table 11. RCTs Evaluating Orthotic Devices for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Dynamic othotic devices versus conventional therapy or task-specific training		

Willigenburg et al. (2017)
RCT (4)
N_{start}=12
N_{end}=12
TPS=Chronic
	E: Myoelectric brace
	C: Repetitive task-specific practice (RTP)
	Duration: 45min, 3d/wk for 8wks
		• Stroke Impact Scale:
		  • Arm: (-)
		  • Hand: (-)
		  • Activities of Daily Living: (-)
		  • Recovery: (+exp)
		• Kinematics reach out task:
		  • Range shoulder flex: (-)
		  • Range elbow extension: (-)
		  • Hand velocity: (-)
		• Kinematics reach up task:
		  • Range shoulder flex: (-)
		  • Range elbow extension: (-)
		  • Hand velocity: (+con)

Lannin et al. (2016) RCT (5) N_{Start}=9 N_{End}=6 TPS=Acute	E: Task-specific training + training with the Saebo-Flex device C: Task-specific training Duration: 45-60min/session, 1-3sessions/d, 5-7d/wk for 4-12wk	• Motor Assessment Scale (-) • Box and Block Test (-) • Grip Strength (-)
Bartolo et al. (2014) RCT (8) N_{Start}=28 N_{End}=28 TPS=Acute	E: Arm orthosis C: Conventional physiotherapy Duration: 30min/d, 6d/wk for 2wk	• Arm abduction (+exp) • Arm adduction (+exp) • Arm flexion (+exp) • Arm extension (+exp) • Normalized jerk (+exp) • Fugl Meyer Assessment (-) • Modified Ashworth Scale (-)
Page et al. (2013) RCT (6) N_{Start}=16 N_{End}=16 TPS=Chronic	E: Myomo brace C: Repetitive task practice Duration: 30min/d, 3d/wk for 8wk	• Fugl Meyer Assessment (-) • Canadian Occupational Performance Measure (-) • Stroke Impact Scale (-)
Barry et al. (2012) RCT (7) N_{start}=22 N_{end}=19 TPS=Subacute	E: Dynamic hand orthosis C: Manual assisted therapy Duration: 15min/d, 4d/wk for 6wk	• Grip strength (-) • Action Research Arm Test (-) • Box and Block Test (-) • Stroke Impact Scale (-)

Housman et al. (2009)
RCT (5)
N_{start}= 29
N_{end}= 23
TPS= Chronic
	E: T-wrex gravity support orthosis
	C: Conventional therapy
	Duration: 45min, 3x/wk, 8wks
		• Fugle-Meyers Upper Extremity: (-)
		• Motor Activity Log
		  • Quality of Movement: (-)
		  • Amount of Use: (-)

Pressure gamrents versus conventional therapy		

Ooi et al. (2020)
RCT (6)
N_{start}= 46
N_{end}= 43
TPS= Subacute
	E: Lycra pressure garment
	C: Conventional therapy
	Duration: 2hrs/wk, 6wk rehab + 6hrs/d of garment
		• Modified Ashworth Scale
		  • Wrist: (-)
		  • Finger: (-)
		  • Disabilities of Arm, Shoulder, Hand Outcome: (-)
		  • Jebsen Hand Function Test - Time: (-)

Sling exercise therapy versus conventional therapy or bimanual tracking		
Liu et al. (2020) RCT (7) N_{start}= 50 N_{end}= 50 TPS= Subacute	E: Sling exercise therapy C: Conventional therapy Duration: 30min, 5x/wk for 4wks	• Barthel Index: (-) • Fugl-Meyers Upper Extremity: (+exp)

Jung et al. (2019) RCT (8) N_{start}= 36 N_{end}= 36 TPS= Acute Chap 11	E: Shoulder sling exercise C: Bimanual tracking Duration: 40min, 5x/wk for 4wks	• Subluxation: (+exp) • Shoulder Proprioception: (+exp) • Fugl-Meyers Upper Extremity: (+exp) • Manual Functional Test: (+exp)
Static orthotic (splint) versus conventional therapy or sham splint		
Choi et al. (2016a) RCT (5) N_{Start}=30 N_{End}=30 TPS=Subacute	E: Hand Splints and a General Rehabilitation Program C: General Rehabilitation Program Duration: 30min/d, 5d/wk for 12wk	• Modified Ashworth Scale (-)
Jung et al. (2011) RCT (4) N_{Start}=21 N_{End}=21 TPS=Chronic	E: Hand stretching/splint device C: No splint Duration: 40min/d, 6d/wk for 3wk	• Modified Ashworth Scale (+exp)
Suat et al. (2011) RCT (6) N_{start}= 19 N_{end}= 19 TPS= Chronic	E: Hand splint C: Conventional therapy Duration: 2hrs/d for 6mo	• Forward reach (-)
Lannin et al. (2007) RCT (7) N_{start}=63 N_{end}=63 TPS=Acute	E1: Extension splint E2: Neutral splint C: No splint Duration: 9-12h/d for 4wk	• Wrist contracture (-)
Lannin et al. (2003) RCT (8) N_{start}=28 N_{finish}=27 TPS=Subacute	E: Hand splint C: No hand splint Duration: up to 12h/d, 5d/wk for 4wk	• Wrist flexor (-) • Finger flexor (-)
Poole et al. (1990) RCT (5) N_{start}=18 N_{end}=18 TPS=Acute	E: Splint C: No splint Duration: 30min/d, 5d/wk for 3wk	• Fugl Meyer Assessment (-)
Static splints versus eachother		
Choi et al. (2016b) RCT (4) N_{Start}=52 N_{End}=52 TPS=Chronic Ch11	E: Dorsal Resting Hand Splint C: Volar Resting Hand Splint Duration: 30min/d, 5dwk for 8wk	• Modified Ashworth Scale (+exp) • Active Range of Motion (+exp)
Basaran et al.(2012) RCT (6) N_{start}=39 N_{end}=39 TPS=Chronic	E1: Volar splint E2: Dorsal splint C: No splint Duration: up to 10h/d for 5wk	E1 vs E2 vs C • Modified Ashworth Scale (-) • Passive range of motion (-)
Langlois et al. (1991) RCT (3) N_{start}=9 N_{end}=9 TPS=Chronic	E1: Spint 22hr/d E2: Splint 12hr/d E3: Splint 6hr/d Duration: 6, 12, or 22h/d for 4wk	• Spasticity (-)
Rose et al. (1987) RCT (4) N=30	E1: Dorsal orthosis E2: Volar orthosis C: No orthosis	E1/E2 vs C • Passive range of motion (+exp) E1 vs C • Spontaneous flexion (+exp)

	Duration: 2h	<u>E2 vs C</u> • Spontaneous flexion (-)
3D versus "Regular" orthosis		

<u>Zheng et al. (2020)</u>
RCT (7)
N_{start}=44
N_{end}=40
TPS=Mixed
	E: 3D orthosis
	C: Regular orthosis
	Duration: 6wks
		• Passive Range of Motion:
		  • Extension: (+exp)
		  • Flexion: (-)
		  • Radial deviation: (-)
		  • Ulnar deviation: (-)
		• Fugl-Meyer Upper Extremity: (+exp)
		• Modified Ashworth Scale: (+exp)

Taping and strapping techniques versus conventional therapy		

<u>Huang et al. (2019)</u>
RCT (6)
N_{start}= 36
N_{end}= 31
TPS= Subacute
	E: Kinesio taping
	C: Conventional therapy
	Duration: 7d/wk tape - 40min stretch, 5d/wk for 3wks
		• Fugl-Meyers Upper Extremity
		  • Proximal: (-)
		  • Distal: (-)
		• Modified Ashworth Scale: (-)
		• Brunnstrom (distal): (-)

<u>Comley-White et al. (2018)</u>
RCT (5)
N_{start}= 56
N_{end}= 33
TPS= Acute
	E1: Longitudinal strapping
	E2: Circumferential strapping
	C: Conventional therapy
	Duration: 2wk s
		<u>E1 Vs C</u>
		• Shoulder subluxation: (-)
		• Modified Ashworth Scale: (-)
		• Motor Assessment Scale
		  • Upper arm: (-)
		  • Hand: (-)
		  • Advanced hand: (-)
		<u>E2 Vs C</u>
		• Shoulder subluxation: (-)
		• Modified Ashworth Scale: (-)
		• Motor Assessment Scale
		  • Upper arm: (-)
		  • Hand: (-)
		  • Advanced hand: (-)
		<u>E1 Vs E2</u>
		• Shoulder subluxation: (-)
		• Modified Ashworth Scale: (-)
		• Motor Assessment Scale
		  • Upper arm: (-)
		  • Hand: (-)
		  • Advanced hand: (-)

<u>Dall'Agnol et al. (2018)</u>
RCT (7)
N_{start}= 16
N_{end}= 16
TPS= Chronic
	E: Kinesio tape + acupuncture
	C: Acupuncture
	Duration:
	30min, 3x/wk for 12wks
		• Motor Activity Scale
		  • Shoulder Adduction: (-)
		  • Shoulder Extensions: (-)
		  • Shoulder in Rotation: (-)
		  • Elbow flexion: (-)
		  • Pronation: (-)
		  • Wrist flex: (-)
		  • Thumb flexion: (-)
		• Finger flexion (2,3,4,5): (-)
		• Active Range of Motion:
		  • Shoulder Flexion: (-)
		  • Shoulder Extension: (-)
		  • Shoulder Abduction: (-)
		  • Elbow Extension: (-)
		  • Wrist extension: (-)
		  • Radial Deviation: (-)
		  • 3rd Finger Extension: (-)
		• Wolf Motor Function Test (time): (-)

<u>Appel et al. (2015)</u> RCT (5) N_{start}= 20 N_{end}=17 TPS= Acute	E: Shoulder strap C: Placebo Duration: Straps with conventional therapy: 4.5hr, 5x/wk for 4wks	• Action Research Arm Test: (-)

Kim et al. (2015) RCT (7) N_{Start}=30 N_{End}=30 TPS=Subacute	E: Taping C: No taping Duration: 30min/d, 3d/wk for 28wk	• Manual Function Test (+) • Modified Motor Assessment Scale (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp₂ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Orthotic Devices

MOTOR FUNCTION

LoE	Conclusion Statement	RCTs	References
1a	**Dyanmic Orthotic devices** may not have a difference in efficacy when compared to **conventional therapy, repetitive task practice** for improving motor function.	5	Willigenburg et al. 2017; Bartolo et al. 2014; Page et al. 2013; Barry et al. 2012; Housman et al. 2009
1b	**Pressure garments** may not have a difference in efficacy when compared to **conventional therapy** for improving motor function.	1	Ooi et al. 2020
1a	**Sling exercise therapy** may improve motor function when compared to **conventional therapy or bimanual training.**	2	Liu et al. 2020; Jung et al. 2019
1b	**Static splints** may not have **a** difference in efficacy when compared to **conventional therapy or sham splints** for improving motor function	2	Staut et al. 2011; Poole et al. 1990
1b	**3-Dimensional orthotics** may improve motor fuinction when compared to **regular orthotics.**	1	Zheng et al. 2020
1a	**Tapping and strapping techniques** may not have a difference in efficacy when compared to **conventional or sham therapy** for imporving motor function.	3	Huang et al. 2019; Appel et al. 2015; Kim et al. 2015

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1a	**Dyanmic Orthotic devices** may not have a difference in efficacy when compared to **conventional therapy, repetitive task practice** for improving dexterity	2	Lannin et al. 2016; Barry et al. 2012
1b	**Pressure garments** may not have a difference in efficacy when compared to **conventional therapy** for improving dexterity.	1	Ooi et al. 2020

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1b	**Dyanmic Orthotic devices** may not have a difference in efficacy when compared to **conventional therapy, repetitive task practice** for improving spasticity.	1	Bartolo et al. 2014

1b	**Pressure garments** may not have a difference in efficacy when compared to **conventional therapy,** for improving spasticity.	1	Ooi et al. 2020
1b	**Static splints** may not have **a** difference in efficacy when compared to **conventional therapy or sham splints** for spasticity.	3	Choi et al. 2016; Jung et al. 2011; Lanin et al. 2007
1b	There is conflicting evidence about the effect of the **duration of splinting** and **type of splinting (dorsal or volar)** for improving spasticity.	3	Choi et al 2016; Basaran et al. 2012; Langlois et al. 1991
1b	**3-Dimensional orthotics** may improve spasticity when compared to **regular orthotics.**	1	Zheng et al. 2020
1a	**Tapping and strapping techniques** may not have a difference in efficacy when compared to **conventional or sham therapy** for imporving spasticity.	1	Comley-white et al. 2018

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
1a	**Dyanmic Orthotic devices** may improve range of motion when compared to **conventional therapy** or **repetitive task practice**.	1	Bartolo et al. 2014;
1b	**Sling exercise therapy** may improve range of motion function when compared to **conventional therapy or bimanual training.**	2	Liu et al. 2020; Jung et al. 2019
1b	**Static splints** may not have **a** difference in efficacy when compared to **conventional therapy or sham splints** for range of motion.	1	Lanin et al. 2007
1b	There is conflicting evidence about the effect of the **duration of splinting** and **type of splint (dorsal or volar)** for improving range of motion.	3	Choi et al 2016; Basaran et al. 2012; Rose et al. 1987
1b	**3-Dimensional orthotics** may not have a difference in efficacy when compared to **regular orthotics** for improving range of motion.	1	Zheng et al. 2020

PROPRIOCEPTION

LoE	Conclusion Statement	RCTs	References
1b	**Sling exercise therapy** may improve proprioception when compared to **conventional therapy or bimanual training.**	1	Jung et al. 2019

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
1a	**Dyanmic Orthotic devices** may not have a difference in efficacy when compared to **conventional therapy, repetitive task practice** for improving performance on activities of daily living.	5	Willigenburg et al. 2017; Lanin et al. 2016; Page et al. 2013; Barry et al. 2012; Housman et al. 2009

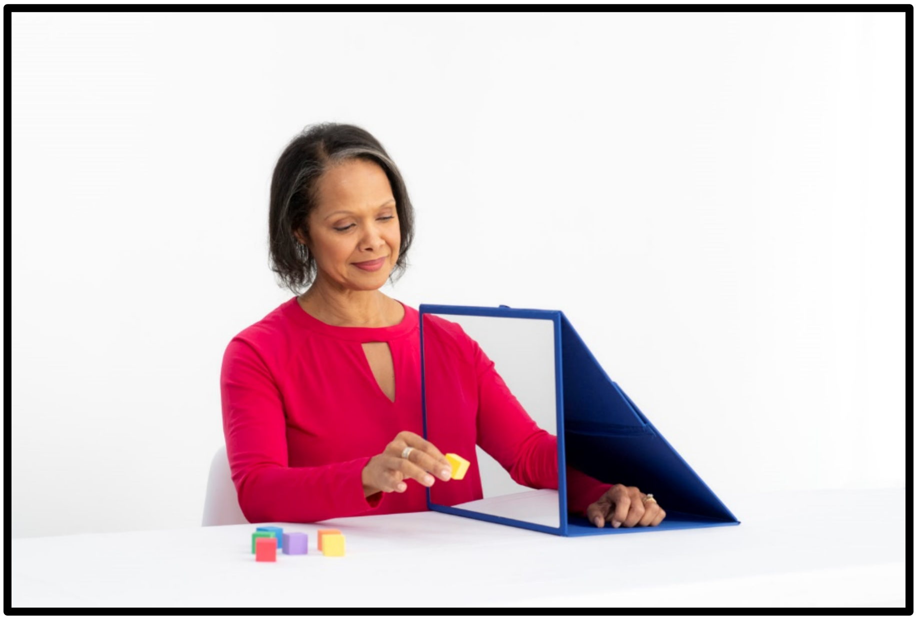
1b	**Sling exercise therapy** may not have a difference in efficacy when compared to **conventional therapy or bimanual training** for improving performance on activities of daily living.	1	Liu et al. 2020
1a	There is conflicting evidence about the effect of **Tapping and strapping techniques** when compared to **conventional or sham therapy** for performance on activities of daily living.	2	Comley-white et al. 2018; Kim et al. 2015

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Dyanmic Orthotic devices** may not have a difference in efficacy when compared to **conventional therapy, repetitive task practice** for muscle strength.	2	Lannin et al. 2016; Barry et al. 2012

Key points

Orthotics may not be beneficial for upper limb rehabilitation following stroke.

Mirror Therapy



Adopted from: https://www.saebo.com/shop/saebo-mirror-box/

In mirror therapy, a mirror is placed beside the unaffected limb, blocking view of the affected limb and creating an illusion of two limbs as if they are both functioning normally. Mirror therapy functions through a process known as mirror visual feedback wherein the movement of one limb is perceived as movement from the other limb (Deconinck et al. 2015). In the brain, mirror therapy is thought to induce neuroplastic changes that promote recovery by increasing excitability of the ipsilateral motor cortex which projects to the paretic limb (Deconinck et al. 2015). Ramachandran et al. (1995) first used this method to understand the effect of vision on phantom sensation and pain in arm amputees. This method has since been adapted from its original use as a means to enhance upper-limb function following stroke (Sathian et al. 2000).

A total of 47 RCTs were found that evaluated mirror therapy for upper extremity rehabilitation poststroke. Of these, 30 RCTs looked at mirror therapy compared to conventional rehabilitation or the Bobath concept approach (Chinnavan et al. 2020; Madhoun et al. 2020; Antoniottie et al 2019; Bai et al. 2019; Chauhari et al. 2019; Ding et al. 2019; Jan et al. 2019; Arya et al. 2018; Ding et al. 2018; Oliveira et al. 2018; Radajewska et al. 2017; Colomer et al. 2016; Gurbuz et al. 2016; Kim et al. 2016; Lim et al. 2016; Pervane Vural et al. 2016; Arya et al. 2015; Cristina et al. 2015; Park et al. 2015; Invernizzi et al. 2013; Radajewska et al. 2013; Timmerman et al. 2013; Wu et al. 2013a; Lee et al. 2012; Michielsen et al. 2011; Dohle et al. 2009; Yavuzer et al. 2008; Altschuler et al. 1999).Two RCTs looked at mirror therapy compared to bilateral arm training (Fong et al. 2019; Li et al. 2109). Two RCTs looked at mirror therapy with bilateral arm training (Rodrigues et al. 2016; Samuelkamaleshkumar et al. 2014). Two studies looked at mirror therapy combined with: transcranial direct current stimulation (Jin et al. 2019; D'agata et al. 20916), one study at functional electrical stimulation (Kim et al. 2015), two studies at neuromuscular electrical stimulation (Amasyali et al. 2016; Yun et al. 2011). Three studies looked at mirror therapy with mesh glove (Lee et al. 2015; Lin et al. 2014a; Lin et al. 2014b) rTMS (Ji et al. 2014), and in a group or individual setting (Thieme et al. 2012). One RCT looked at movement versus task-based mirror therapy (Bai et al. 2019). One RCT looked at mirror therapy combined with strength versus strength alone (Ehrensberger et al. 2019). One study looked at mirror Therapy combined with extracorpeal shockwave (Guo et al. 2019).

The methodological details and results of these 45 RCTs are presented in Table 12.

Table 12. Summary of RCTs Evaluating Mirror Therapy for the Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Mirror therapy compared to conventional rehabilitation		
Chinnavan et al. (2020) RCT (4) N_{start}= 25 N_{end}= 25 TPS= Chronic	E: Mirror Therapy C: Conventional Therapy Duration: 45min, 3x/wk for 6wks	• Fugl-Meyers Assessment: (+exp) • Functional Independence Measure: (+exp)

Madhoun et al. (2020)
RCT (5)
N_{start}= 35
N_{end}= 30
TPS= Subacute
	E: Mirror therapy
	C: Conventional therapy
	Duration: 25min, 7d/wk for 4wks
		• Brunnstrom Recovery Stages
		  • Upper extremity: (-)
		  • Hand: (-)
		• Barthel Index: (-)
		• Fugl-Meyer Upper Extremity: (+exp)
		• Modified Ashworth Scale:
		  • Elbow: (-)
		  • Wrist: (-)
		  • Finger: (-)
		  • Thumb - extension and flexion: (-)

Antoniotti et al. (2019) RCT (7) N_{start}= 40 N_{end}= 35 TPS= Acute	E: Mirror therapy C: Sham therapy Duration: 30min 5x/wk for 4wks	• Fugl-Meyers Upper Extremity: (-) • Action Research Arm Test: (-) • Functional Independence Measure: (-)

Bai et al. (2019)
RCT (7)
N_{start}=34
N_{end}= 34
TPS= Subacute
	E1: Movement based mirror therapy
	E2: Task based mirror therapy
	C: Conventional therapy
	Duration: 30min 5x/wk for 4wks
		E1 vs C
		• Fugl-Meyers Upper Extremity: (+exp1)
		• Wolf Motor Function Test: (-)
		• Grip strength: (-)
		• Modified Barthel Index: (-)
		• Modified Ashworth Scale
		  • Arm: (-)
		  • Hand: (-)
		E2 vs C
		• Fugl-Meyers Upper Extremity: (-)
		• Wolf Motor Function Test: (-)
		• Grip strength: (-)
		• Modified Barthel Index: (-)
		• Modified Ashworth Scale
		  • Arm: (-)
		  • Hand: (-)
		E1 vs E2
		• Fugl-Meyers Upper Extremity: (+exp1)
		• Wolf Motor Function Test: (-)
		• Grip strength: (-)
		• Modified Barthel Index: (-)
		• Modified Ashworth Scale
		  • Arm: (-)
		  • Hand: (-)

Chaudhari et al. (2019) RCT (5)	E: Mirror therapy C: Conventional therapy	• Brunstom Recovery Stage: • Hand (+exp)

N_{start}= 50 N_{end}= 50/Not reported TPS= Not reported	Duration: 3x/wk, 4wks conventional, + mirror (nr)	• Upper Extremity (+exp)
Ding et al. (2019) RCT (7) N_{start}= 20 N_{end}= 19 TPS= Subacute Multi-Site	E: Camera mirror therapy C: Conventional therapy Duration: 1.5hrs, 5d/wk, 4wks	• Fugl-Meyers Assessment: • Upper Limb: (+exp) • Wrist & Hand: (+exp) • Functional Independence Measure: (+exp) • Self care: (-) • Sphincter control (-) • Transfers: (+exp) • Locomotion: (+exp) • Communication: (-) • Social cog ability: (-) • Manual Muscle Testing: (-) • Modified Ashworth Scale: (-)
Jan et al. (2019) RCT (5) N_{start}= 66 N_{end}= 66 TPS= Not reported	E: Mirror therapy C: Motor relearning program Duration: 2hrs, 3x/wk, 6wks	• Motor Assessment Scale • Upper limb: (+con) • Hand: (+con) • Advance Hand: (+con)
Arya et al. (2018) RCT (8) N_{start}= 31 N_{end}=30 TPS= Chronic	E: Mirror therapy C: Conventional therapy Duration: 40min, 5x/wk for 6wks	• Fugl-Meyer Upper Extremity: (+exp)
Chan et al. (2018) RCT (8) N_{start}= 41 N_{end}= 35 TPS= Acute	E: Mirror therapy C: Conventional therapy Duration: 1hr, 5d/wk for 4wks	• Fugl-Meyer Assessment (-) • Proximal (-) • Wrist (-) • Hand (-) • Cordination (-) • Wolf Motor Function Test • Time (-) • Score (-)
Ding et al. (2018) RCT (7) N_{start}= 90 N_{end}= 79 TPS= Subacute	E: Camera mirror therapy C: Conventional therapy Duration: 1hr, 5d/wk, 4wks	• Fugl Meyers Upper Limb: (+exp) • Barthel's Index: (-) • Reaction Time: (-) • Accuracy: (-)
Oliveira et al. (2018) RCT (3) N_{start}= 21 N_{end}= 21 TPS= Chronic	E1: Mirror therapy E2: Vibration therapy C: Conventional therapy Duration: 15min, 3x/wk, 4wks	E1 Vs C • Rivermead Mobility Index: (+exp1) • Jebsen Hand Function Test - Time: (+exp1) • Wolf Motor Function Test • Time: (+exp1) • Score: (+exp1) E2 Vs C • Rivermead Mobility Index: (+exp2) • Jebsen Hand Function Test - Time: (+exp2) • Wolf Motor Function Test • Time: (+exp2) • Score: (+exp2) E1 Vs E2 • Rivermead Mobility Index: (-) • Jebsen Hand Function Test - Time: (-) • Wolf Motor Function Test • Time: (-) • Score: (-)
Radajewska et al. (2017) RCT (5)	E: Mirror therapy C: Conventional rehabilitation	• Frenchay Arm Test (+exp)

N_{Start}=60 N_{End}=60 TPS=Subacute	Duration: 30min/d, 5d/wk for 3wk	
Colomer et al. (2016) RCT (7) N_{Start}=34 N_{End}=31 TPS=Chronic	E: Mirror Therapy C: Passive Mobilization Duration: 45min/d, 3d/wk for 8wk	• Nottingham Sensory Assessment (+exp) • Fugl-Meyer Assessment (-)
Gurbuz et al. (2016) RCT (6) N_{Start}=31 N_{End}=31 TPS=Subacute	E: Mirror Therapy C: Conventional Therapy Duration: 60-120min/d, 5d/wk for 4wk	• Brunnstrom Recovery Stage (-) • Fugl-Meyer Assessment (+exp) • Function Independence Measure (-)
Kim et al. (2016) RCT (5) N_{Start}=25 N_{End}=25 TPS=Chronic	E: Mirror Therapy C: Conventional Therapy Duration: 30min/d, 5dwk for 4wk	• Action Research Arm Test (+exp) • Fugl-Meyer Assessment (+exp) • Box and Block Test (+exp) • Functional Independence Measure (+exp)
Lim et al. (2016) RCT (5) N_{Start}=60 N_{End}=60 TPS=?	E: Mirror Therapy C: Sham Therapy Duration: 20min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Modified Barthel Index (+exp) • Brunnstrom Recovery Stage (-)
Pervane Vural et al. (2016) RCT (6) N_{Start}=30 N_{End}=30 TPS=Subacute	E: Mirror Therapy C: Conventional rehabilitation Duration: 4h/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Brunnstrom Recovery Stage (+exp) • Functional Independence Measure (+exp) • Modified Ashworth Scale (+exp)
Arya et al. (2015) RCT (8) N_{Start}=33 N_{End}=32 TPS=Chronic	E: Task-based mirror therapy C: Standard Rehabilitation Duration: 90min/d, 5d/wk for 8wk	• Fugl-Meyer Assessment (+exp)
Cristina et al. (2015) RCT (6) N_{Start}=15 N_{End}=15 TPS=Subacute	E: Mirror therapy C: Conventional therapy Duration: 30min/d, 5d/wk for 6wk	• Modified Ashworth Scale: writ (+exp) • Bhakta finger flexion scale (+exp)
Park et al. (2015) RCT (6) N_{Start}=30 N_{End}=30 TPS=Chronic	E: Mirror therapy C: Non-reflecting mirror Duration: 5d/wk for 6wk	• Manual Function Test (+exp) • FIM (+exp)
Invernizzi et al. (2013) RCT (7) N_{Start}=26 N_{End}=25 TPS=Acute	E: Mirror therapy C: Conventional therapy Duration: 30-60min/d, 5d/wk for 4wk	• Action Research Arm Test (+exp) • Motricity Index (+exp) • Fugl-Meyer Assessments (+exp)
Radajewska et al. (2013) RCT (3) N_{Start}=60 N_{End}=60 TPS=?	E: Mirror therapy C: Conventional therapy Duration: 30min/d, 5d/wk for 3wk	• Frenchay Arm Test (+exp)
Timmerman et al. (2013) RCT (7) N_{Start}=42 N_{End}=42 TPS=Subacute	E: Mirror therapy C: Bobath concept Duration: 30min/d, 3d/wk for 6wk	• Frenchay Arm Test (-) • Functional Assessment Scale (-) • Wolf Motor Function Test (-)
Wu et al. (2013) RCT (6)	E: Mirror therapy C: Conventional therapy	• Fugl-Meyer Assessment (+exp) • Modified Ashworth Scale (-)

N_{Start}=33 N_{End}=21 TPS=Chronic	Duration: 1.5h/d, 5d/wk for 4wk	• ABILHAND (-)
In et al. (2012) RCT (4) N_{start}= 24 N_{end}= 19 TPS= Chronic	E: Virtual mirror therapy C: Sham Duration: 30min, 5x/wk, 4wk	• Fugl-Meyers Upper Extremity: (+exp) • Modified Ashworth Scale: (-) • Box and Block Test: (-) • Jebsen Hand Function Test: (-) • Manual Function Test: (-)
Lee et al. (2012) RCT (5) N_{start}=28 N_{end}=26 TPS=Subacute	E: Mirror therapy C: Standard care Duration: 50min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Brunnstrom recovery stages (+exp) • Manual Function Test (+exp)
Michielsen et al. (2011) RCT (7) N_{Start}=40 N_{End}=40 TPS=Chronic	E: Mirror therapy C: Control therapy Duration: 1h/d, 5d/wk for 6wk	• Action Research Arm Test (-) • ABILHAND (-) • Grip force (-) • Tardieu Scale (-) • Fugl-Meyer Assessment (+exp)
Dohle et al. (2009) RCT (7) N_{Start}=36 N_{End}=36 TPS=Acute	E: Mirror therapy C: Control therapy Duration: 30min/d, 5d/wk for 6wk	• Fugl-Meyer Assessment (-)
Yavuzer et al. (2008) RCT (7) N_{Start}=40 N_{End}=40 TPS=Subacute	E: Mirror Therapy C: Sham Therapy Duration: 2-5h/d, 5d/wk for 4wk	• Brunnstrom Recovery Stages (+exp) • Funtional Indepence Measure (+exp) • Modified Ashworth Scale (-)
Altschuler et al. (1999) RCT (7) N_{Start}=40 N_{End}=40 TPS=Chronic	E: Mirror therapy C: Sham therapy Duration: 30min/d, 6d/wk for 4wk	• Brunnstrom Recovery Stage (+exp) • Fugl Meyer self-care Score (+exp) • Modified Ashworth Scale (-)
Mirror therapy versus bilateral arm training		

Fong et al. (2019)
RCT (7)
N_{start}= 101
N_{end}= 96
TPS= Chronic
	E: Mirror therapy
	C: Bilateral arm training
	Duration: 30min, 2x/wk for 6wks
		• Fugl-Meyers Assessment
		  • Upper Limb: (-)
		  • Hand: (+exp)
		• Action Research Arm Test
		  • Grasp:(-)
		  • Grip: (-)
		  • Pinch: (-)
		  • Gross: (-)
		• Wolf Motor Function Test:
		  • Functional Ability Sub Score:(-)
		  • Grip Sub Score: (-)

Li et al. (2019)
RCT (8)
N_{start}= 23
N_{end}= 20
TPS= Chronic
	E: Mirror therapy
	C: Bilateral arm training
	Duration: 130min, 3d/wk for 4wks (+home practice 5d/wk 30-40min)
		• Fugl-Meyer Upper Extremity: (-)
		  • Proximal: (-)
		  • Distal: (-)
		• Revised Nottingham Sensory Assessment - Tactile total: (-)
		• Chedoke Arm and Hand Activity Inventory: (-)
		• Motor Activity Log
		  • Amount of use: (-)
		  • Quality of movement: (-)
		• Stroke Impact Scale: (+exp)

Mirror therapy combined with bilateral arm training		
Rodrigues et al. (2016) RCT (7) N_{Start}=16	E: Mirror therapy and Bilateral Training C: Bilateral Training	• Upper extremity function test (-)

N_{End}=16 TPS=Chronic	Duration: 1h/d, 3d/wk for 4wk	
Samuelkamaleshkumar et al. (2014) RCT (7) N_{Start}=20 N_{End}=20 TPS=Subacute	E: Mirror therapy + bilateral arm training C: Control group Duration: 6h/d, 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Brunnstrom Recovery Stage (+exp) • Box and Block Test (+exp) • Modified Ashworth Scale (-)
Mirror therapy combined with tDCS		
Jin et al. (2019) RCT (8) N_{start}= 30 N_{end}= 28 TPS= Chonic	E1: Dual tDCSs + mirror therapy (before) E2: Dual tDCSs + mirror therapy (during) C: Sham + mirror therapy Duration: 30 min (stimulation and mirror each) 5x/wk, 2wks	E1 Vs C • Fugle-Meyers Upper Extremity: (-) • Action Research Arm Test: (-) • Box and Block Test: (-) E2 Vs C • Fugle-Meyers Upper Extremity: (-) • Action Research Arm Test: (+exp2) • Box and Block Test: (-) E1 Vs E2 • Fugle-Meyers Upper Extremity: (-) • Action Research Arm Test: (+exp2) • Box and Block Test: (-)
D'Agata et al. (2016) RCT crossover (7) N_{start}= 36 N_{end}= 36 TPS= Chronic	E1: rTMS E2: tDCS + Mirror therapy C: Sham + mirror therapy Duration: 5x/wk, 2wks (6mo washout for E1 and E2 groups)	E1 Vs C • Action Research Arm Test: (-) E2 Vs C • Action Research Arm Test: (-) E1 Vs E2 • Action Research Arm Test: (-)
Mirror therapy combined with functional electrical stimulation		
Kim et al. (2015) RCT (6) N_{Start}=28 N_{End}=23 TPS=Chronic	E: FES + mirror therapy C: FES + sham mirror therapy Duration: 30min/d, 5d/wk for 4wk	• Box and Block Test (-) • Fugl-Meyer Assessment (+exp) • Brunnstrom Recovery Stage (-) • Manual Function Test (+exp)
Mirror therapy combined with neuromuscular electrical stimulation		

Amasyali et al. (2016)
RCT (7)
N_{start}= 24
N_{end}= 25
TPS= Subacute
	E: Mirror therapy + NMES
	E2: EMG + NMES
	C: Conventional physiotherapy
	Duration: 30min 5x/wk for 3 wks
		E1 Vs C
		• Wrist Extension: (+exp1)
		• Grip Force: (-)
		• Box and Block Test: (+exp1)
		• Fugl-Meyers Upper Extremity: (+exp1)
		  • Shoulder/Elbow: (-)
		  • Wrist: (-)
		  • Hand: (-)
		  • Coordination: (-)
		E2 Vs C
		• Wrist Extension: (+exp2)
		• Grip Force: (-)
		• Box and Block Test: (-)
		• Fugl-Meyers Upper Extremity: (-)
		  • Shoulder/Elbow: (-)
		  • Wrist: (-)
		  • Hand: (-)
		  • Coordination: (-)
		E1 Vs E2
		• Wrist Extension: (-)
		• Grip Force: (-)
		• Box and Block Test: (+exp1)
		• Fugl-Meyers Upper Extremity: (-)
		  • Shoulder/Elbow: (-)
		  • Wrist: (-)
		  • Hand: (-)
		  • Coordination: (-)

Yun et al. (2011) RCT (4) N=60 TPS=Acute	E1: Cyclic NMES + mirror therapy E2: Cyclic NMES E3: Mirror therapy Duration: 30min/d, 5d/wk for 3wk	E1 vs. E2/E3 • Fugl-Meyer Assessment (+exp) • Hand flexion (-) • Wrist flexion (-) • Wrist extension (-)
Mirror therapy combined with mesh glove		
Lee et al. (2015) RCT (7) N_{Start}=48 N_{End}=47 TPS=Chronic	E1: Mirror Therapy with Mesh Glove Afferent Stimulation E2: Mirror Therapy C: Mirror Therapy with Sham Stimulation Duration: 90min/d, 5d/wk for 4wk	E1 vs E2/C • Extensor Digitorum Muscle Tone (+exp) E1/C vs E2 • Box and Block Test: (+exp, +con) • Muscle stiffness on the flexor carpi radialis (+exp, +con) • Functional Independence Measure (+exp, +con) • Fugl-Meyer Assessment (-) Revised Nottingham Sensory Assessment (-)
Lin et al. (2014a) RCT (7) N_{Start}=16 N_{End}=16 TPS=Chronic	E: Mirror therapy + Mesh glove C: Mirror therapy Duration: 90min/d, 5d/wk for 4wk	• Modified Ashworth Scale (-) • Box and Block Test (+exp) • Functional Independence Measure (-) Action Research Arm Test (+exp)
Lin et al. (2014b) RCT (7) N_{Start}=43 N_{End}=42 TPS=Chronic	E1: Mirror therapy + Mesh glove E2: Mirror therapy C: Therapeutic exercises Duration: 90min/d, 5d/wk for 4wk	E1 vs C • Fugl-Meyer Assessment (+exp) E1 vs E2 & E1 vs C • Box and Block Test (+exp) E1 vs E2 • Wolf Motor Function Test (-)
Mirror therapy combined with rTMS		
Ji et al. (2014) RCT (7) N_{Start}=35 N_{End}=35 TPS=Chronic	E1: Mirror therapy + rTMS E2: Mirror therapy C: Sham therapy Duration: 30min/d, 5d/wk for 4wk	E1 vs. E2 • Fugl-Meyer Assessment (+exp) • Box and Block Test (+exp) E2 vs. C • Fugl-Meyer Assessment (+exp_2) • Box and Block Test (+exp_2)
Group vs individual mirror therapy		
Thieme et al. (2012) RCT (6) N_{Start}=60 N_{End}=49 TPS=Subacute	E1: Individual mirror therapy E2: Group mirror therapy C: Sham mirror therapy Duration: 30min/d, 4dwk for 5wk	• Action Research Arm Test (-) • Fugl-Meyer Assessment (-) • Barthel Index (-) • Stroke Impact Scale (-) E1 vs. E2 • Modified Ashworth Scale (+exp)
Movement vs Task Based Mirror Therapy		

Bai et al. (2019)
RCT (7)
N_{start}=34
N_{end}= 34
TPS= Subacute
	E1: Movement based mirror therapy
	E2: Task based mirror therapy
	C: Conventional therapy
	Duration: 30min 5x/wk for 4wks
		E1 vs C
		• Fugl-Meyers Upper Extremity: (+exp1)
		• Wolf Motor Function Test: (-)
		• Grip strength: (-)
		• Modified Barthel Index: (-)
		• Modified Ashworth Scale
		  • Arm: (-)
		  • Hand: (-)
		E2 vs C
		• Fugl-Meyers Upper Extremity: (-)
		• Wolf Motor Function Test: (-)
		• Grip strength: (-)
		• Modified Barthel Index: (-)
		• Modified Ashworth Scale
		  • Arm: (-)
		  • Hand: (-)
		E1 vs E2

		• Fugl-Meyers Upper Extremity: (+exp1)
		• Wolf Motor Function Test: (-)
		• Grip strength: (-)
		• Modified Barthel Index: (-)
		• Modified Ashworth Scale
		  • Arm: (-)
		  • Hand: (-)

Mirror combined with Strength Therapy		
Ehrensberger et al. (2019) RCT (7) N_{start}= 35 N_{end}= 32 TPS= Chronic	E: Mirror + strength therapy C: Strength therapy only Duration: 20min, 3x/wk for 4wks	• Isometric Strength: (-) • Modified Ashworth Scale (Shoulder, Elbow, Wrist): (-) • Chedoke Arm and Hand Activity: (-) • Abihland: (-) • London Handicap Scale: (-)
Mirror Therapy combined with extracorpeal shockwave versus conventional therapy or mirror/shockwave alone		
Guo et al. (2019) RCT (6) N_{start}= 120 N_{end}= 120 TPS=Chronic	E1: Mirror therapy + extracorporeal shock E2: Mirror therapy E3: shock alone C: Conventional therapy Duration: 30min 5d/wk, 4wks conv + 20min 5d/wk, 4wks additional	E1 Vs C • Fugl-Meyer Upper Extremity Assessment: (+exp1) • Modified Ashworth Scale: (+exp1) E2 Vs C • Fugl-Meyer Upper Extremity Assessment: (+exp2) • Modified Ashworth Scale: (-) E3 Vs C • Fugl-Meyer Upper Extremity Assessment: (+exp3) • Modified Ashworth Scale: (+exp3) E1 vs E2 Vs E3 • Fugl-Meyer Upper Extremity Assessment: (+exp1) • Modified Ashworth Scale: (+exp1)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Mirror Therapy

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Mirror therapy** may produce greater improvements in motor function than **conventional therapy.**	27	Chinnavan et al. 2020; Madhoun et al. 2020; Antoniotti et al. 2019; Bai et al. 2019; Chaudhai et al. 2019; Ding et al. 2019; Guo et al. 2019; Arya et al. 2018; Chan et al. 2018; Ding et al. 2018; Oliveira et al. 2018; Colomer et al. 2016; Gurbuz et al. 2016; Kim et al. 2016; Lim et al. 2016; Pervane Vural et al. 2016; Arya et al. 2015; Park et al. 2015; Ji et al. 2014; Invernizzi et al. 2013; Timmerman et al. 2013; Wu et al. 2013a; In et al. 2012; Lee et al. 2012; Michielsen et al. 2011; Dohle et al. 2009; Altschuler et al. 1999
1a	**Mirror therapy** may not have a difference in efficacy compared to **bilateral arm training** for improving motor function.	2	Fong et al. 2019; Li et al 2019

1a	There is conflicting evidence about the effect of **mirror therapy combined with bilateral arm training** to improve motor function when compared to **bilateral arm training or conventional therapy**.	2	Rodrigues et al. 2016; Samuelkamaleshkumar et al. 2014
1a	**Mirror therapy combined with tDCS** may not have a difference in efficacy compared to **sham mirror therapy combined with tDCS** for improving motor function.	2	Jin et al. 2019; D'Agata et al. 2016
1b	**Mirror therapy combined with high frequency rTMS** may produce greater improvements in motor function than **mirror therapy on its own or sham stimulation**.	1	Ji et al. 2014
1b	**Mirror therapy combined with FES** may produce greater improvements in motor function than **sham mirror therapy with FES**.	1	Kim et al. 2015
1b	**Mirror therapy combined with cyclic NMES** may produce greater improvements in motor function than **mirror therapy or cyclic NMES on their own**.	2	Amasyali et al. 2016 Yun et al. 2011
1a	There is conflicting evidence about the effect of **mirror therapy combined with Mesh Gloves** to improve motor function when compared to **mirror therapy on its own**.	3	Lee et al. 2015; Lin et al. 2014a, Lin et al. 2014b
1b	**Mirror therapy provided in a group setting** may not have a difference in efficacy when compared to **mirror therapy in a one on one setting** to improve motor function.	1	Thieme et al. 2012
1b	There is conflicting evidence about the effect of **Movement based mirror therapy** on producing greater improvements in motor function than **task-based mirror therapy or conventional therapy**.	1	Bai et al. 2019
1b	**Mirror therapy combined with strength training** may not have a difference in efficacy when compared to **strength therapy** to improve motor function.	1	Ehrensberger et al. 2019

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**There is conflicting evidence about the effect of mirror therapy** when compared to **conventional therapy or Bobath concept approaches** for producing greater improvements in dexterity.	3	Oliveira et al. 2018; Kim et al. 2016; In et al. 2012
1b	**Mirror therapy combined with bilateral arm training** may produce greater improvements in dexterity than **bilateral arm training or conventional therapy**.	1	Samuelkamaleshkumar et al. 2014
1b	**Mirror therapy combined with tDCS** may not have a difference in efficacy when compared to **sham mirror therapy combined with tDCS** for improving dexterity.	1	Jin et al. 2019;

1b	**Mirror therapy combined with FES** may not have a difference in efficacy compared to **sham mirror therapy with FES** for improving dexterity.	1	Kim et al. 2015
2	**Mirror therapy combined with cyclic NMES** may not have a difference in efficacy when compared to **cyclic NMES or mirror therapy on their own** for improving dexterity.	1	Amasyali et al. 2016
1a	**Mirror therapy combined with Mesh Gloves** may produce greater improvements in dexterity than **mirror therapy on its own**.	3	Lee et al. 2015; Lin et al. 2014a; Lin et al. 2014b
1b	**Mirror therapy combined with high frequency rTMS** may produce greater improvements in dexterity than **mirror therapy on its own or sham stimulation**.	1	Ji et al. 2014

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1a	**Mirror therapy** may not have a difference in efficacy when compared to **conventional therapy or Bobath concept approaches** for improving spasticity.	11	Madhoun et al. 2020; Bai et al. 2019; Ding et al. 2019; Guo et al. 2019; Pervane Vural et al. 2016; Cristina et al. 2015; Wu et al. 2013a; In et al. 2012; Michielsen et al. 2011; Yavuzer et al. 2008; Altschuler et al. 1999
1b	**Mirror therapy combined with bilateral arm training** may not produce greater improvements in spasticity than **bilateral arm training or conventional therapy**.	1	Samuelkamaleshkumar et al. 2014
1a	**Mirror therapy combined with Mesh Gloves** may produce greater improvements in dexterity than **mirror therapy on its own**.	2	Lee et al. 2015; Lin et al. 2014a
1b	**Mirror therapy provided in a group setting** may produce greater improvements in spasticity than **mirror therapy administered in a one on one setting**.	1	Thieme et al. 2012
1b	**Movement based mirror therapy** may not have a difference in efficacy when compared **to task-based mirror therapy** for improving spasticity.	1	Bai et al. 2019
1b	**Mirror therapy combined with strength training** may not have a difference in efficacy when compared to **strength therapy** to improve spasticity.	1	Ehrensberger et al. 2019

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
2	**Mirror therapy combined with cyclic NMES** may not have a difference in efficacy when compared to **cyclic NMES or mirror therapy on their own** for improving range of motion.	2	Amasyali et al. 2016; Yun et al. 2011

PROPRIOCEPTION

LoE	Conclusion Statement	RCTs	References
1b	**Mirror therapy** may produce greater improvements in proprioception than **conventional therapy or Bobath concept approaches**.	1	Colomer et al. 2016
1b	**Mirror therapy combined with Mesh Gloves** may noy have a difference in efficacy when compared to **mirror therapy on its own** to produce greater improvements in dexterity than	1	Lee et al. 2015

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **mirror therapy** to improve performance of activities of daily living when compared to **conventional therapy or Bobath concept approaches**.	19	Chinnavan et al. 2020; Madhoun et al. 2020; Antoniotti et al. 2019; Bai et al. 2019; Ding et al. 2019; Ding et al. 2018; Oliverira et al. 2018; Radajewska et al. 2017; Gurbuz et al. 2016; Kim et al. 2016; Lim et al. 2016; Pervane Vural et al. 2016; Park et al. 2015; Tyson et al. 2015; Radajewska et al. 2013; Timmerman et al. 2013; Wu et al. 2013a; Michielsen et al. 2011; Yavuzer et al. 2008
1a	**Mirror therapy** may not have a difference in efficacy compared to **bilateral arm training** for improving activities of daily living.	2	Fong et al. 2019; Li et al 2019
1a	There is conflicting evidence about the effect of **mirror therapy combined with Mesh Gloves** to improve performance of activities of daily living when compared to **mirror therapy on its own**.	2	Lee et al. 2015; Lin et al. 2014a
1b	**Mirror therapy in a group setting** may not have a difference in efficacy compared to **mirror therapy in a one on one setting** to improve performance of activities of daily living.	1	Thieme et al. 2012
1b	**Movement based mirror therapy** may not have a difference in efficacy when compared **to task-based mirror therapy or conventional therapy** for improving activities of daily living.	1	Bai et al. 2019
1b	**Mirror therapy combined with strength training** may not have a difference in efficacy when compared to **strength therapy** to activities of daily living.	1	Ehrensberger et al. 2109

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References
1b	**Mirror therapy combined with bilateral arm training** may produce greater improvements in stroke severity than **bilateral arm training or conventional therapy**.	1	Samuelkamaleshkumar et al. 2014

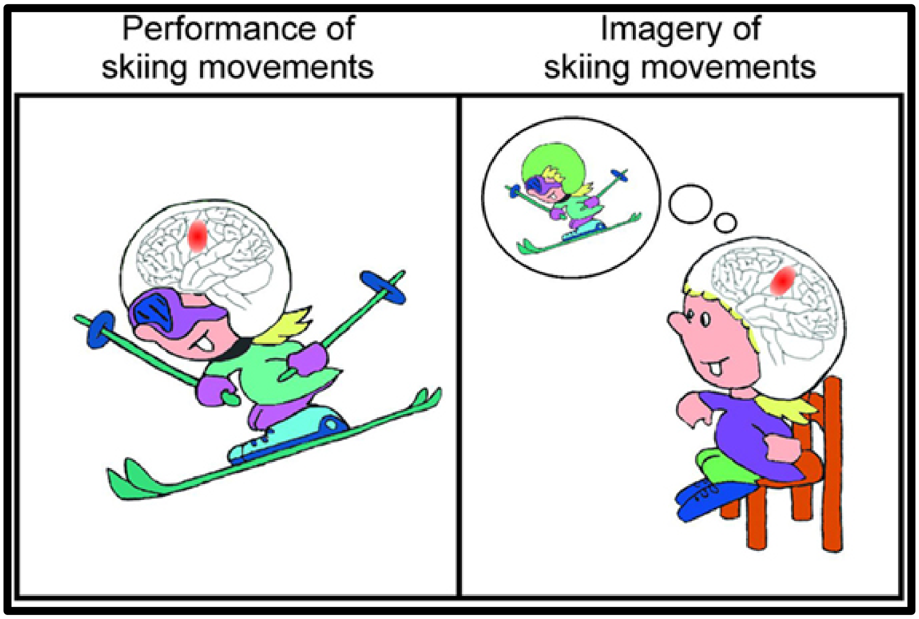
1b	**Mirror therapy combined with FES** may not have a difference in efficacy compared to **sham mirror therapy with FES** for improving stoke severity.	1	Kim et al. 2015

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Mirror therapy** may not improve muscle strength when compared to **conventional therapy or Bobath concept approaches**.	4	Bai et al. 2019; Ding et al. 2019; Tyson et al. 2015; Invernizzi et al. 2013; Michielsen et al. 2011
2	**Mirror therapy combined with cyclic NMES** may not have a difference in efficacy when compared to **cyclic NMES or mirror therapy on their own** for improving range of motion.	1	Amasyali et al. 2016;
1b	**Movement based mirror therapy** may not have a difference in efficacy when compared **to task-based mirror therapy or conventional therapy** for improving muscle strength.	1	Bai et al. 2019
1b	**Mirror therapy combined with strength training** may not have a difference in efficacy when compared to **strength therapy** to improve muscle strength	1	Ehrensberger et al. 2109

Key points

Mirror therapy on its own or in combination with other interventions may some aspects of upper limb function following stroke.

Mental Practice



Adopted from: https://www.ucbmsh.com/motor-imagery-for-improvement-of-gait-in-stroke-patient/

Mental practice as the name suggests, involves cognitively rehearsing a specific task by repetitively imagining oneself performing the precise movements involved in the task in the absence of performing the physical movement (Page et al. 2014). Mental practice is speculated to be effective because of its ability to use the same motor schema as when physically practicing the same task through the activation of similar neural regions and networks during mental practice (Page et al. 2014). The use of mental practice 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 (Page et al. 2014). The technique is believed to be advantageous in stroke survivors because certain motor skills may be difficult to physically practice; stroke survivors spend a majority of their time inactive and alone; and repetitive task-specific practice is a prerequisite for cortical plasticity and subsequent motor changes (Page et al. 2014). Mental practice can be used to supplement conventional therapy and can be used at any stage of recovery.

21 RCTs evaluated mental practice compared to conventional rehabilitation or a sham intervention for upper extremity motor rehabilitation (Wang et al. 2020; Nam et al. 2019; Li et al. 2018; Oh et al. 2016; Park et al. 2015b; Mihara et al. 2013; Oostra et al. 2013; Sun et al. 2013; Nielsen et al. 2012; Letswaart et al. 2011; Page et al. 2011; Wellfringer et al. 2011; Bovend'Eerdt et al. 2010; Riccio et al. 2010; Liu et al. 2009b; Muller et al. 2007; Page et al. 2007; Page et al. 2005; Liu et al. 2004; Page et al. 2001; Page et al. 2000). Three RCTs combined mental practice with modified constraint induced movement therapy (mCIMT) compared to mCIMT on its own (Kim et al. 2018; Park et al. 2015a; Page et al. 2009). Another RCT combined mental practice with Nintendo Wii virtual reality interactive game training compared to Nintendo Wii training on its own (Park et al. 2016). Three RCTs combined mental imagery with NMES (Park et al. 2109; Park et al. 2017; Hong et al. 2012). One RCT examined mental practice of the unaffected and the affected side (Lie et al. 2014). One study looked at motor imagery combined with brain computer interface (Pichiorri et al. 2015)

The methodological details and results of all 20 RCTs evaluating mental practice interventions for upper extremity motor rehabilitation are presented in Table 13.

Table 13. RCTs Evaluating Mental Practice Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Wang et al. (2020) RCT (7) N_{start}=34 N_{end}=31 TPS=Subacute	E: Motor imagery C: Conventional therapy Duration: 3hrs/d, 5d/wk for 4wks rehab, Motor imagery 30min 5d/wk, 4wks	• Fugl-Meyer Upper Extremity: (+exp) • Modified Barthel Index: (-) • Functional magnetic resonance imaging data: (+exp)
Nam et al. (2019) RCT (6) N_{start}= 24 N_{end}= 20 TPS= Subacute	E: Mental practice C: Conventional therapy Duration: 20min, 5x/wk for 4wks, +30min rehab	• Fugl-Meyer Upper Extremity: (-) • Manual Function Test: (-) • Functional Independence Measure: (-)
Li et al. (2018) RCT (6) N_{start}= 20 N_{end}= 20 TPS= Subacute	E: Mental practice C: Conventional therapy Duration: 45min, 5x/wk for 4wks (+rehab same time)	• Action Research Arm Test: (+exp) • Fugle-Meyers Upper Extremity: (+exp)
Oh et al. (2016) RCT Crossover (7) N_{Start}=10 N_{End}=10 TPS=Chronic	E: Mental Practice C: Conventional Therapy Duration: 20min/d, 3d/wk for 3wk	• Fugl-Meyer Assessment (-) • Motor Activity Log (-)
Park et al. (2015b) RCT (6) N_{Start}=29 N_{End}=29 TPS=Chronic	E: Mental practice C: Physical therapy Duration: 10min/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (+exp) • Modified Barthel Index (+exp)
Mihara et al. (2013) RCT (9) N_{Start}=20 N_{End}=20 TPS=Chronic	E: Mental practice C: Sham intervention Duration: 20min/d, 3d/wk for 2wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm test (-)
Oostra et al. (2013) RCT (8) N_{Start}=20 N_{End}=20 TPS=Chronic	E: Mental practice C: Physical training Duration: 30min/d, 5d/wk for 6wk	• Action Research Arm Test (+exp)
Sun et al. (2013) RCT (6) N_{start}= 20 N_{end}= 18 TPS= Subacute	E: Motor imagery C: Conventional therapy Duration: rehab 3hr/d, 5d/wk, 4wks (+30min MI)	• Fugl-Meyer Upper Extremity: (+exp)

Nilsen et al. (2012)
RCT (6)
N_{start}= 19
N_{end}= 16
TPS= Chronic
	E1: Mental Imagery internal
	E2: Mental imagery external
	C: Relaxation control
	Duration: ~20min, 2x/wk, 6wks
		E1 Vs C
		• Fugl-Meyers Assessment Upper Extremity: (+exp1)
		• Jebsen Hand Function Test: (+exp1)
		• Canadian Occupational Performance Measure
		  • Performance: (-)
		  • Satisfaction: (-)
		E1 Vs C
		• Fugl-Meyers Assessment Upper Extremity: (+exp2)
		• Jebsen Hand Function Test: (+exp2)

		• Canadian Occupational Performance Measure • Performance: (-) • Satisfaction: (-) E1 Vs E2 • Fugl-Meyers Assessment Upper Extremity: (-) • Jebsen Hand Function Test: (-) • Canadian Occupational Performance Measure • Performance: (-) • Satisfaction: (-)
Ietswaart et al. (2011) RCT (7) N_{start}=121 N_{end}=101 TPS=Subacute	E1: Motor imagery E2: Attention placebo C: Usual care Duration: 45min/d, 3d/wk for 4wk	• Action Research Arm Test (-)
Page et al. (2011) RCT (6) N_{start}=32 N_{end}=29 TPS=Subacute	E: Audiotaped mental practice C: Audiotaped sham intervention Duration: 30min/d, 3d/wk for 10wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-)
Welfringer et al. (2011) RCT (7) N_{start}=30 N_{end}=30 TPS=Subacute	E: Visuomotor imagery therapy C: No therapy Duration: 30min, 2x/d, 4-5d/ wk, 3wks(exp) - con 45min 4x/wk	• Representation tests: • Body touching: (-) • Visual arm imagery: (-) • Kinaesthetic imagery: (-) • Body identification sensation: (-) • Action Research Arm Test: (-)
Bovend'Eerdt et al. (2010) RCT (8) N_{start}=50 N_{end}=48 TPS=Chronic	E: Mental practice C: Conventional therapy Duration: 30min/d, 2-3d/wk for 5wk	• Barthel Index (-) • Nottingham Extended ADL (-) • Action Research Arm Test (-)
Riccio et al. (2010) RCT Crossover (5) N_{start}=36 N_{end}=36 TPS=Chronic	E: Mental practice C: Conventional rehabilitation Duration: 1h/d, 5d/wk for 3wk	• Motricity Index (+exp) • Arm Function Test (+exp)
Liu et al. (2009b) RCT (5) N_{start}=35 N_{end}=35 TPS=Subacute	E: Mental Imagery C: Conventional Functional Rehabilitation Duration: 1h, 5d/wk for 3wk	• Improvement in Trained Tasks (+exp)
Müller et al. (2007) RCT (4) N_{start}=17 N_{end}=17 TPS=Acute	E1: Mental practice E2: Motor practice C: Conventional therapy Duration: 30min/d, 5d/wk for 4wk	E1/E2 vs. C • Jebsen Hand Function Test: (+exp_1, +exp_2) • Pinch grip: (+exp_1, +exp_2)
Page et al. (2007) RCT (6) N_{start}=32 N_{end}=32 TPS=Chronic	E: Mental Practice C: Sham Relaxation Exercise Intervention Duration: 30min/d, 2d/wk for 6wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (+exp)
Page et al. (2005a) RCT (6) N_{start} =11 N_{end}=8 TPS=Chronic	E: Mental practice C: Relaxation techniques Duration: 30min/d, 2d/wk for 6wk	• Action Research Arm Test (+exp) • Motor Activity Log: Amount of Use (+exp), Quality of Movement (+exp)
Liu et al. (2004) RCT (4) N_{start}=49 N_{end}=46 TPS=Acute	E: Mental Imagery C: Functional training Duration: 1h/d, 5d/wk for 3wk	• Fugl-Meyer Assessment (-)

Page et al. (2001) RCT (5) N_{start}=13 N_{end}=13 TPS=Subacute	E: Imagery training C: Occupational therapy Duration: 10min/d, 4d/wk for 6wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (+exp)
Page et al. (2000) RCT (4) N_{start}=16 N_{end}=13 TPS=Chronic	E: Imagery training C: Occupational therapy Duration: 30min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (+exp)
Mental practice combined with mCIMT		

Kim et al. (2018)
RCT (6)
N_{start}= 16
N_{end}= 14
TPS= Chronic
	E: Mental practice plus modified constraint-induced movement (mCIMT) therapy
	C: mCIMT therapy
	Duration: 6 hours plus 10 min for experimental group, 5x/wk for 2wks
		• 3D motion analysis
		  • Speed: (-)
		  • Time: (-)
		  • Smoothness: (-)
		• Jebsen –Taylor Hand Function Test
		  • Writing: (+exp)
		  • Page turning: (+exp)
		  • Small objects: (-)
		  • Feeding: (-)
		  • Stacking: (-)
		  • Large lightweight objects: (-)
		  • Large heavy objects: (-)
		• Motor activity log
		  • Amount of Use: (+exp)
		  • Quality of Movement: (+exp)

Park et al. (2015a) RCT (7) N_{Start}=26 N_{End}=26 TPS=Chronic	E: Mental practice + mCIMT C: mCIMT Duration: 30min/d, 5d/wk for 6wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (+exp) • Modified Barthel Index (+exp)
Page et al. (2009) RCT (4) N_{start}=10 N_{end}=10 TPS=Chronic	E: Mental practice + Modified Constraint Induced Movement Therapy C: Modified Constraint Induced Movement Therapy Duration: 30min/d, 5d/wk for 10wk	• Action Research Arm Test (+exp) • Fugl-Meyer Assessment (+exp)
Nintendo Wii combined with mental practice		
Park et al. (2016) RCT (7) N_{Start}=30 N_{End}=30 TPS=Chronic	E: Nintendo Wii + mental practice C: Nintendo Wii Duration: 5min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (-) • Motor Activity Log (-)
Mental Imagery combined with NMES vs Functional Electrical Stimulation		
Park et al. (2019) RCT (8) N_{start}=68 N_{end}=68 TPS=Chronic	E: Mental imagery + EMG-NMES C: Electromyogram-triggered neuromuscular electrical stimulation Duration: 30min, 5d/wk, 6wks	• Action Research Arm Test: (-) • Fugl-Meyer upper extremity: (-) • Korean version of Modified Barthel Index: (-)
Park et al. (2017) RCT (2) N_{Start} =40 N_{End} =32 TPS=NR	E: Mental Practice + EMG NMES C: Conventional Rehabilitation Program Duration: 30min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp)
Hong et al. (2012) RCT (8) N_{start}= 14 N_{end}= 14 TPS= Chronic	E: Mental imagery +EMG-NMES C: Functional electric stimulation Duration: 40min, 5d/wk for 4wks	• Fugl-Meyers Upper Extremity: (-) • Motor Activity Log (Quality of Movement, Amount of Use):(-) • Modified Ashworth Scale: (-) • Modified Barthel Index: (-)
Mental practice of affected versus unaffected side		

Liu et al. (2014) RCT (7) N_{Start}=20 N_{End}=20 TPS=Subacute	E: Motor imagery + mental practice of affected hand C: Motor imagery + mental practice of unaffected hand Duration: 45min/d, 5d/wk for 4wk	• Action Research Arm test (+exp)
Motor imagery combined with Brain computer interface		
Pichiorri et al. (2015) RCT (6) N_{start}=32 N_{end}=28 TPS=Subacute	E: Brain-computer interface + motor imagery C: Motor imagery Duration: 30min, 3x/wk, 4wks	• Fugl Meyer Assessment: (+exp) • Medical Research Council Scale: (+exp) • National Institute of Health Stroke Scale: (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Mental Practice

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Mental practice** may produce greater improvements in motor function than **conventional rehabilitation or a sham intervention**.	20	Wang et al. 2020; Nam et al. 2019; Li et al. 2018; Oh et al. 2016; Park et al. 2015b; Mihara et al. 2013; Oostra et al. 2013; Sun et al. 2013; Lee et al. 2012; Nilsen et al. 2012; Page et al. 2011; Wellfringer et al. 2011; Bovend'Eerdt et al. 2010; Riccio et al. 2010; Muller et al. 2007; Page et al. 2007; Page et al. 2005; Liu et al. 2004; Page et al. 2001; Page et al. 2000;
1a	**Mental practice combined with mCIMT** may produce greater improvements in motor function than **mCIMT** on its own.	2	Park et al. 2015a; Page et al. 2009;
1b	**Mental practice combined with Nintendo Wii training** may not have a difference in efficacy compared to **Nintendo Wii training on its own** for improving motor function.	1	Park et al. 2016
1b	**Mental practice combined with EMG-NMES training** may not have a difference in efficacy compared to **FES on its own** for improving motor function.	1	Hong et al. 2012
2	**Mental practice combined with EMG-NMES training** may improving motor function when compared to **conventional therapy on its own.**	1	Park et al. 2017
1b	**Mental practice combined with EMG-NMES training** may not have a difference in efficacy compared to **EMG-NMES on its own** for improving motor function.	1	Park et al. 2019
1b	**Motor imagery combined with mental practice of the affcted hand** may improve motor function when compared to **motor imagery combined with mental practice of unaffected hand.**	1	Liu et al. 2014

1b	**Motor imagery combined with brain computer interface** may improve motor function compared to **motor imagery** alone.	1	Pichiorri et al. 2015

DEXTERITY			
LoE	Conclusion Statement	RCTs	References
1b	**Mental practice combined with mCIMT** may not produce greater improvements in dexterity than **mCIMT on its own**.	1	Kim et al. 2018

ACTIVITIES OF DAILY LIVING			
LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **mental practice** to improve performance of activities of daily living when compared to **conventional rehabilitation or a sham intervention**.	8	Wang et al. 2020; Oh et al. 2016; Park et al. 2015b; Rajeesh et al. 2015; Bovend'Eerdt et al. 2010; Liu et al. 2009b; Page et al. 2005
1a	**Mental practice combined with mCIMT** may produce greater improvements in performance of activities of daily living than **mCIMT on its own**.	2	Park et al. 2015a Kim et al. 2018
1b	**Mental practice combined with Nintendo Wii** training may not have a difference in efficacy compared to **Nintendo Wii training on its own** for improving performance of activities of daily living.	1	Park et al. 2016
1b	**Mental practice combined with EMG-NMES training** may not have a difference in efficacy compared to **EMG-NMES on its own** for improving performance on activities of daily living.	1	Park et al. 2019
1b	**Mental practice combined with EMG-NMES training** may not have a difference in efficacy compared to **FES on its own** for improving performance of activities of daily living.	1	Hong et al. 2012

MUSCLE STRENGTH			
LoE	Conclusion Statement	RCTs	References
2	**Mental practice** may produce greater improvements in muscle strength than **conventional rehabilitation or a sham intervention**.	1	Muller et al. 2007
1b	**Motor imagery combined with brain computer interface** may improve muscle strength compared to **motor imagery** alone.	1	Pichiorri et al. 2015

PROPRIOCEPTION			
LoE	Conclusion Statement	RCTs	References

1b	**Mental practice** may not have a difference in efficacy compared to **conventional rehabilitaton or no therapy** for improving proprioception.	1	Wellfringer et al. 2011

RANGE OF MOTION			
LoE	Conclusion Statement	RCTs	References
1b	**Mental practice combined with mCIMT** may not produce greater improvements in range of motion than **mCIMT on its own**.	1	Kim et al. 2018

SPASTICITY			
LoE	Conclusion Statement	RCTs	References
1b	**Mental practice combined with EMG-NMES training** may not have a difference in efficacy when compared to **FES** for improving spasticity.	1	Hong et al. 2012

STROKE SEVERITY			
LoE	Conclusion Statement	RCTs	References
1b	**Motor imagery combined with brain computer interface** may improve muscle strength compared to **motor imagery** alone.	1	Pichiorri et al. 2015

Key points

Mental practice, alone or in combination with constraint-induced movement therapy, may be beneficial for upper limb rehabilitation following stroke.

Mental practice in combination with other therapies training may not be more beneficial for upper limb function than CIMT on its own.

Action Observation

Adopted from: https://www.youtube.com/watch?v=QE3CUhmKi7U

Action observation is a form of therapy whereby an individual observes another individual performing a motor task, either on a video or a real demonstration, and then may attempt to perform the same task themselves. For example, the patient may be instructed to watch a video showing an adult stretching out his hand to pick up a cup, bringing the cup to his mouth, and then returning the cup to its initial position - the act of drinking. After observing the video sequence for a time, the participants may or may not be asked to perform the same action (Borges et al. 2018).

The therapy is considered a multisensory approach designed to increase cortical excitability in the primary motor cortex by activating central representations of actions through the mirror neuron system (Kim and Kim, 2015). Although action observation has been evaluated mainly in healthy volunteers, a few studies have evaluated its benefit in motor relearning following stroke.

Thirteen RCTs were found that evaluated action observation techniques in total. Ten RCTs compared action observation to conventional rehabilitation or sham action observation for upper extremity motor rehabilitation (Zhu et al. 2020; Fu et al. 2017; Kuk et al. 2016; Kim and Kim, 2015; Zhu et al. 2015; Sale et al. 2014; Cowles et al. 2013; Franceschini et al. 2012; Celnik et al. 2008; Ertelt et al. 2007). Two RCTs compared action observation to Task-specifc training (Kim and Bang 2016; Ahmad et al. 2014) and one RCT compared action observation with intrinsic muscle stimulation to action observation alone (Kim et al. 2020). Their methodological details and results are presented in Table 14.

Table 14. RCTs Evaluating Action Observation Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Zhu et al. (2020) RCT (7) N_{start}=46 N_{end}=31 TPS= Subacute	E: Action Observation C: Conventional therapy Duration: 30min, 6x/wk for 8wks	• Fugl-Meyer Upper Extremity: (+exp) • Barthel Index: (+exp)
Fu et al. (2017) RCT (5) N_{Start}=70 N_{End}=53 TPS=Subacute	E: Video clip of 30 actions relating to shoulder, elbow, wrist, forearm and hand movements. C: Conventional therapy Duration: 20min, 6x/wk for 8 wk	• Fugl-Meyer Assessment (-) • Wolf motor function test (-) • Modified Barthel Index (-)
Kuk et al. (2016) RCT (5) N_{Start}=22 N_{End}=20	E: Video clip of a motor task followed by execution of the same motor task C: Pictures of landscapes followed by execution of the motor task Duration: 1min/d for 5d	• Box and Block Test (+exp)
Kim and Kim (2015) RCT (6) N_{Start}=12 N_{End}=12 TPS= Not reported	E: Action observation + occupational therapy C: Placebo observation + occupational therapy Duration: 30min/d, 5d/wk for 6wk	• Wolf Motor Function Test (-)
Zhu et al. (2015) RCT (5) N_{Start}=70 N_{End}=61 TPS=Acute	E: Upper Limb Action Observation Therapy C: Conventional Rehabilitation Therapy Duration: 30min/d, 6d/wk for 8wk	• Fugl-Meyer Assessment (+exp) • Barthel Index (+exp) • Modified Ashworth Scale (+exp)
Sale et al. (2014) RCT (7) N_{Start}=67 N_{End}=67 TPS=Acute	E: Action observation C: Standard rehabilitation Duration: 3min/d, 5d/wk for 4wk	• Box and Block Test (+exp) • Fugl Meyer Assessment (+exp)
Cowles et al. (2013) RCT (7) N=29 TPS=Acute	E: Action observation C: Conventional therapy Duration: 1h/d, 5d/wk for 3wk	• Motricity Index (-) • Action Research Arm Test (+con)
Franceschini et al. (2012) RCT (8) N=102 TPS=Acute/Subacute	E: Video footage C: Static images Duration: 15min/d, 5d/wk for 4wk	• Box and Block Test (+exp) • Frenchay Arm Test (-) • Modified Ashworth Scale (-) • Functional Idependence Measure (-)
Celnik et al. 2008 RCT (5) crossover N_{start}= 18 N_{end}= 18 TPS= Chronic	E1: Congruent AO (same movements) E2: Incongruent AO (different movements) C: Conventional therapy Duration: 30min, 1x/condition, 7d washout period	E1 Vs C • Limb Kinematics (-) E2 Vs C • Limb Kinematics (-) E1 Vs E2 • Limb Kinematics (+exp1)
Ertelt et al. (2007) RCT (5) N=15 TPS=Chronic	E: Action observation therapy C: Traditional therapy Duration: 12min/d, 5d/wk for 18d	• Frenchay Arm Test (+exp) • Wolf Motor Function Test (+exp) • Stroke Impact Scale (+exp)
Action observation compared to task-oriented training		
Kim and Bang, 2016 RCT (5) N_{Start}=22 N_{End}=22 TPS=Subacute	E: Action observation C: Task-oriented training Duration: 40min, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Box and block test (+exp) • Modified Barthel Index (+exp) • Modified Ashworth Scale (-)

Ahmad et al. (2014)
RCT (4)
N_{start}= 40
N_{end}= 40
TPS= Not reported
	E1: Auditory imagery
	E2: Visual imagery
	E3: Both imagery
	C: Task specific training
	Duration: single session unspecified length
		E1 Vs C
		• Action Research Arm Test: (-)
		• Motor Activity Log: (-)
		  • Quality of Movement: (-)
		  • Amount of Use: (-)
		• Barthels Index: (-)
		E2 Vs C
		• Action Research Arm Test: (-)
		• Motor Activity Log: (-)
		  • Quality of Movement: (-)
		  • Amount of Use: (-)
		• Barthels Index: (-)
		E3 Vs C
		• Action Research Arm Test: (-)
		• Motor Activity Log: (-)
		  • Quality of Movement: (-)
		  • Amount of Use: (-)
		• Barthels Index: (-)
		E1 Vs E2 Vs E3
		• Action Research Arm Test: (-)
		• Motor Activity Log: (-)
		  • Quality of Movement: (-)
		  • Amount of Use: (-)
		• Barthels Index: (-)

Action Observation combined with Muscle Stimulation		
Kim et al. (2020) RCT (5) N_{start}= 22 N_{end}= 22 TPS= Chronic	E: Action observation training with intrinsic muscle stimulation C: Action observation training Duration: 70min 5x wk for 4 wks	• Manual Function Test: (-) • 2-point Discrimination: (-) • Proprioception: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Action Observation

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **action observation interventions** to improve motor function when compared to **conventional rehabilitation or sham action observation**.	8	Zhu et al. 2020; Fu et al. 2017; Kim and Kim, 2015; Zhu et al. 2015; Sale et al. 2014; Cowles et al. 2013; Celnik et al. 2008; Ertelt et al. 2007
2	There is conflicting evidence about the effect of **action observation interventions** to improve motor function when compared to **task-specific training.**	2	Kim and Bang, 2016; Ahmad et al. 2014
2	**Action observation with intrinsic muscle electrical stimulation** may not produce greater improvements in motor function than **action observation alone**.	1	Kim et al. 2020

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**

1a	**Action observation** may produce greater improvements in dexterity than **sham stimulation or conventional therapy**.	3	Kuk et al. 2016; Sale et al. 2014; Franceschini et al. 2012
2	**Action observation** may produce greater improvements in dexterity than **task-oriented training**.	1	Kim and Bang, 2016

ACTIVITIES OF DAILY LIVING			
LoE	Conclusion Statement	RCTs	References
1b	There is conflicting evidence about the effect of **action observation interventions** to improve activities of daily living when compared to **sham stimulation or conventional therapy**.	5	Zhu et al. 2020; Fu et al. 2017; Zhu et al. 2015; Franceschini et al. 2012; Ertelt et al. 2007
2	**Action observation** may not have a difference in efficacy when compared to **task-oriented training** for improving performance on activities of daily living.	2	Kim and Bang, 2016; Ahmad et al. 2014

SPASTICITY			
LoE	Conclusion Statement	RCTs	References
1b	There is conflicting evidence about the effect of **action observation interventions** to improve spasticity when compared to **sham stimulation or conventional therapy**.	2	Zhu et al. 2015; Francesschini et al. 2012
2	**Action observation** may not have a difference in efficacy when compared to **task-oriented training** for improving spasticity.	1	Kim and Bang, 2016

PROPRIOCEPTION			
LoE	Conclusion Statement	RCTs	References
2	**Action Observation with intrinsic muscle stimulation** may not produce greater improvements in proprioception than **action observation alone.**	1	Kim et al. 2020

Key points

There is conflicting evidence for the use of action observation for improving some aspects of upper limb function following stroke.

Music Therapy

Adopted from: https://steinhardt.nyu.edu/site/ataglance/2017/03/music-therapy-helps-with-recovery-post-stroke.html

Music therapy is defined as listening, singing, and creating music with/without rhythm and percussion instruments, and is based on four rehabilitation principles: extended repetition of simple finger and arm movements, auditory-motor coupling to reinforce motor learning due to instant auditory feedback, individualized training, and emotional/motivational support due to the emotions invoked by music and the acquisition of a new skill (Zhang et al. 2016). As such 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 music pieces based on individual performance (Jun et al. 2013).

Four RCTs (Tong et al. 2015; Thielbar et al. 2014; Van Vugt et al. 2014; Altenmuller et al. 2009) examined the efficacy of musical instruction and playing compared to conventional or sham therapy.

Five RCTs (Fukioka et al. 2018; Street et al. 2018; Scholz et al. 2016; Jun et al. 2013; Chouhan et al. 2012) evaluated the effects of music therapy cueing compared to conventional therapy and graded repetitive arm supplementary programs.

The methodological details and results of all nine RCTs are presented in Table 15.

Table 15. RCTs Evaluating Music Therapy Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Musical instruction and playing versus sham or conventional therapy		
Van Vugt et al. (2016) RCT (5) N$_{start}$= 43 N$_{end}$= 34 TPS= Subacute	E: Piano playing with normal audio feedback C: Piano playing with jittered audio feedback Duration: 10 sessions of 30mins for 5 hrs total over 4 weeks	• Finger Tapping and Finger Tapping Speed (-) • Nine Hole Peg Test (-)
Tong et al. (2015) RCT (5) N$_{Start}$=33 N$_{End}$=30 TPS=Chronic	E: Audible Music Instrumental Training C: Mute Music Instrumental Training Duration: 30min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (-) • Wolf Motor Function Test (+exp)
Thielbar et al. (2014) RCT (6) N$_{Start}$=14 N$_{End}$=14 TPS=Chronic	E: Virtual keyboard music playing C: High intensity, task oriented occupational therapy Duration: 1hr/d, 3d/wk for 6wk	• Action Research Arm Test (-) • Fugl Meyer Assessment (+exp) • Jebsen Taylor Hand Function Test (+exp) • Grip strength (-) • Pinch strength (-)
Van Vugt et al. (2014) RCT (4) N$_{Start}$=36 N$_{End}$=28 TPS=Subacute	E: Playing piano together C: Playing piano sequentially Duration: 30min/d, 5d/wk for 2wk	• Nine Hole Peg Test (-)
Altenmüller et al. (2009) RCT (5) N$_{Start}$=62 N$_{End}$=62 TPS=Acute	E: MIDI piano and electronic drum training + conventional therapy C: Conventional therapy only Duration: 1hr/d, 5d/wk for 3wk	• Box and Block Test (+exp) • Nine Hole Pegboard Test (+exp) • Action Research Arm Test (+exp) • Finger/Hand tapping (+exp)
Musical movement cueing versus conventional therapy or graded repetitive arm supplementary programs		

Fujioka et al. (2018)
RCT (8)
N$_{start}$= 29
N$_{end}$= 27
TPS= Chronic
	E: Music therapy
	C: Graded Repetitive Arm Supplementary Program
	Duration: 1hr, 3x/wk for 10wks
		• Chedoke-McMaster Stroke Assessment
		  • Hand: (-)
		  • Arm: (-)
		• Action Research Arm Test: (-)
		• Trail Making: (+exp)
		• Stoke Impact Scale
		  • Mobility: (-)
		  • Memory/Thinking: (-)
		  • Emotion: (-)
		  • Communication: (-)
		  • Social: (-)

Street et al. (2018) RCT (6) N$_{start}$= 11 N$_{end}$= 10 TPS= Chronic	E: Home based music therapy C: Conventional therapy Duration: 2x/wk, 6wks, 20-30min	• Action Research Arm Test: (-) • Nine Hole Peg Test: (-)
Scholz et al. (2016) RCT (4) N$_{Start}$=25 N$_{End}$=25 TPS=Acute	E: Music Sonification Therapy C: Sham Movement Training Duration: 30min/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Nine Hold Peg Test (-) • Stroke Impact Scale (-)
Jun et al. (2013) RCT (4) N$_{Start}$=40 N$_{End}$=30	E: Music movement therapy C: Routine intervention Duration: 1hr/d, 3d/wk for 8wk	• Shoulder and elbow flexion (+exp) • Arm strength (-) • Modified Barthel Index (-)

TPS=Acute		
Chouhan et al. (2012) RCT (6) N_{start}= 45 N_{end}= 45 TPS= Subacute	E1: Rhythmic auditory cueing E2: Visual cueing C: Conventional therapy Duration: 2hrs, 3x/wk for 3wks	E1 Vs C • Fugl-Meyers Upper Extremity: (+exp1) E2 Vs C • Fugl-Meyers Assessment Upper Extremity: (+exp2) E1 Vs E2 • Fugl-Meyers Upper Extremity: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Music Therapy

MOTOR FUNCTION			
LoE	Conclusion Statement	RCTs	References
1b	**Musical training** may improve motor function when compared to **sham or conventional therapy.**	3	Tong et al. 2015; Thielbar et al. 2014 Altenmuller et al. 2009
1a	**Music cueing therapy** may not have a difference in efficacy for improving motor function when compared to **conventional therapy, task-oriented therapy, visual cueing and sham interventions**.	4	Fujioka et al. 2018; Street et al. 2018; Scholz et al. 2016; Chouhan et al. 2012;

ACTIVITIES OF DAILY LIVING			
LoE	Conclusion Statement	RCTs	References
1a	**Music cueing therapy** may not have a difference in efficacy for improving performance on activities of daily living when compared to **conventional therapy, task-oriented therapy, visual cueing and sham interventions**.	3	Fujioka et al. 2018; Scholz et al. 2016; Jun et al. 2013

MUSCLE STRENGTH			
LoE	Conclusion Statement	RCTs	References
1b	**Musical training** may not have a difference in efficacy for improving muscle strength when compared to **sham or conventional therapy.**	1	Thielbar et al. 2014
2	**Music cueing therapy** may not have a difference in efficacy for improving muscle strength when compared to **conventional therapy, task-oriented therapy, visual cueing and sham interventions**.	1	Jun et al. 2013

DEXTERITY			
LoE	Conclusion Statement	RCTs	References

2	**Musical training** may not have a difference in efficacy for improving dexterity when compared to **sham or conventional therapy.**	2	Altenmuller et al. 2009, Van Vugt et al. 2016
1a	**Music cueing therapy** may not improve dexterity when compared to **conventional therapy, task-oriented therapy, visual cueing and sham interventions**.	2	Street et al. 2018; Scholz et al. 2016;

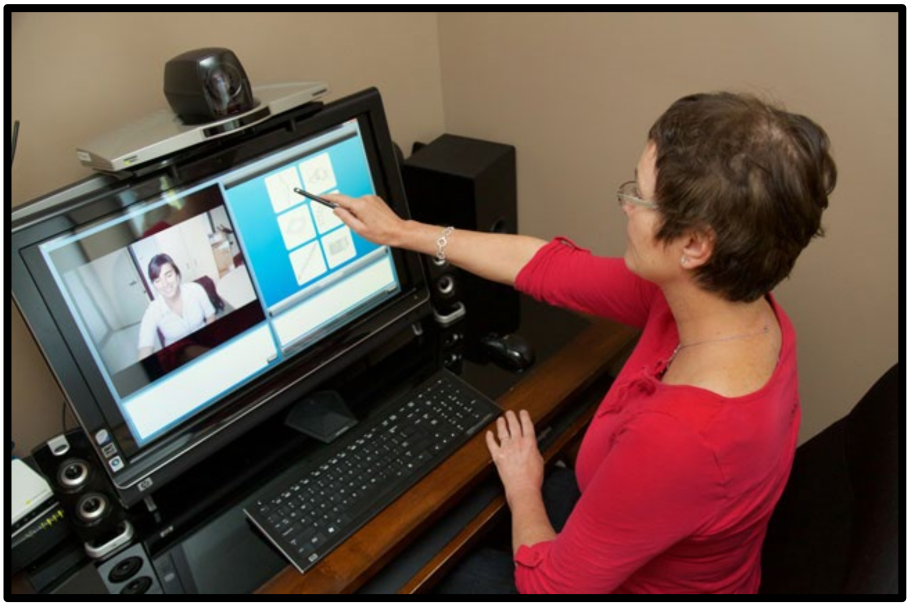
RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Music cueing therapy** may not improve range of motion when compared to **conventional therapy, task-oriented therapy, visual cueing and sham interventions**.	1	Jun et al. 2013

Key points

Musical training may be beneficial for improving motor function aspects of upper limb rehabilitation post-stroke.
Musical cueing may not be beneficial for improving upper limb rehabilitation post-stroke.

<u>**Technology based interventions**</u>

Telerehabilitation



Adopted from: http://www.telereadaptation.com/en/projet/telerehabilitation-in-speech-therapy/

Telerehabilitation is the process of providing rehabilitation services remotely through information and communication technologies (e.g. a kiosk, telephone and computer) (Dodakian et al. 2017; Emmerson et al. 2017). This rehabilitation method is particularly useful for patients who cannot access a rehabilitation center (Benvenuti et al. 2014). Additionally, this intervention 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).

Only two RCTs looked at upper limb rehabilitation using telerehabilitation (Emerson et al. 2017; Wolg et al. 2015), though several RCT protocols and observational studies have been published. In one RCT the intervention group was a home exercise program delivered through a tablet (Emerson et al. 2017), while the other RCT delivered a home exercise program through a novel hand robot system (Wolf et al. 2015). Both RCTs were compared to home exercise programs on their own,

The methodological details and results of the two RCTs evaluating telerehabilitation for the upper extremity motor rehabilitation are presented in Table 16.

Table 16. RCTs Evaluating Telerehabilitation for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Emmerson et al. (2017) RCT (7) N$_{Start}$=62 N$_{End}$=58 TPS=Chronic	E: Home exercise program using an electronic tablet with automated reminders C: Paper-based home exercise program Duration: 45min/d, 5d/wk for 4wk	• Wolf Motor Function Test (-) • Grip Strength (-)
Wolf et al. (2015) RCT (7) N$_{Start}$=99 N$_{End}$=92 TPS=Subacute	E: Telerehabilitation through an upper extremity hand robot with home exercise program C: Home exercise program only Duration: 3h/d, 5d/wk for 8-12wk	• Fugl Meyer Assessment (-) • Action Research Arm Test (-) • Wolf Motor Function Test (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Telerehabilitation

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **telerehabilitation** to improve motor function when compared to **conventional therapy, task-oriented therapy and sham interventions**.	2	Emmerson et al. 2017; Wolf et al. 2015

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Telerehabilitation** may not have a difference in efficacy compared to **home exercise programs** for improving muscle strength.	1	Emmerson et al. 2017

Key points

The literature is mixed regarding telerehabilitation for upper limb rehabilitation following stroke.

Robotics

Adopted from: https://www.strokengine.ca/wp-content/uploads/2015/05/robotics_ARMin-300x226;.jpg http://www.gentle.rdg.ac.uk/103-0325_IMG.JPG; https://cpmsales.net/wp-content/uploads/CENTURA.jpg; http://img.medicalexpo.com/images_me/photo-g/74722-10591286.jpg

Robotic devices can be used to help facilitate passive range of motion, to help maintain range and flexibility, to temporarily reduce hypertonia, and to provide resistance during passive movement. Assistance can also be provided during active movements when a patient 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) robotic devices may be the most beneficial in severely impaired patients where unassisted movement is not possible, and especially during the acute phase of recovery during which spontaneous recovery occurs. Krebs et al. (2003) noted that robotic devices rely on the repetition of specific movements to improve functional outcomes.

Upper limb robotic devices can be classified based on the type of robot, the actuation method, the form of transmission, and the sensor used (Yue et al. 2017). The type of robot is based on the alignment of the device and the use and includes end-effectors and exoskeletons (Yue et al. 2017). End-effectors are external to the patient and are connected at a single distal point, whereas exoskeletons are worn by the patient and include mechanical joints that align to the human limb joints (Sicuri et al. 2014; Yue et al. 2017). Actuation of the robot refers to the way in which the energy is produced and includes use of an electric motor, hydraulics, pneumatics, or human muscle (Yue et al. 2017). Transmission refers to the way in which the robot transfers the motion of the actuator to that of the arm, and includes linkages and cables (Yue et al. 2017). Lastly, sensors detect the force and position of the upper limb to provide feedback in response, and these include physical or bioelectrical signals such as through an electroencephalogram or an electromyogram (Yue et al. 2017).

A table of various robotic devices used in stroke rehabilitation is outlined below (Table 17).

Table 17. Robotic Devices Used for Upper Limb Rehabilitation Post-Stroke

Robotic Devices	Description
Arm/Shoulder End-Effectors • MIT-Manus (InMotion) • GENTLE/S (Haptic Master) • MIME (Mirror Image Movement Enhancer) • Neuro-X • Arm Assist • Bi-Manu-Track • Arm Guide • NeReBot • Armeo Boom • Continuous Passive Motion Devices (CYBEX and NORM, Shoulder 600)	MIT-Manus was one of the first robotic devices to be developed and is the most commonly used end-effector (Sicuri et al. 2014). It is a 2-degree-of-freedom robot manipulator that assists in goal-directed shoulder and elbow movements within the horizontal plane, while providing visual, auditory and tactile feedback (Masiero et al. 2007). A commercially available unit (InMotion[2]) of this device is also available.
	GENTLE/S or the Haptic Master is a 3-degree-of-freedom haptic interface arm with a wrist attachment mechanism, two embedded computers, a monitor and speakers and an overhead arm support system (Coote et al. 2008). The affected arm is de-weighted through a free moving elbow splint attached to the overhead frame (Coote et al. 2008). The subject is connected to the device by a wrist splint and feedback is provided during task-oriented training (Coote et al. 2008)..
	MIME is a 6-degree-of-freedom robotic manipulator that is attached at the forearm through a splint. It provides bimanual movements as well as unilateral passive, active-assisted, and resisted movements of the hemiparetic upper extremity (Kahn et al. 2006; Burgar et al. 2011). More force is applied to the more affected forearm during goal-directed movements.
	Neuro-X is a 2-degree-of-freedom upper limb rehabilitation robot that assists in performing shoulder abduction-adduction and elbow flexion-extension movements in a horizontal plane. Feedback is provided through use of a monitor on which tasks are performed (Lee et al, 2016).
	Arm Assist is a low-cost robotic system for rehabilitation of the shoulder and elbow post-stroke. The arm is supported through a device while playing interactive games (Tomic et al. 2017).
	Bi-Manu-Track is a 1 degree-of-freedom device that enables bilateral and passive/active practice of forearm and wrist movement (Van Delden et al. 2012).
	The ARM Guide offers 3 degrees of freedom and uses a motor and chain drive to move the user's hand along a linear rail, which assists reaching in a straight-line trajectory (Kahn et al. 2006).
	The NeReBot is a 3-degrees-of-freedom, cable-driven device that produces sensorimotor stimulation and spatial movements of the shoulder and elbow. It is portable and can be used when the patient is either prone or sitting (Rosati et al. 2007; Masiero et al. 2007).
	Armeo Boom is a 3-degree-of-freedom cable-driven manipulator (Sicuri et al. 2014).
	A continuous passive motion device mobilizes a joint through supporting repetitive and reproducible movements (Hu et al. 2009).
Arm/Shoulder Exoskeletons • ARMin • Pneu-WREX • Armeo Spring	ARMin is 7-degree-of-freedom exoskeleton robot that provides intensive and task-specific training to target improvements in motor function (Klamroth-Marganska et al. 2014).
	Pneu-WREX is 4-degree-of-freedom pneumatically actuated upper extremity orthosis that provides robot assisted movement rehabilitation (Reinkensmeyer et al. 2012).
	Armeo Spring is 5-degree-of-freedom exoskeleton robot with an adjustable suspension system (Gijbels et al. 2011). Auditory and visual feedback are provided through the virtual reality system while various functional tasks are performed (Gijbels et al. 2011).
Hand End-Effectors • Amadeo	The Amadeo assists in hand rehabilitation, having an end-effecter design. It helps with finger movements to allow for synchronization (Sale et al. 2014).
Hand Exoskeletons • Music Glove	The Music Glove is used with a game that promotes specific pinching movements to match musical notes displayed on a screen (Zondervan et al. 2016).
	The Gloreha hand rehabilitation glove provides repetitive and passive mobilization of the fingers with multisensory feedback through a computing device (Vanoglio et al. 2017).

• Gloreha (HAnd REhabilitation GLOve) • RAPAEL Smart Glove • FINGER Robot • Modified Hand Exoskeleton Robot • Hand Mentor	The RAPAEL Smart Glove provides a 9-axis movement and position sensors along with acceleration channels, angular rate channels, magnetic field channels to assess wrist movement, and bending sensors to assess finger movement (Shin et al. 2016). The glove is worn during video games that are specifically designed to encourage specific rehabilitation exercises within the wrist and fingers (Shin et al. 2016).
	The FINGER robotic exoskeleton provides assistance with flexion and extension of the finger while playing a musical computer game (Rowe et al. 2017).
	The modified hand exoskeleton robot enables individual finger control through joint movement sensing (Susanto et al., 2015). The robot is used to assist with gestures such as hand grasping/opening as well as finger pinching/opening (Susanto et al. 2015).
	The Hand Mentor robotic device facilitates and assists in movement of the wrist and fingers. While the arm unit stabilizes the forearm, movement in the wrist and fingers are isolated. Visual and auditory feedback are provided through a computer control box (Linder et al. 2015).

A total of 112 RCTs evaluating robotic interventions for upper extremity motor rehabilitation were found, the characteristics of these interventions are described below.

52 RCTs examined arm and shoulder end-effectors (Amatya et al. 2020; Aprile et al. 2020; Carpinella et al. 2020; Chinembiri et al. 2020; Esquenazi et al. 2020; Takebayashi et al. 2020; Dehem et al. 2019; Hung et al. 2019; Hsu et al. 2019; Kim et al. 2019; Duanoraviciene et al. 2018; Hsieh et al. 2018; Lee et al. 2018; Ellis et al. 2018; Schuster-Amft et al. 2018; Hsieh et al. 2017; Tomic et al. 2017; Fan et al. 2016; Lee et al. 2016; Takahashi et al. 2016; McCabe et al. 2015; Prange et al. 2015; Hesse et al. 2014; Lemmens et al. 2014; Masiero et al. 2014a; Timmermans et al. 2014; Sale et al. 2014; Hsieh et al. 2012; Liao et al. 2012l; Abdullah et al. 2011; Burgar et al. 2011; Conroy et al. 2011; Hsieh et al. 2011; Masiero et al. 2011; Wagner et al. 2011; Lo et al. 2010; Ellis et al. 2009; Hu et al. 2009; Coote et al. 2008; Iwamuro et al. 2008; Rabadi et al. 2008; Volpe et al. 2008; Masiero et al. 2007; Kahn et al. 2006; Lum et al. 2006; Masiero et al. 2006; Fasoli et al. 2004; Volpe et al. 2004; Lum et al. 2002; Burgar et al. 2000; Volpe et al. 2000a; Volpe et al. 1999). One RCT compared arm end-effector with task specific training to the robot alone (Conroy et al. 2019). Five RCTs examined arm end-effectors under various assistive force conditions (Cho et al. 2019; Abdollahi et al. 2018; Wright et al. 2018; Rowe et al. 2017; Stein et al. 2004). Eight RCTs examined arm or shoulder exoskeletons (Horsley et al. 2019; Duanoraviciene et al. 2018; Villafane et al. 2018; Taveggia et al. 2016; Brokaw et al. 2014; Klamroth-Marganska et al. 2014; Reinkensmeyer et al. 2012; De Araujo et al. 2011). One RCT compared a single joint exoskeleton to a multijointed exoskeleton). Six RCTs examined hand end-effectors (Calabro et al. 2019; Hsieh et al. 2018; Neuendorf et al. 2017; Orihuela-Espina et al. 2016; Sale et al. 2014; Hwang et al. 2012). 15 RCTs examined hand exoskeletons (Lee et al. 2020; Page et al. 2020; Park et al. 2018; Jung et al. 2017; Thielbar et al. 2017; Vanoglio et al. 2017; Shin et al. 2016; Zondervan et al. 2016; Linder et al. 2015; Susanto et al. 2015; Wolf et al. 2015; Friedman et al. 2014; Carmeli et al. 2011; Kutner et al. 2010; Talahashi et al. 2008). Six RCTs examined robotic exoskeletons with EEG brain computer interfaces (Cheng et al. 2020; Wang et al. 2018; Ang et al. 2015; Curado et al. 2015; Ang et al. 2014; Ramos-Murguialday et al. 2013). Two RCTs compared robotics in combination with electrical stimulation (Huang et al. 2020; Hayward et al. 2013), and two RCTs examined robotics versus functional electrical sitmulation (Hesse et al. 2005; Hesse et al. 2008). Five RCTs examined robotics in combination with tDCS (Edwards et al. 2019; Mazzoleni et al. 2019; Dehem et al. 2018; Mazzoleni et al. 2017; Triccas et al. 2015). One RCT compared an arm end-

effector to an arm exoskeleton (Lee et al. 2020). Three RCTs examined robotics with constraint induced movement therapy (Hung et al. 2019; Hung et al. 2019b; Hsieh et al. 2014). Six other RCTs examined robotics in combination with various other interventions (Straudi et al. 2020; Capone et al. 2017; Kim et al. 2017; Bustamante Valles et al. 2016; Liu et al. 2009; Carry et al. 2007).

The methodological details and results of all 112 RCTs are presented in Table 18.

Table 18. RCTs Evaluating Robotics for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
	Arm/Shoulder End-Effectors	

Amatya et al. (2020)
RCT (6)
N_{start}= 92
N_{end}=86
TPS= Acute
	E: Enriched environment using robotics (NAO robot, arm end effector)
	C: Conventional therapy
	Duration: Conventional (30min once per week), Experimental (20 min of NAO robot)
		• Action Research Arm Test: (-)
		• Functional Independence Measure: (-)
		  • Motor: (-)
		  • Cognition: (-)

Aprile et al. (2020)
RCT (6)
N_{start}= 247
N_{end}=122
TPS= Acute
	E: Arm end effector
	C: Conventional therapy
	Duration: 45min 5x/wk for 6wks
		• Fugl-Meyer Assesment Upper Extremity: (-)
		• Motricity index: (+exp)
		• Modified Barthel Index: (-)
		• Medical Research Council
		  • Shoulder: (-)
		  • Elbow: (-)
		  • Wrist: (-)
		• Frenchay arm test: (-)
		• Action Research Arm Test: (-)
		• Modified Ashworth Scale: (-)
		  • Shoulder Abduction: (-)
		  • Shoulder Intra-Rotation: (-)
		  • Elbow: (-)
		  • Wrist: (-)

Carpinella et al. (2020)
RCT (8)
N_{start}= 40
N_{end}= 38
TPS= Subacute/Chronic
	E: Robot arm end effector (braccio di ferro)
	C: Conventional therapy
	Duration: 45min, 5d/wk, 4wks
		• Elbow: Flexion (-) & Extension (+exp)
		• Trunk compensation index: (+exp)
		• Fugl-Meyer Assessment Upper Extremity: (-)
		  • Proximal (-)
		  • Distal (-)
		• Reaching performance scale: (-)
		• Proximal Modified Ashworth Scale: (+exp)
		• Distal Modified Ashworth Scale: (-)
		• Functional Independence Measure (-)

Chinembiri et al. (2020)
RCT (5)
N_{start}= 50
N_{end}= 45
TPS= *Not reported*
	E: Robot End Effector (Fourier M2) + Occupational therapy (50min)
	C: Occupational therapy only (50min)
	Duration: Not reported
		• Barthel's Index (+exp):
		  • Bowel: (+exp)
		  • Bladder: (+exp)
		  • Hygiene: (-)
		  • Toileting: (-)
		  • Eating: (+exp)
		  • Transfers: (+exp)
		  • Mobility: (+exp)
		  • Dressing: (+exp)
		  • Stair climb: (-)
		  • Bathing: (+exp)
		• Fugle Meyers Upper Extremity: (+exp)
		  • Upper: (-)

		• Wrist: (+exp) • Elbow: (-) • Fingers: (+exp) • Coordination: (-)
Esquenazi et al. (2020) RCT (6) N_{start}= 45 N_{end}= 40 TPS= Acute	E: Robot assisted therapy (Armeo) C: Conventional table top exercise Duration: 1hr, 4x/wk until discharge (~3wks)	• Functional Independence Measure: (-) • Fugl-Meyer Assessment Upper Extremity: (-) • Modified Ashworth Scale • Elbow flexion: (-) • Elbow extension: (-) • Active Range of Motion: • Elbow flexion: (+exp) • Elbow extension: (-) • Passive Range of Motion • Elbow flexion: (+exp) • Elbow extension: (-)
Takebayashi et al. (2020) RCT (7) N_{start}=60 N_{end}=56 TPS=Subacute	E: Robot arm end effectors (ReoGO) C: Conventional therapy Duration: 40min/d 6wks	• Fugl Meyer Assessment Total Upper Extremity Motor Score: • Mild: (-) • Moderate: (-) • Severe: (-) • Fugl Meyer Assessment Proximal Upper Extremity Motor Score: • Mild: (-) • Moderate: (-) • Severe: (-) • Fugl Meyer Assessment Upper Extremity Flexor Synergy Motor Score: • Mild: (-) • Moderate: (-) • Severe: (-)
Dehem et al. (2019) RCT (7) N_{start}= 45 N_{end}= 28 TPS= Acute	E: REAplan end-effector robot assisted therapy C: Conventional therapy Duration: 45min, 4x/wk, 9wks (stats only for 6mo follow up)	• Fugl Meyers Assessment Upper Extremity: (-) • Box and Block Test: (+exp) • Wolf Motor Function Test-Functional Ability Scale: (+exp) • Stroke Impact Scale (social participation): (+exp)
Hung et al. (2019) RCT (7) N_{start}= 30 N_{end}= 30 TPS= Chronic	E1: Robot assisted therapy (inMotion) E2: Bimanual tracking C: Conventional therapy Duration: 70-75min, 5d/wk, 4wks	E1 Vs C • Fugle-Meyers Assessment Upper Extremity: (+exp1) • Proximal: (+exp1) • Distal: (-) • Modified Ashworth Scale: (+exp1) • Proximal: (+exp1) • Distal: (-) • Medical Research Council Scale: (-) • Motor Activity Log: (-) E2 Vs C • Fugle-Meyers Assessment Upper Extremity: (-) • Proximal: (-) • Distal: (-) • Modified Ashworth Scale: (-) • Proximal: (-) • Distal: (-) • Medical Research Council Scale: (-) • Motor Activity Log): (-) E1 Vs E2 • Fugle-Meyers Assessment Upper Extremity: (-) • Proximal: (-)

		• Distal: (-) • Modified Ashworth Scale: (+exp1) • Proximal: (+exp1) • Distal: (-) • Medical Research Council Scale: (-) • Motor Activity Log: (-)
Hsu et al. (2019) RCT (8) N_{start}= 43 N_{end}= 43 TPS= Chronic	E: Robot assisted therapy (bimanual tracking) C: Conventional therapy Duration: 40min, 3x/wk for 4wks	• Motor Activity Log • Quality of Movement: (-) • Amount of Use: (-) • Fugl-Meyers Assessment: (-) • Shoulder/Elbow: (-) • Wrist: (+exp) • Hand: (+con) • Coordination: (-)
Kim et al. (2019) RCT (6) N_{start}= 38 N_{end}= 36 TPS= Subacute Ch11	E: Robotic-assisted shoulder rehabilitation therapy C: Conventional therapy Duration: 30min, 10x plus 5x of additional robotic-assisted shoulder rehabilitation therapy for 4wks	• Passive Range of Motion • Flexion: (-) • Abduction: (+exp) • External rotation: (-) • Internal rotation: (-)
Daunoraviciene et al. (2018) RCT (6) N_{start}= 34 N_{end}= 34 TPS= Subacute	E: Robot assisted therapy (Armeo Spring) C: Conventional therapy Duration: 30min, 5d/wk, 2wks	• Fugl-Meyer Assessment Upper Extremity: (-) • Shoulder Passive Range of Motion: (+exp) • Elbow Passive Range of Motion: (+exp) • Wrist Passive Range of Motion: (-) • Modified Function Independence Measure: (-)
Hsieh et al. (2018) RCT (7) N_{start}= 44 N_{end}= 40 TPS= Chronic	E1: Proximal robot (inMotion arm) E2: Distal robot (inMotion wrist) C: Conventional therapy Duration: 45min, 5d/wk, 4wks	E1 Vs C • Fugl-Meyers Assessment (-) • Medical Research Council (-) • Motor Activity Log (-) • Wrist Accelerometer: (-) E2 Vs C • Fugl-Meyers Assessment (-) • Medical Research Council (-) • Motor Activity Log (-) • Wrist Accelerometer: (-) E1 Vs E2 • Fugl-Meyers Assessment (-) • Medical Research Council (+exp2) • Motor Activity Log: (+exp2) • Wrist Accelerometer: (-)
Lee et al. (2018) RCT (6) N_{start}= 30 N_{end}= 30 TPS= Chronic	E: Robot assisted therapy (REJOYCE) C: Conventional occupational therapy Duration:30min 5x/wk for 8wks	• Fugle-Meyers Assessment: (+exp) • Modified Barthel Index: (+exp)
Ellis et al. 2018 RCT (8) N_{Start}=32 N_{End}=32 TPS=Chronic	E: Progressive Abduction Loading Therapy and Horizontal-Plane Viscous Resistance using Robotic Device (Haptic Master) C: Progressive Abduction Loading Therapy Duration: 30min/d, 3d/wk for 8wk	• Maximum Reaching Distance (+exp) • Elbow Extension and Rotation (+exp) • Shoulder Extension, Abduction (+exp) • Fugl-Meyer Assessment (-) • Motor Activity Log (-) • Quality of Movement (-) • Rancho Los Amigos Functional Test for the Hemiparetic Upper Extremity (-)
Schuster-Amft et al. (2018) RCT (8) N_{start}= 54 N_{end}= 52	E: VR robot - Bi-Manu trainer C: Conventional therapy Duration: 45min, 4x/wk, 4wks	• Box and Block Test: (-) • Cheodke Mcmaster Arm Hand Inventory: (-) • Stroke Impact Scale • Strength: (-)

TPS= Chronic		• Activites of Daily Living: (-) • Mobility: (-) • Hand Function: (-) • Stroke Recovery: (-)
Hsieh et al. (2017) RCT (6) N_{Start} =31 N_{End} =21 TPS=Subacute	E: Bilateral priming robot-aided (Bi-Manu-Track) therapy with task-oriented therapy C: Task-oriented therapy Duration: 90min/d, 5d/wk for 4wk	• Stroke Impact Scale (-) • Fugl-Meyer Assessment (-) • Box and Block Test (-) • Grip Strength (-) • Modified Rankin Scale (-) • Functional Independence Measure (-)
Tomic et al. (2017) RCT (7) N_{Start} =26 N_{End} =26 TPS=Subacute	E: ArmAssist Robot C: Conventional Therapy Duration: 30min/d, 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp) • Barthel Index (-)
Fan et al. (2016) RCT (4) N_{Start}=6 N_{End}=6 TPS=Chronic	E: Robot-assisted bilateral arm therapy (Bi-Manu-Track) C: Dose-matched control therapy Duration: 45min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (-) • Wolf Motor Function Test (-)
Lee et al. (2016) RCT (4) N_{Start}=58 N_{End}=44 TPS=Acute	E: Robotic-assisted therapy (Neuro-X) C: Conventional rehabilitation Duration: 1hr/d, 5d/wk for 2wk	• Manual Muscle Test (-) • Manual Function Test (-) • Modified Barthel Index (-)
Takahashi et al. (2016) RCT (5) N_{start}=60 N_{end}=56 TPS=Subacute	E: Robot arm end effectors (ReoGO) C: Conventional therapy Duration: 40min/d 6wks	• Fugl Meyer Assessment Upper Extremity (-) • Wolf Motor Function Test Total: (-) • Motor Activity Log-Amount of use: (-) • Motor Activity Log-Quality of use: (-)
McCabe et al. (2015) RCT (6) N_{Start}=39 N_{End}=35 TPS=Chronic	E1: Robotic training (InMotion ARM) + motor learning E2: Motor learning + functional electrical stimulation C: Motor learning Duration: 5hr/d, 5d/wk for 12wk	• Arm Motor Ability Test (-) • Fugl-Meyer Assessment (-)
Prange et al. (2015) RCT (7) N_{Start}=70 N_{End}=68 TPS=Acute	E: Arm training with robot (ArmeoBoom) C : Conventional training Duration : 30min/d, 4d/wk for 6wk	• Stroke Upper Limb Capacity Scale (-) • Reaching Distance (-) • Fugl-Meyer Assessment (-)
Hesse et al. (2014) RCT (8) N_{Start}=50 N_{End}=46 TPS=Acute	E: Group robot therapy (Bi-Manu-Track) + individual arm therapy C: Individual arm therapy Duration: 30min/d, 5d/wk for 6wk	• Box and Block Test (-) • Action Research Arm Test (-)
Lemmens et al. (2014) RCT (7) N_{Start}=16 N_{End}=16 TPS=Chronic	E: Robotic therapy (Haptic Master) C: No robotic therapy Duration: 30min (2x/d), 4d/wk for 8wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Motor Activity Log (-)
Masiero et al. (2014a) RCT (7) N_{Start}=34 N_{End}=30 TPS=Chronic	E: Robotic therapy (NeReBot) C: Standard therapy Duration: 2hr/d, 5d/wk for 5wk	• Fugl-Meyer Assessment (-) • Box and Block test (-) • Frenchay Arm Test (-) • Medical Research Council Scale (-) • Functional Independence Measure (-)
Timmermans et al. (2014) RCT (8) N_{Start}=22	E: Robotic arm training (Haptic Master) C: Task oriented arm training	• Fugl-Meyer Assessment (-) • Action Research Arm test (-) • Motor Activity Log (-)

N_{End}=22 TPS=Chronic	Duration: 30min (2x/d), 4d/wk for 8wk	
Sale et al. (2014) RCT (6) N_{Start}=53 N_{End}=53 TPS=Acute	E: Robot aided therapy (MIT-Manus) + reaching tasks C: Reaching tasks Duration: 1hr/d, 2d/wk for 10wk	• Fugl-Meyer Assessment (+exp) • Motricity Index (+exp)
Hsieh et al. (2012) RCT (7) N_{start}=54 N_{end}=53 TPS=Chronic	E1: High intensity robotic therapy (Bi-Manu-Track) E2: Low intensity robotic therapy C: Conventional therapy Duration: 90min/d, 5d/wk for 3wk	E1 vs E2 • Fugl-Meyer Assessment: (+exp) E1 vs C • Fugl-Meyer Assessment: (+exp) E1 vs E2 & E1 vs C • Medical Research Council Scale (-) • Motor Activity Log (-) • Stroke Impact Scale (-)
Liao et al. (2012) RCT (7) N_{start}=20 N_{end}=20 TPS=Chronic	E: Robotic therapy (Bi-Manu-Track) C: Dose-matched conventional therapy Duration: 100min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp) ABILHAND (+exp)
Abdullah et al. (2011) RCT (5) N_{start}=20 N_{end}=20 TPS=Acute	E: Robot assisted therapy C: Dose-matched conventional therapy Duration: *Not Specified*	• Chedoke Arm and Hand Activity Inventory (-)
Burgar et al. (2011) RCT (5) N=54 TPS=Acute	E1: High intensity robotic therapy (MIME) E2: Low intensity robotic therapy C: Conventional therapy Duration: 1hr/d, 3d/wk for 8wk	E1 vs C • Functional Independence Measure (+exp) • Modified Ashworth Scale (-) • Fugl-Meyer Assessment (-)
Conroy et al. (2011) RCT (6) N_{start}=62 N_{end}=54 TPS=Chronic	E1: Robot-assisted (InMotion ARM) planar reaching E2: Robot-assisted planar and vertical reaching C: Intensive conventional arm therapy Duration: 1hr/d, 3d/wk for 6wk	• Fugl-Meyer Assessment (-)
Hsieh et al. (2011) RCT (8) N_{start}=18 N_{end}=18 TPS=Chronic	E1: High intensity robot-assisted therapy (Bi-Manu-Track) E2: Low intensity robot-assisted therapy C: Conventional therapy Duration: 45min/d, 3d/wk for 6wk	E1 vs E2 • Fugl-Meyer Assessment: (+exp) E2 vs. C • Fugl-Meyer Assessment (-) E1 vs C • Motor Activity Log (+exp) E1 vs E2/C • Motor Activity Log (-) • ABILHAND (-) • Medical Research Council Scale (-)
Masiero et al. (2011) RCT (5) N_{start}=21 N_{end}=21 TPS=Acute	E: Robotic arm therapy (NeReBot) C: Conventional therapy Duration: *Not Specified*	• Medical Research Council Scale (+exp) • Fugl-Meyer Assessment (-) • Functional Independence Measure (-) • Modified Ashworth Scale (-) • Frenchay Arm Test (-) Box and Block Test (-)
Wagner et al. (2011) RCT (5) N_{start}=127 N_{end}=127 TPS=Chronic	E: Intensive robot assisted therapy C1: Intensive comparison therapy C2: Conventional therapy Duration: 1hr, 3x/wk, 12wks	• Stroke Impact Scale: (+exp)
Lo et al. (2010) RCT (7) N_{start}=127	E1: Intensive robot assisted therapy (MIT-Manus) E2: Intensive comparison therapy	E1 vs C • Fugl-Meyer Assessment (-) • Wolf Motor Function Test (-)

N_{end}=127 TPS=Chronic	C: Usual care Duration: 1hr/d, 3d/wk for 12wk	• Stroke Impact Scale (+exp) • Modified Ashworth Scale (-) E1 vs E2 • Fugl-Meyer Assessment (-) • Wolf Motor Function Test (-) • Stroke Impact Scale (-) • Modified Ashworth Scale (-)
Ellis et al. (2009) RCT (4) N_{start}= 14 N_{end}= Not reported TPS= Not reported	E: Haptic master robot (progressive abduction shoulder loading) C: Robot sham Duration: 3x/wk, 8wks	• Work Area: (+exp) • Shoulder Strength: (-) • Elbow Strength: (-)
Hu et al. (2009) RCT (5) N_{start}=27 N_{end}=27 TPS=Chronic	E: EMG-driven robot (CYBEX and NORM Continuous Passive Motion) C: Passive motion device Duration: 20min/d, 5d/wk for 7wk	• Fugl-Meyer Assessment (+exp) • Modified Ashworth Scale (+exp)
Coote et al. (2008) RCT (6) N_{start}=23 N_{end}=20 TPS=Chronic	E: Robot-mediated therapy (GENTLE/s) C: Sling suspension phase Duration: 30min/d, 3d/wk for 9wk	• Fugl-Meyer Assessment (+exp)
Iwamuro et al. (2008) RCT Cross over (6) N_{start}= 10 N_{end}= 10 TPS= NR	E: Robot arm end effector C: No robot Duration: 1 session	• Speed: (+con) • Accuracy: (+exp)
Rabadi et al. (2008) RCT (5) N_{start}=30 N_{end}=30 TPS=Acute	E1: Robot (MIT-Manus)-unilateral group E2: Ergometer (bilateral) group C: Conventional therapy Duration: 3hr/d, 3d/wk for 4wk	E1 vs E2/C • Fugl-Meyer Assessment (-)
Volpe et al. (2008) RCT (5) N_{start}=21 N_{end}=21 TPS=Chronic	E: Sensorimotor arm training delivered by robotic device (MIT-Manus) C: Sensorimotor arm training delivered by a therapist Duration: 1hr/d, 3d/wk for 6wk	• Fugl-Meyer Assessment (-) • Motor Power Scale (-)
Masiero et al. (2007) RCT (5) N_{start}=20 N_{end}=20 TPS=Acute	E: Robotic Training (NeReBot) C: Exposure to robotic device Duration: 1hr/d, 4d/wk for 5wk	• Fugl-Meyer Assessment (+exp) • Medical Research Council (+exp) • Functional Independence Measure (+exp) • Modified Ashworth Scale (-)
Kahn et al. (2006) RCT (4) N_{start}=19 N_{end}=19 TPS=Chronic	E: Active-assistive reaching exercise using a robotic device (Arm Guide) C: Task-matched amount of reaching without assistance Duration: 40min/d, 6d/wk for 4wk	• Rango Los Amigos Functional Test (-)
Lum et al. (2006) RCT (4) N_{start}=30 N_{end}=23 TPS=Subacute	E1: Robot-unilateral (MIME) E2: Robot-bilateral E3: Robot-combined C: Conventional therapy Duration: 30min/d, 3d/wk for 4wk	E3 vs C • Fugl-Meyer Assessment (+exp_3) • Motor Status Score (+exp_3) • Functional Independence Measure (-) • Motor power examination (-) • Modified Ashworth Scale (-) E3 vs E1 • Fugl-Meyer Assessment (-) • Motor Status Score (-) • Functional Independence Measure (-) • Motor power examination (-) • Modified Ashworth Scale (-)

Masiero et al. (2006) RCT (5) N_{start}=35 N_{end}=35 TPS=Acute	E: Additional sensorimotor robotic training (NeReBot) C: Exposure to robotic device with no training Duration: 1hr/d, 4d/wk for 8wk	• Fugl-Meyer Assessment (+exp) • Motricity Index (+exp) • Functional Independence Measure (+exp) Medical Research Council Scale (-)
Fasoli et al. (2004) RCT (6) N_{start}=56 N_{end}=56 TPS=Acute	E: Robot assisted (MIT-Manus) movement training C: Robot exposure Duration: 90min/d, 2d/wk for 12wk	• Fugl-Meyer Assessment (+exp) • Motor status score (-) • Medical Research Council score (-)
Volpe et al. (2004) RCT (4) N_{start}=32 N_{end}=32 TPS=Acute	E: Continuous Passive Motion Device (Shoulder 600) C: Control Duration : 30min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (-) • Motor Status score (-) • Modified Ashworth Scale (-)
Lum et al. (2002) RCT (6) N_{start}=30 N_{end}=27 TPS=Chronic	E: Robot (MIME)-assisted movement training C: Conventional therapy Duration: 1hr/d, 5d/wk for 6wk	• Fugl-Meyer Assessment (+exp) • Strength upper extremity (+exp) • Reach upper extremity (+exp) • Functional Independence Measure (-)
Burgar et al. (2000) RCT (5) N_{start}=21 N_{end}=21 TPS=Chronic	E: Robotic (MIME) device therapy C: Conventional care (physical therapy) Duration: 2hr/d, 3d/wk for 10wk	• Fugl-Meyer Assessment (-) • Functional Independence Measure (-) • Barthel Index (-)
Volpe et al. (2000a) RCT (6) N_{start}=56 N_{end}=56 TPS=Acute	E: Robotic training (MIT-Manus) C: Exposure to the robotic device without training Duration: 30min/d, 3d/wk for 4wk	• Motor Power score: shoulder and elbow (+exp), wrist and hand (-) • Motor Status score: shoulder and elbow (+exp), wrist and hand (-) • Functional Independence Measurer (+exp) • Fugl-Meyer Assessment: (-)
Volpe et al. (1999) RCT (6) N_{start}=20 N_{end}=12 TPS=Acute	E: Robot (MIT-Manus) C: Sham treatment Duration: 45min/d, 5d/wk for 6wk	• Motor Status score (+exp) • Motor Status score (-) • Motor Power score (+exp) • Fugl-Meyer Assessment (-)
Arm End Effectors Combined with Task Specific Training		

Conroy et al. (2019)
RCT (6)
N_{start}= 45
N_{end}= 41
TPS= Chronic
Multi-Site
	E: Robot + task training (Inmotion)
	C: Robot only
	Duration:1hr, 3x/wk, 12wks
		• Fugl Meyers Assessment Upper Extremity: (-)
		  • Shoulder/Elbow: (-)
		  • Wrist/Hand: (-)
		• Log Wolf Motor Function Test: (+exp)
		• Stroke Impact Scale hand item: (+exp)

Arm/Shoulder End Effectors combined with Forcefield/Feedback		
Cho et al. (2019) RCT (8) N_{start}= 42 N_{end}= 38 TPS= Chronic	E: Robot therapy with assistance as needed C: Robot therapy with guidance forces all times (EE) Duration: 40min, 3x/wk for 6wks	• Fugle Meyers Assessment Upper Extremity: (+exp) • Box and Block Test: (-) • Action Research Arm Test: (+exp) • Movement Velocity: (-)
Abdollahi et al. (2018) RCT (6) N_{start}= 28 N_{end}=26 TPS= Chronic	E: Arm end effector + error augmentation C: Arm end effector Duration: 45min, 3x/wk for 2wks	• Wolf Motor Function Test: (-) • Motor Activity Log (-) • Box and Block Test: (-) • Fugl-Meyer Assessment Upper Extremity: (-)

Wright et al. (2018)
RCT (8)
N_{start}=23
N_{end}=22
	E: Robot training with force field
	C: Robot training without force field
	Duration: ~45min, 5 sessions over 5 wks
		• Fugl Meyer Upper Extremity: (-)
		• Action Research Arm Test:
		  • Time: (-)
		  • Score: (-)

TPS=Chronic		• Chedoke McMaster Stroke Assessment-Arm: (-)
		• Elbow Range of Motion:
		  • Flexion: (-)
		  • Extension: (-)
		• Modified Ashworth Scale:
		  • Biceps: (-)
		  • Triceps: (+exp)

Rowe et al. (2017) RCT (7) N_{Start} =30 N_{End} =30 TPS=Chronic	E: High Robotic Assistance Finger Training (FINGER robot) C: Low Robotic Assistance Finger Training Duration: 90min/d, 5d/wk for 8wk	• Fugl-Meyer Assessment (+exp) • Box and Block Test (-) • Action Research Arm Test (-) • Nine-Hole Peg Test (-) • Finger Tapping (-) • Motor Activity Log (-) • National Institutes of Health Stroke Scale (-)

Stein et al. (2004)
RCT (6)
N_{start}= 18
N_{end}= 18
TPS= Chronic
	E: Resistance robot training end eff
	C: Active asissted robot training
	Duration: 1hr, 3x/wk, 6wks
		• Modified Ashworth Scale: (-)
		• Fugl Meyers Upper Extremity: (-)
		• Motor Status Score
		  • Shoulder/Elbow: (-)
		  • Wrist/Hand (-)
		• Manual Muscle Testing (-)
		• Peak Force (N) (-)

Arm/Shoulder Exoskeletons		

Horsley et al. (2019)
RCT (8)
N_{start}= 50
N_{end}= 45
TPS= Acute
Chap11
	E: Repetitive task practice with SMART arm device
	C: Conventional therapy
	Duration: 60min, 5d/wk, 5wks + same amount of time for smart arm (not equal)
		• Passive Range of Motion
		  • Wrist Extension: (-)
		  • Elbow Extension: (+con)
		  • Shoulder Flexion: (-)
		  • Shoulder External rotation: (-)
		• Motor Assessment Scale: (-)

Daunoraviciene et al. (2018) Lithuania RCT (5) N_{Start} =34 N_{End} =34 TPS= Subacute	E: Robot-assisted Training (Armeo Spring) C: Conventional Therapy Duration: 1hr/d, 4d/wk for 5wk	• Functional Independence Measure (-) • Fugl-Meyer Assessment (-) • Shoulder Flexion, Abduction, Adduction, and Internal Rotation (+exp) • Elbow Flexion, Supination, and Pronation (+exp) • Wrist Range of Motion (-)
Villafane et al. (2018) RCT (7) N_{start}=32 N_{end}=32 TPS=NR	E: Robot passive mobilization (exo) C: Conventional therapy Duration: 30min 5x/wk, 3wks	• National Institutes of Health Stroke Scale: (-) • Modified Ashworth Scale: (-) • Barthel Index: (-) • Motricity Index: (-) • Quick DASH: (-)
Taveggia et al. (2016) RCT (7) N_{start}=54 N_{end}=54 TPS=Mixed	E: Robot arm exoskeletons C: Conventional rehabilitation Duration: dose matched, 30min, 5d/wk for 6wks (+30min PT)	• Functional Independence Measure: (-) • Motricity Index: (-) • Modified Ashworth Scale: (-)
Brokaw et al. (2014) RCT (3) N_{Start}=12 N_{End}=10 TPS=Chronic	E: Robotic therapy (ARMin) C: Conventional therapy Duration: 90min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (+exp) • Box and Bock Test (-)
Klamroth-Marganska et al. (2014) RCT (8) N_{Start}=77 N_{End}=73 TPS= Chronic	E: Robotic therapy (ARMin) C: Conventional treatment Duration: 1hr/d, 3d/wk for 8wk	• Fugl-Meyer Assessment (+exp) • Strength (+exp) • Motor Activity Log (-) • Modified Ashworth Scale (-) • Wolf Motor Function test (-)
Reinkensmeyer et al. (2012) RCT (7)	E: Robotic training (Pneu-WREX) C: Conventional tabletop therapy	• Fugl-Meyer Assessment (-) • Nottingham sensory test (-)

N_{start}=26 N_{end}=26 TPS=Chronic	Duration: 1hr/d, 3d/wk for 8wk	• Grip strength (-) • Box and Block Test (-)

de Araújo et al. (2011)
RCT (5)
N_{start}= 12
N_{end}= 12
TPS= Chronic
	E: Electromechanical orthosis (Exo-Robot)
	C: Conventional Therapy
	Duration: 3x/wk, 8wks, 50min
		• Fugl Meyers Assessment Upper Extremity: (-)
		  • Shoulder/Elbow: (-)
		  • Wrist/Hand: (-)
		  • Velocity/Coordination: (-)
		• Modified Ashworth Scale:
		  • Elbow: (-)
		  • Wrist/Hand: (-)

Single Vs Multijoint Arm Exoskeleton		

Milot et al. (2013)
RCT (7)
N_{start}= 20
N_{end}= 20
TPS= Chronic
	E: Single joint arm exoskeleton
	C: Multijointed arm exoskeleton
	Duration: 60min, 3x/wk for 4wks
		• Box and Block Test: (-)
		• Fugl-Meyers Assessment Upper Extremity: (-)
		• Wolf Motor Function Test: (-)
		  • Time: (-)
		  • Score: (-)
		• Motor Activity Log:
		  • Amount of Use (-)
		  • Quality of Life: (-)
		• Grip Strength: (-)
		• Pinch Strength: (+exp)

Hand End-Effectors		
Calabrò et al. (2019) RCT (7) N_{start}= 50 N_{end}= 50 TPS= Chronic	E: Hand end effector (Amadeo) C: Conventional therapy Duration: Robot (45min/5x/8wk); conv (2h/5x/8wk)	• Nine Hole Peg Test: (+exp) • Fugl-Meyers Assessment Upper Extremity: (+exp)

Hsieh et al. (2018)
RCT (7)
N_{start}= 44
N_{end}= 40
TPS= Chronic
	E1: Proximal robot (inMotion arm)
	E2: Distal robot (inMotion wrist)
	C: Conventional therapy
	Duration: 45min, 5d/wk, 4wks
		E1 Vs C
		• Fugl-Meyers Assessment (-)
		  • Proximal (-)
		  • Distal (-)
		• Medical Research Council (-)
		• Motor Activity Log (-)
		• Wrist Accelerometer: (-)
		E2 Vs C
		• Fugl-Meyers Assessment (-)
		  • Proximal (-)
		  • Distal (+exp)
		• Medical Research Council (-)
		• Motor Activity Log (-)
		• Wrist Accelerometer: (-)
		E1 Vs E2
		• Fugl-Meyers Assessment (-)
		  • Proximal (-)
		  • Distal (-)
		• Medical Research Council (+exp2)
		• Motor Activity Log: (+exp2)
		• Wrist Accelerometer: (-)

Neuendorf et al. (2017) RCT (4) N_{start}= 25 N_{end}= 20 TPS= Chronic	E: Robotic ball C: Conventional therapy Duration: 45min, 2x/wk 12wks each condition	• Grip Strength: (+exp) • Round Block Test: (+exp) • Quick Disabilities of Arm Shoulder Hand (Quick DASH): (-)
Orihuela-Espina et al. (2016) RCT Cross overs (6) N_{start}= 17 N_{end}= 17 TPS= Subacute	E: Robot assisted therapy (Amadeo Robot) C: Conventional therapy Duration: 40x ,1hr, 5x/wk for 8-10wks	• Fugl-Meyers Assessment Upper Extremity: (+exp) • Motricity Index: (-)

Sale et al. (2014) RCT (7) N_{Start}=20 N_{End}=20 TPS=Acute	E: Amadeo robotic therapy + physiotherapy C: Occupational therapy Duration : 1hr/d, 3d/wk for 4wk	• Box and Block Test (+exp) • Fugl-Meyer Assessment (+exp)
Hwang et al. (2012) RCT (6) N_{start}=17 N_{end}=17 TPS=Chronic	E: Active Amadeo robot training C: Early passive therapy Duration : 45min/d, 5d/wk for 2wk	• Jebsen-Taylor Hand Function (-) • Fugl-Meyer Assessment (-) • Ashworth Scale (-) • Nine Hole Peg Test (-) • Stroke Impact Scale (-)
Hand Exoskeletons		
Lee et al. (2020) RCT (8) N_{start}= 36 N_{end}= 36 TPS= Chronic Multi-site	E: VR glove (RAPAEL) C: Conventional therapy Duration: 30min, 3x/wk, 8wks	• Box and Block Test: (+exp) • Grip Strength: (+exp) • Jebsen-Taylor Hand Function Test: (-) • Wolf Motor Function Test: (+exp)
Page et al. (2020) RCT (7) N_{start}= 35 N_{end}= 31 TPS= Chronic	E1: Myomo electromyography (EMG) powered orthosis with repetitive task practice (RTP) E2: Myomo EMG powered orthosis C: RTP Duration: 1hr, 3x/wk, 8wk	• Fugl-Meyers Assessment Upper Extremity: (-) • Action Research Arm Test: (-)

Park et al. (2018)
RCT (7)
N_{start}=26
N_{end}=25
TPS=Chronic
	E: Robot Rapael smart board VR
	C: Conventional therapy
	Duration: 30min, 5d/wk, 4wks
		• Fugl Meyer Assessment Upper Extremity (-)
		  • Proximal: (-)
		  • Distal: (-)
		  • Coordination: (-)
		• Wolf Motor Function Test (-)
		• Active Range of Motion-shoulder: (-)
		• Modified Barthel Index: (-)
		• SIS total: (+exp)
		  • Strength: (-)
		  • Hand function: (-)
		  • Mobility: (-)
		  • Activities of daily living: (+exp)
		  • Memory and thinking: (-)
		  • Communication: (-)
		  • Emotion: (-)
		  • Social participation: (-)
		  • Recovery: (-)

Jung et al. (2017) RCT (6) N_{start}= 14 N_{end}= 13 TPS= Chronic	E: VR glove (RAPAEL) C: Conventional therapy Duration: 30min, 5x/wk, 3wks	• Wolf Motor Function Test: (+exp) • Active Range of Motion: (-)
Thielbar et al. (2017) RCT (6) N_{Start} =23 N_{End} =22 TPS=Chronic	E: EMG-driven actuated glove + conventional occupational therapy C: Occupational therapy Duration: 1 hr/d, 3d/wk for 6wk	• Hand Aperture (+exp) • Action Research Arm Test (-) • Wolf Motor Function Test (-) • Fugl-Meyer Assessment (-) • Chedoke McMaster Stroke Assessment (-) • Grip/Pinch Strength (-)
Vanoglio et al. (2017) RCT (7) N_{Start} =30 N_{End} =27 TPS=Acute	E: Robotic Glove with Multisensory Feedback (Gloreha hand rehab glove) C: Conventional Therapy Duration: 30min/d, 3d/wk for 5wk	• Motricity Index (+exp) • Nine Hole Peg Test (+exp) • Grip Strength (+exp) • Pinch Test (+exp) • Quick Version of Disabilities of the Arm, Shoulder, and Hand Questionnaire (+exp)
Shin et al. (2016) RCT (8) N_{Start}=46	E: RAPAEL SmartGlove virtual reality task training C: Conventional therapy	• Fugl-Meyer Assessment (+exp) • Jebsen Taylor Hand Function Test (+exp) • Stroke Impact Scale (+exp)

N_{End}=46 TPS=Chronic	Duration: 40min/d, 5d/wk for 4wk	• Purdue Pegboard Test (-)
Zondervan et al. (2016) RCT (6) N_{Start}=18 N_{End}=17 TPS=Chronic	E: Home-based training with a MusicGlove C: Conventional tabletop exercise Duration: 25min/d, 6d/wk for 4wk	• Motor Activity Log (+exp) • Box and Block Test (-) • 9-Hole Peg Test (-) • Action Research Arm Test (-)
Linder et al. (2015) RCT (5) N_{Start}=99 N_{End}=99 TPS=Acute	E: Robot-assisted therapy program + home exercise program (Hand Mentor) C: Home exercise program Duration: 30min/d, 2d/wk for 5wk	• Stroke Impact Scale (+exp)
Susanto et al. (2015) RCT (7) N_{Start}=19 N_{End}=19 TPS=Chronic	E: Robotic paretic hand therapy (exoskeleton device) C: Task therapy without robotic aid Duration: 1hr/d, 5d/wk for 4wk	• Wolf Motor Function Test (+exp)
Wolf et al. (2015) RCT (6) N_{Start}=99 N_{End}=92 TPS=Acute	E: Telemonitored robotic assisted home exercise therapy program (Hand Mentor) C: Dose-matched usual care home program Duration; 3hr/d, 5d/wk for 8wk	• Wolf Motor Function Test (+exp) • Fugl-Meyer Assessment (-) • Action Research Arm Test (-)
Friedman et al. (2014) RCT (6) N_{Start}=12 N_{End}=12 TPS=Chronic	E1: IsoTrainer E2: Music glove training C: Control Duration: 1hr/d, 3d/wk for 2wk	• Wolf Motor Function Test (-) • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) E2 vs C • Box and Block Test: (+exp_2) • Nine Hole Peg Test:(+exp_2) E1 vs E2 • Box and Block Test: (-) • Nine Hole Peg Test:(-) E1 vs C • Box and Block Test: (-) • Nine Hole Peg Test:(-)
Carmeli et al. (2011) RCT (6) N_{start}= 34 N_{end}= 31 TPS= Acute	E: Hand exoskeleton robot (hand tutor) C: Convential therapy Duration: 20-30min, 5x/wk, 3wks	• Fugl Meyers Assessment Upper Extremity: (+exp) • Box and block test: (+exp) • Movement speed: (+exp) • Trajectory accuracy: (+exp)
Kutner et al. (2010) RCT (7) N_{start}=30 N_{end}=26 TPS=Subacute/Chronic	E: Robot therapy (Hand Mentor) C: Conventional therapy Duration: 1hr/d, 5d/wk for 6wk	• Stroke Impact Scale (+exp)

Takahashi et al. (2008)
RCT (5)
N_{start}=13
N_{end}=12
TPS=Chronic
	E: Robot hand exoskeletons (active)
	C: Sham
	Duration: 7.5d, 3x/wk, 1.5hrs
		• Action Research Arm Test: (+exp)
		• Block and Block Test: (-)
		• Fugl Meyer Assessment Upper Extremity: (+exp)
		• Modified Ashworth Scale:
		  • Wrist: (+exp)
		  • Elbow: (-)
		• Active Range of Motion- Wrist: (-)
		• National Institutes of Health Stroke Scale- (-)
		• Stroke Impact Scale: (+exp)
		• Grasp force: (-)
		• Pinch force: (+exp)

EEG guided brain computer interface with Hand Exoskeleton		
Cheng et al. (2020) RCT (6) N_{start}= 11	E: EEG Motor Imagery Brain Computer Interface assisted Exo-glove	• Fugl Meyers Upper Extremity: (-) • Action Research Arm Test: (-)

N_{end}= 10 TPS= Chronic	C: Robot exo-glove only Duration: 30min standard, 90min, 3x/wk, 6wks	
Wang et al. (2018) RCT (6) N_{start}=24 N_{end}=24 TPS=Chronic	E: Action observation with EEG guided robot (hand exo) C: Robot (hand exo) Duration: 20x, 3-5x/wk, 5-7wks	• Fugl Meyer Assessment Upper Extremity: (-)
Ang et al. (2015) RCT (7) N_{Start}=26 N_{End}=25 TPS=Chronic	E: Brain computer interface + MIT-Manus robotic training C: MIT-Manus robotic training Duration: 90min/d, 3d/wk for 4wk	• Fugl Meyer Assessment Upper Extremity: (-)
Curado et al. (2015) RCT (4) N_{start}= 32 N_{end}= Not reported TPS= Chronic	E: Brain Machine Interface + robotic orthosis C: Sham + robot Duration: 1hr, 5x/wk for 4wks	• EMG facilitation (-)
Ang et al. (2014) RCT (8) N_{Start}=22 N_{End}=21 TPS=Chronic	E1: Brain-computer interface + haptic knob (HK) robot E2: HK robot C: Standard Arm Therapy (SAT) Duration: 90min/d, 3d/wk for 6wks	E1 vs C • Fugl-Meyer Assessment (-) E2 vs C • Fugl-Meyer Assessment (-) E1 vs E2 • Fugl-Meyer Assessment (-)
Ramos-Murguialday et al. (2013) RCT (8) N_{Start}=32 N_{End}=30 TPS=Chronic	E: Brain machine interface (BMI) + arm and hand orthosis C: Sham BMI Duration: 5d/wk for 4wk	• Fugl Meyer Assessment (+exp) • Motor Activity Log (-) • Ashworth Scale (-)
Robotics with Electrical Stimulation		

Huang et al. (2020)
RCT (7)
N_{start}= 30
N_{end}= 30
TPS= Chronic
	E: Electromyography -NMES robot (hand exoskelton)
	C: Electromyography -robot (hand exo)
	Duration: 20 sessions, 3-5x/wk for up to 7wks, 60min
		• Fugl-Meyers Assessment: (+exp)
		  • Shoulder/Elbow: (+exp)
		  • Wrist/Hand: (-)
		• Action Research Arm Test: (-)
		• Modified Ashworth Scale:
		  • Elbow: (+exp)
		  • Wrist: (-)
		  • Finger: (-)
		• Functional Independence Measure: (+exp)

Hayward et al. (2013) RCT (7) N_{start}= 10 N_{end}= 8 TPS= Subacute	E: SMART robot end effector with electric stimulation C: SMART robot end effector without electric stimulation Duration: 60min, 5d/wk, 4wks	• Motor Assessment Scale - 6 (Upper Limb Function): (-)
Arm End Effector versus Functional Electrical Stimulation		
Hesse et al. (2005) RCT (8) N_{start}=44 N_{end}=39 TPS=Subacute	E: Computerized arm training enabling repetitive practice (Bi-Manu-Track) C: Electrical stimulation Duration: 20min/d, 5d/wk for 6wk	Fugl-Meyer Assessment (+exp)
Hesse et al. (2008) RCT (8) N_{start}=54 N_{end}=47 TPS=Subacute	E: Computerized arm trainer (Reha-Slide Mechanical Arm Trainer) C: Electrical stimulation Duration: 25min/d, 5d/wk for 6wk	• Fugl-Meyer Assessment (-) • Barthel Index (-)
Robot combined with Anodal tDCS versus Robot		

Edwards et al. (2019) RCT (8) N_{start}= 82 N_{end}= 69 TPS= Chronic Multi-site	E: Robot (MIT-MANUS) + tDCS (anodal) C: Robot + sham Duration: 1hr, 3x/wk, 12wks + 20 min stim before	• Fugle-Meyers Assessment Upper Extremity: (-) • Wolf Motor Function Test: (-)

Mazzoleni et al. (2019)
RCT (6)
N_{start}= 40
N_{end}= 39
TPS= Acute
	E: Robot assisted therapy (InMotion robot wrist + anodal tDCS)
	C: Robot assisted therapy + sham
	Duration: 30min, 5x/wk for 6wks
		• Fugl-Meyers Assessment
		  • Wrist: (-)
		  • Shoulder/Elbow: (-)
		  • Upper Extremity: (-)
		• Modified Ashworth Scale - Wrist: (-)
		• Motricity Index: (-)
		• Box and Block Test: (-)

Dehem et al. (2018) RCT-crossover (6) N_{Start} =21 N_{End} =20 TPS=Chronic	E: Dual tDCS with Upper Limb Robotic Assisted Therapy C: Sham tDCS with Upper Limb Robotic Assisted Therapy Duration: 45min/d, 5d/wk for 6wk	• Box and Block Test (+exp) • Purdue Pegboard Test (-) •
Mazzoleni et al. 2017 RCT (7) N_{Start} =24 N_{End} =24 TPS=Acute	E: Anodal tDCS with Wrist Robot-Assisted Training C: Wrist Robot-Assisted Training Duration: *Not Specified*	• Fugl-Meyer Assessment (-) • Modified Ashworth Scale (-) • Motricity Index (-) • Box and Block Test (-)
Triccas et al. (2015) RCT (8) N_{start}=23 N_{end}=22 TPS=Subacute	E: Anodal tDCS + robotic ArmeoSpring C: Sham tDCS + robotic ArmeoSpring Duration: 45min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Motor Activity Log (-) • Stroke Impact Scale (-)
End Effectors versus Exoskeleton		

Lee et al. (2020)
RCT (7)
N_{start}= 39
N_{end}= 38
TPS= Chronic
	E: Robot End Effector (inMotion2)
	C: Robot exoskeleton (Amreo Power)
	Duration: 30min, 5d/wk 4wks + same time Occupational therapy
		• Fugl-Meyer Assessment Upper Extremity: (-)
		  • Proximal: (-)
		• Wolf Motor Function Test
		  • Functional Ability Score: (+exp)
		  • Time: (+exp)
		  • Weights: (-)
		• Motor status score (-)
		  • Proximal: (-)
		• Stroke Impact Scale: (-)
		  • Hand: (-)
		  • Strength: (-)
		  • Activities of Daily Living: (-)
		  • Social participation: (-)

Robotic and Constraint Induced Movement Therapy		

Hung et al. (2019)
RCT (6)
N_{start}= 45
N_{end}= 44
TPS= Chronic
	E1: Unilateral robot assisted therapy + CIMT (unilateral arm)
	E2: Bilateral robot assisted therapy + BAT (Bimanual tracking)
	C: Robot assisted therapy alone (both modes)
	Duration: 45min robot, 45min bat/cimt (robot group 90min robot) 3x/wk, 6wks
		E1 Vs C
		• Fugl-Meyers Assessment: (-)
		• Stroke Impact Scale (all domains): (-)
		• Wolf Motor Function Test (-)
		• Nottingham Extended Activities of Daily Living Scale: (-)
		  • Kitchen: (-)
		  • Living affairs: (-)
		  • Leisure: (-)
		  • Mobility: (-)
		E2 Vs C
		• Fugl-Meyers Assessment: (-)
		• Stroke Impact Scale (all domains): (-)
		• Wolf Motor Function Test (time, functional ability scale): (-)

		• Nottingham Extended Activities of Daily Living Scale: (-) • Kitchen: (-) • Living affairs: (-) • Leisure: (-) • Mobility: (+con) E1 Vs E2 • Fugl-Meyers Assessment Total: (+exp2) • Stroke Impact Scale (all domains): (-) • Wolf Motor Function Test (time, functional ability scale): (-) • Nottingham Extended Activities of Daily Living Scale: (-) • Kitchen: (-) • Living affairs: (-) • Leisure: (-) • Mobility: (-)
Hung et al. (2019b) RCT (7) N_{start}= 30 N_{end}= 30 TPS= Chronic	E1: Unilateral robot assisted therapy + CIMT (unilateral arm) E2: Bilateral robot assisted therapy + BAT (Bimanual tracking) C: Robot assisted therapy alone (both modes Duration: 45min robot, 45min bat/cimt (robot group 90min robot) 3x/wk, 6wks	E1 Vs C • Fugle-Meyers Assessment: (-) • Chedoke Arm and Hand Activity Inventory: (-) • Goal Attainment Scale: (+exp1) E2 Vs C • Fugle-Meyers Assessment (-) • Chedoke Arm and Hand Activity Inventory: (-) • Goal Attainment Scale: (+exp2) E1 Vs E2 • Fugle-Meyers Assessment (-) • Chedoke Arm and Hand Activity Inventory: (-) • Goal Attainment Scale: (+exp2)
Hsieh et al. (2014) RCT (8) N_{Start}=48 N_{End}=48 TPS=Chronic	E1: Robotic training (Bi-Manu-Track) + dCIT (distributed constraint induced therapy) E2: Robotic therapy C: Conventional therapy Duration: 1hr/d, 5d/wk for 5wk	E1 vs E2 • Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp) E1 vs C • Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp) E2 vs C • Fugl-Meyer Assessment: (+exp_2) • Wolf Motor Function Test (+exp_2) E1 vs E2, E1 vs C & E2 vs C • Motor Activity Log (-)
	Other Robotic Combinations and Comparisons	
Bustamante Valles et al. (2016) RCT (3) N_{Start}=27 N_{End}=20 TPS=Chronic	E: Rehabilitation using a technology-assisted rehabilitation gymnasium (circuit with various robots) C: Traditional therapy Duration: 2hr/d, 4d/wk for 6wk	• Fugl-Meyer Assessment (-) • Box and Block Test (-)
Straudi et al. (2020) RCT (6) N_{start}= 40 N_{end}= 39 TPS= Subacute	E: Robot arm end effector + FES C: Conventional Duration: 1hr40min, 5x/wk, 6wks	• Fugl-Meyers Upper Extremity: (-) • Box and Block Test: (-) • Wolf Motor Ffunction Test (-) • Barthel Idex (-)
Capone et al. (2017) Quasi-RCT (8) N_{Start}=14 N_{End}=12 TPS= Chronic	E: Robot-Assisted Therapy with Transcutaneous Stimulation of Vagus Nerve (tVNS) C: Robot-Assisted Therapy with Sham-tVNS	• Fugl-Meyer Assessment (+exp)

	Duration: 1h, 1d/wk for 10d	
Carry et al. (2007) RCT (3) N_{start}= 25 N_{end}= 20 TPS= Chronic	E: Finger tracking training (telerehab) C: Sham (no tracking) (telerehab) Duration: 180 reps, 5d/wk 2wks	• Box and block test (+con) • Jebsen hand function test (-) • Finger range of motion (+exp)
Liu et al. (2009) RCT (5) N_{start}= 9 N_{end}= 9 TPS= Chronic	E: Sensory robot (inMotion) C: Robot only Duration: 40min, 3x/wk, 6wks	• Motor Status: (-) • Shoulder/Elbow: (-) • Wrist/Hand: (-)
Kim et al. (2017) RCT (5) N_{Start} =33 N_{End} =30 TPS=Chronic	E: External Focus with Robotic Arm (InMotion ARM) C: Internal Focus with Robotic Arm Duration: 45min/d, 3d/wk for 4wk	• Joint Independence (-) • Fugl-Meyer Assessment (-) • Wolf Motor Function Test (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Robotics

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Arm end effectors** may not have a difference in efficacy when compared to **conventional therapy or tast specific training** for improving motor function.	52	Amatya et al. 2020; Aprile et al. 2020; Carpinella et al. 2020; Esquenazi et al. 2020; Takebayashi et al. 2020; Dehem et al. 2019; Hung et al. 2019; Hsu et al. 2019; Duanoravacine et al. 2018; Ellis et al. 2018; Hsieh et al. 2018; Lee et al. 2018; Schuster-Amft et al. 2018; Hsieh et al. 2017; Tomic et al. 2017; Fan et al. 2016; Lee et al. 2016; Takahashi et al. 2016; McCabe et al. 2015; Prange et al. 2015; Ang et al. 2014Hesse et al. 2014; Hsieh et al. 2014; Lemmens et al. 2014; Masiero et al. 2014; Sale et al. 2014; Timmermans et al. 2014; Hsieh et al. 2012; Liao et al. 2012; Abdullah et al. 2011; Burgar et al. 2011; Conroy et al. 2011; Hsieh et al. 2011; Masiero et al. 2011; Lo et al. 2010; Ellis et al. 2009; Hu et al. 2009; Coote et al. 2008; Iwamuro et al. 2008; Rabadi et al. 2008; Volpe et al. 2008; Masiero et al. 2007; Kahn et al. 2006; Lum et al. 2006; Masiero et al. 2006; Fasoli et al. 2004; Volpe et al. 2004; Lum et al. 2002; Burgar et al. 2000; Volpe et al. 1999
1b	There is conflicting evidence about the effect of an **arm/shoulder end-effector with task specific training** to improve motor function when compared to the **robot alone**.	1	Conroy et al. 2019
1b	**Arm/shoulder end-effectors (Bi-Manu-Track, MIT-Manus/InMotion) provided in a group setting** may not have a difference in efficacy when compared to **arm/shoulder end-effectors provided in a one on one setting** for improving motor function.	2	Kim et al. 2017; Hesse et al. 2014
1a	**Arm/shoulder end-effectors with force feedback/ assistance** may not have a difference in efficacy when	5	Cho et al. 2019; Abdollahi et al. 2018; Wright et al. 2018;

	compared to **robotic training without assistance** for improving motor function.		Rowe et al. 2017; Stein et al. 2004
1b	There is conflicting evidence about the effect of a specific **arm/shoulder end-effector (Bi-Manu-Track)** to improve motor function when compared to **cyclic NMES**.	2	Hesse et al. 2008; Hesse et al. 2005
1a	**Arm/shoulder exoskeletons** may not have a difference in efficacy when compared to **conventional therapy** for improving motor function.	5	Daunoraviciene et al. 2018; Villafane 2018; Klamroth-Marganska et al. 2014; Reinkensmeyer et al. 2012; Brokaw et al. 2014
1b	**Multijoint arm exokeletons** may not have a difference in efficacy when compared to **single joint exoskeletons** for improving motor function.	1	Milot et al. 2013
1a	There is conflicting evidence about the effect of **hand end-effectors** to improve motor function when compared to **conventional therapy**.	6	Calabro et al. 2019; Hsieh et al. 2018; Neuendorf et al. 2017; Orihuela-Espina et al. 2016; Sale et al. 2014; Hwang et al. 2012
1a	There is conflicting evidence about the effect of **hand exoskeletons** to improve motor function when compared to **conventional therapy**.	6	Rowe et al. 2017; Shin et al. 2016; Zondervan et al. 2016; Wolf et al. 2015; Susanto et al. 2015; Friedman et al. 2014
1a	**EEG brain computer interface hand exoskeletons** may not have a difference in efficacy when compared to **hand exoskeletons alone** for improving motor function.	5	Cheng et al. 2020; Wang et al. 2018; Ang et al. 2015; Ang et al. 2014; Ramos-Murguialday et al. 2013
1b	There is conflicting evidence about the effect of **hand exoskeleton with electrical sitmulation** to improve motor function when compared to **hand exoskeleton alone**	1	Huang et al. 2020
1a	**Robotics with tDCS** may not have a difference in efficacy when compared to **robotics alone** for improving motor function.	4	Edwards et al. 2019; Mazzoleni et al. 2019; Mazzoleni et al. 2017; Triccas et al. 2015
1b	**Arm exokeletons** may not have a difference in efficacy when compared to **arm end-effectors** for improving motor function.	1	Lee et al. 2020
1a	**Unilateral robotics with CIMT** may not have a difference in efficacy when compared to **bilateral robotics with bilateral arm training** for improving motor function.	2	Hung et al. 2019; Hung et al. 2019

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **arm/shoulder end-effectors** to improve muscle strength when compared to **conventional therapy or task specific training.**	19	Aprile et al. 2020; Hung et al. 2019; Hsieh et al. 2018; Hsieh et al. 2017; Lee et al. 2016; Masiero et al. 2014; Sale et al. 2014; Hsieh et al. 2012; Hsieh et al. 2011; Masiero et al. 2011; Ellis et al. 2009; Volpe et al. 2008; Masiero et al. 2007; Lum et al. 2006; Masiero et al. 2006; Fasoli et al. 2004;

			Lum et al. 2002; Volpe et al. 2000; Volpe et al. 1999
2	**Arm/shoulder end-effectors (MIT-Manus//InMotion)** may not have a difference in efficacy when compared to **active control therapies (sensorimotor arm training, progressive resistance training)** for improving muscle strength.	2	Volpe et al. 2008; Stein et al. 2004
2	**Arm/shoulder end-effectors with force feedback/ assistance** may not have a difference in efficacy when compared to **robotic training without assistance** for improving muscle strength.	1	Stein et al. 2004
1a	**Arm/shoulder exoskeletons** may not have a difference in efficacy when compared to **conventional therapy** for improving muscle strength.	4	Villafane 2018; Taveggia et al. 2016; Klamroth-Marganska et al. 2014; Reinkensmeyer et al. 2012
1b	**Multijoint arm exokeletons** may not have a difference in efficacy when compared to **single joint exoskeletons** for improving muscle strength.	1	Milot et al. 2013
1b	**Hand end-effector** may not have a difference in efficacy when compared to **conventional therapy** for improving muscle strength.	3	Hsieh et al. 2018; Neuendorf et al. 2017; Orihuela-Espina et al. 2016
1b	**Hand exoskeletons (Gloreha)** may produce greater improvements in muscle strength than **conventional therapy**.	1	Vanoglio et al. 2017
1a	**Robotics with tDCS** may not have a difference in efficacy when compared to **robotics alone** for improving muscle strength.	2	Mazzoleni et al. 2019; Mazzoleni et al. 2017

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Arm/shoulder end-effectors** may not have a difference in efficacy when compared to **conventional therapy or task specific training** for improving dexterity.	6	Dehem et al. 2019; Schuster-Amft et al. 2018; Hsieh et al. 2017; Hesse et al. 2014; Masiero et al. 2014; Masiero et al. 2011
2	**Arm/shoulder end-effectors (Bi-Manu-Track, MIT-Manus/InMotion) provided in a group setting** may not have a difference in efficacy when compared to **arm/shoulder end-effectors provided in a one on one setting** for improving dexterity.	1	Hesse et al. 2014
1a	**Arm/shoulder end-effectors with force feedback/ assistance** may not have a difference in efficacy when compared to **robotic training without assistance** for improving dexterity.	3	Cho et al. 2019; Abdollahi et al. 2018; Rowe et al. 2017
1b	**Arm/shoulder exoskeletons** may not have a difference in efficacy when compared to **conventional therapy** for improving dexterity.	2	Brokaw et al. 2014; Reinkensmeyer et al. 2012

1b	**Multijoint arm exokeletons** may not have a difference in efficacy when compared to **single joint exoskeletons** for improving dexterity.	1	Milot et al. 2013
1a	There is conflicting evidence about the effect of **hand end-effectors (Amadeo hand robot)** to improve dexterity when compared to **conventional therapy**.	2	Sale et al. 2014; Hwang et al. 2012
1a	There is conflicting evidence about the effect of **hand exoskeletons (Glohera, SmartGlove, Music Glove)** to improve dexterity when compared to **conventional therapy**.	7	Lee et al. 2020; Vanoglio et al. 2017; Shin et al. 2016; Zondervan et al. 2016; Friedman et al. 2014; Carmeli et al. 2011; Takehashi et al. 2008
1a	**Robotics with tDCS** may not have a difference in efficacy when compared to **robotics alone** for improving dexterity.	3	Mazzoleni et al. 2019; Dehem et al. 2018; Mazzoleni et al. 2017

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **arm/shoulder end-effectors** to improve range of motion when compared to **conventional therapy or task specific training.**	5	Carpinella et al. 2020; Esquenazi et al. 2020; Kim et al. 2019; Duanoravacine et al. 2018; Ellis et al. 2018
1b	**Arm/shoulder end-effectors with force feedback/ assistance** may not have a difference in efficacy when compared to **robotic training without assistance** for improving range of motion.	1	Wright et al. 2018
1b	There is conflicting evidence about the effect of **Arm/shoulder exoskeletons** to improve range of motion when compared to **conventional therapy.**	2	Horsley et al. 2019; Daunoraviciene et al. 2018

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
1a	**Arm/shoulder end-effectors** may not have a difference in efficacy when compared to **conventional therapy or task-oriented training** for improving performance of activities of daily living.	33	Amatya et al. 2020; Aprile et al. 2020; Carpinella et al. 2020; Chinembiri et al. 2020; Esquenazi et al. 2020; Dehem et al. 2019; Hung et al. 2019; Hsu et al. 2019; Duanoravicine et al 2018; Hsieh et al. 2018; Lee et al. 2018; Schuster-Amft et al. 2018; Hsieh et al. 2017; Tomic et al. 2017; Lee et al. 2016; Takahashi et al. 2016; McCabe et al. 2015; Hsieh et al. 2014; Lemmens et al. 2014; Masiero et al. 2014; Timmermans et al. 2014; Hsieh et al. 2012; Liao et al. 2012; Burgar et al. 2011; Hsieh et al. 2011; Masiero et al. 2011; Wagner et al. 2011; Lo et al. 2010; Lum et al. 2006; Masiero et al. 2006; Masiero et al. 2007; Lum et al. 2002; Burgar et al. 2000; Volpe et al. 2000
1a	**Arm/shoulder end-effectors (Haptic Master, MIT-Manus/InMotion)** may not have a difference in efficacy when compared to **active control therapies (progressive abduction loading therapy or motor learning)** for improving performance of activities of daily living.	2	Ellis et al. 2018; McCabe et al. 2015

1b	**Arm/shoulder end-effectors with task specific training** may not have a difference in efficacy when compared to **arm/shoulder end-effectors provided in a one on one setting** for improving performance of activities of daily living.	1	Conroy et al. 2019
1a	**Arm/shoulder end-effectors with force feedback/ assistance** may not have a difference in efficacy when compared to **robotic training without assistance** for improving performance of activities of daily living.	2	Abdollahi et al. 2018; Rowe et al. 2017
1a	**Arm/shoulder exoskeletons** may not have a difference in efficacy when compared to **conventional therapy** for improving performance of activities of daily living.	5	Horsley et al. 2019; Daunoraviciene et al. 2018; Villafane 2018; Taveggia et al. 2016; Klamroth-Marganska et al. 2014
1b	**Multijoint arm exokeletons** may not have a difference in efficacy when compared to **single joint exoskeletons** for improving performance of activities of daily living.	1	Milot et al. 2013
1b	**Hand end-effector (Amadeo hand robot)** may not have a difference in efficacy when compared to **early passive training** for improving performance of activities of daily living.	1	Hwang et al. 2012
1a	**Hand exoskeletons** may produce greater improvements in performance of activities of daily living than **conventional therapy**.	7	Park et al. 2018; Thielbar et al. 2017; Shin et al. 2016; Zondervan et al. 2016; Linder et al. 2015; Kutner et al. 2010; Takehashi et al. 2008
1b	**EEG brain computer interface hand exoskeletons** may not have a difference in efficacy when compared to **hand exoskeletons alone** for improving performance on activities of daily living function.	1	Ramos-Murguialday et al. 2013
1a	There is conflicting evidence about the effect of **robotics with electrical sitmulation** to improve activities of daily living when compared to **robotics alone.**	2	Huang et al. 2020; Hayward et al. 2013
1b	There is conflicting evidence about the effect of a specific **arm/shoulder end-effector (Bi-Manu-Track)** to improve activities of daily living when compared to **cyclic NMES**.	1	Hesse et al. 2008;
1b	**Robotics with tDCS** may not have a difference in efficacy when compared to **robotics alone** for improving performance on activities of daily living function.	1	Triccas et al. 2015
1b	**Arm exokeletons** may not have a difference in efficacy when compared to **arm end-effectors** for improving performance on activities of daily living function.	1	Lee et al. 2020
1a	**Unilateral robotics with CIMT** may not have a difference in efficacy when compared to **bilateral**	2	Hung et al. 2019; Hung et al. 2019

	robotics with bilateral arm training for improving performance on activities of daily living function.		

PROPRIOCEPTION

LoE	Conclusion Statement	RCTs	References
1b	**Arm/shoulder exoskeletons (Pneu-WREX)** may produce greater improvements in proprioception than **conventional therapy**.	1	Reinkensmeyer et al. 2012

SPASTICITY

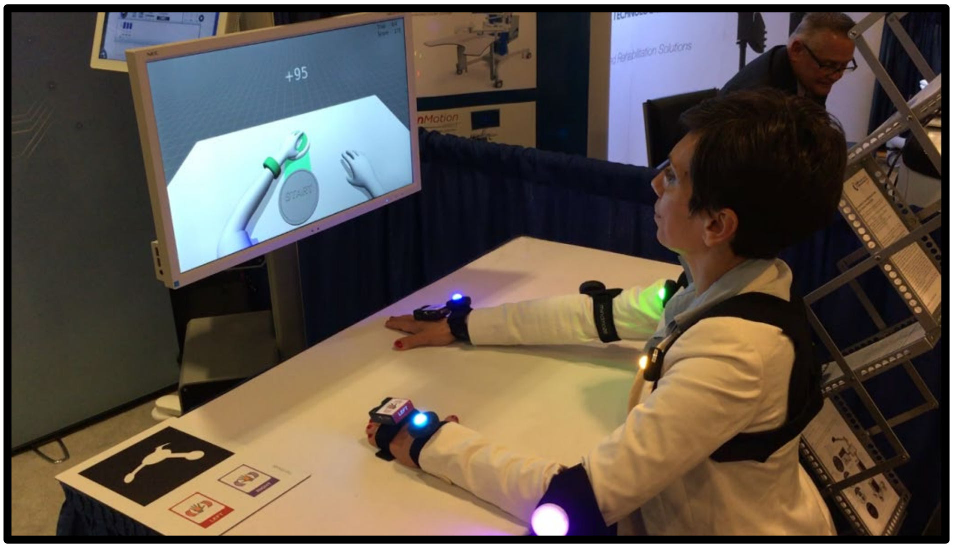
LoE	Conclusion Statement	RCTs	References
1a	**Arm/shoulder end-effectors** may not have a difference in efficacy when compared to **conventional therapy** for improving spasticity.	11	Aprile et al. 2020; Carpinella et al. 2020; Esquenazi et al. 2020; Hung et al. 2019; Burgar et al. 2011; Masiero et al. 2011; Lo et al. 2010; Hu et al. 2009; Masiero et al. 2007; Lum et al. 2006; Volpe et al. 2004
1b	**Arm/shoulder end-effectors with force feedback/ assistance** may not have a difference in efficacy when compared to **robotic training without assistance** for improving spasticity.	2	Wright et al. 2018; Stein et al. 2004
1a	**Arm/shoulder exoskeletons** may not have a difference in efficacy when compared to **conventional therapy** for improving spasticity.	4	Villafane et al. 2018; Taveggia et al. 2016; Klamroth-Marganska et al. 2014; De Araujo et al. 2011
1b	**Hand end-effector (Amadeo hand robot)** may not have a difference in efficacy when compared to **early passive training** for improving spasticity.	1	Hwang et al. 2012
1b	**Hand exoskeletons (Gloreha)** may produce greater improvements in spasticity than **conventional therapy**.	1	Vanoglio et al. 2017
1b	**EEG brain computer interface hand exoskeletons** may not have a difference in efficacy when compared to **hand exoskeletons alone** for improving spasticity.	1	Ramos-Murguialday et al. 2013
1b	**Hand exoskeleton with electrical stimulation** may not have a difference in efficacy when compared to **hand exoskeletons alone** for improving spasticity.	1	Huang et al. 2020
1a	**Robotics with tDCS** may not have a difference in efficacy when compared to **robotics alone** for improving spasticity.	2	Mazzoleni et al. 2019; Mazzoleni et al. 2017

Key points

The evidence is mixed regarding arm/shoulder end-effector robotics, alone or in combination with other therapy approaches, for upper limb rehabilitation following stroke.

The evidence is mixed regarding arm/shoulder exoskeleton, hand exoskeleton, and hand end-effector robotics for upper limb rehabilitation.

Virtual Reality



Adopted from: https://philadelphia.cbslocal.com/2016/05/15/virtual-reality-stroke-rehab/

Virtual reality interventions are described as the use of immersive multimedia created through computer programs that allows users to engage in simulated environments representative of both real-world and imagined places and objects (Iruthayarajah et al. 2017; Laver et al. 2017). These virtual reality interventions are presented typically as games with haptic feedback, that allow for the creation of a multisensory experience. Virtual reality interventions meet as the four guiding principles of rehabilitation: intensity, task-specific training, biofeedback and motivation (Dias et al. 2019). Research on the use of virtual reality for stroke rehabilitation is increasing as technology becomes more accessible and affordable. This includes using existing gaming consoles (e.g. Nintendo Wii, Xbox Kinect, Playstation Eyetoy) for therapeutic purposes or designing new systems specifically for rehabilitation (Laver et al. 2017).

A total of 57 RCTs evaluating virtual reality interventions for upper extremity motor rehabilitation were found, the characteristics of these interventions are described below.

48 RCTs examined virtual reality compared to conventional care or sham (Laffont et al. 2020; Lin et al. 2020; Henrique et al. 2019; Hung et al. 2019; Norouzi-Gheidari et al. 2019; Ogun et al. 2019; Oh et al. 2019; Rogers et al. 2019; Yacoby et al. 2019; Asfar et al. 2018; Askin et al. 2018; Faria et al. 2018; Kim et al. 2018; Kiper et al. 2018; Lee et al. 2018; Adie et al. 2017; Ballester et al. 2017; Brunner et al. 2017; Rand et al. 2017; Standen et al. 2017; Stockley et al. 2017; Turkbey et al. 2017; Wang et al. 2017; Choi et al. 2016; Givon et al. 2016; Kong et al. 2016; Lee et al. 2016a; Lee et al. 2016c; Sapsonik et al. 2016; Bower et al. 2015; Da Silva Ribeiro et al. 2015; Shin et al. 2015; Simsek et al. 2015; Choi et al. 2014; Fan et al. 2014; Kiper et al. 2014; Shin et al. 2014; Thielbar et al. 2014; Duff et al. 2013; Lee et al. 2013; Sin & Lee, 2013; Crosbie et al. 2012; Da Silva et al. 2011; Kiper et al. 2011; Piron et al. 2010; Sapsonik et al. 2010; Yavuzer et al. 2008; Jang et al. 2005). One RCT examined virtual reality combined with bilateral arm training compared to bilateral arm training alone (Lee et al. 2016b). One RCT examined virtual reality combined with FES (Lee et al. 2018). One RCT examined virtual reality combined with tDCS (Lee & Chun, 2014). One RCT examined virtual reality with a hand orthosis (Nijenhuis et al. 2017). One RCT compared virtual reality to mCIMT (McNulty et al. 2015). One

RCT compared asymmetric training with virtual reality compared to symmetric (Lee et al. 2014). One RCT examined virtual reality combined with mirror therapy (Choi et al. 2019). One RCT compared virtual reality combined with stretching (Dos Santos Junior et al. 2019). One RCT compared multi-user virtual reality to a single user virtual reality (Thielbar et al. 2020).

The methodological details and results of all 57 RCTs are presented in Table 19.

Table 19. RCTs Evaluating Virtual Reality Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Virtual reality training compared to conventional therapy, recreational therapy or sham		

Laffont et al. (2020)
RCT (8)
N_{start}= 51
N_{end}= 46
TPS= Acute
	E: VR (video games)
	C: Conventional therapy
	Duration: 90-120min conventional therapy/d, + 15-45min, 5x/wk 6wks of intervention or control exercise
		• Fugle-Meyers Assessment Upper Extremity: (-)
		  • Proximal: (-)
		  • Distal: (+exp)
		• Box and Block Test: (+exp)
		• Motor Activity Log: (-)
		• Barthel Index: (-)
		• Wolf Motor Function Test: (-)

Lin et al. (2020) RCT (7) N_{start}= 152 N_{end}= 145 TPS= Acute	E: Early VR Rehabilitation C: Early conventional rehabilitation Duration: 8hrs/wk for 4wks	• Manual Muscle Test (-) • Barthel Index: (+exp)

Henrique et al. (2019)
RCT (5)
N_{start}= 31
N_{end}= 31
TPS= Chronic
	E: VR motion rehab AVE 3D
	C: Conventional therapy
	Duration: 30min, 2x/wk for 12wks
		• Fugle-Meyers Assessment Upper Extremity: (+exp)
		  • Shoulder/Elbow/ forearm: (+exp)
		  • Wrist: (-)
		  • Hand: (-)

Hung et al. (2019)
RCT (8)
N_{start}= 33
N_{end}= 32
TPS= Chronic
	E: Modified Kinect VR
	C: Conventional therapy
	Duration: 30min, 2-3xwk, 3mo
		• Fugle-Meyers Assessment Upper Extremity: (-)
		  • Proximal: (-)
		  • Distal: (-)
		• Wolf Motor Function Test:
		  • Time: (-)
		  • Functional Activity Scale: (-)
		• Motor Activity Log (Quality of Movement, Amount of Use): (-)

Norouzi-Gheidari et al. (2019)
RCT (6)
N_{start}= 23
N_{end}= 18
TPS= Chronic
	E: Jintronix VR
	C: Conventional therapy
	Duration: 2-3x/wk, 30-45min, 4wks add on to conventional therapy
		• Fugl Meyer Assessment upper extremity: (-)
		• Box and Block Test: (-)
		• MAL:
		  • Amount of Use: (-)
		  • Quality of Movement: (+exp)
		• Stroke Impact Scale total: (+exp)

Ögün et al. (2019) RCT (6) N_{start}= 84 N_{end}= 65 TPS= Chronic	E: Leap motion VR C: Sham Duration: 60min, 3x/wk for 6wks	• Fugl-Meyers Assessment Upper Extremity: (+exp) • Action Research Arm Test: (+exp) • Functional Independence Measure: (+exp) • Performance Assessment of Self-Care Skill – Basic Activities Daily Living: (+exp) • Performance Assessment of Self-Care Skills – Instrumental Activities Daily Living: (+exp)
Oh et al. (2019) RCT (7) N_{start}= 33 N_{end}= 31	E: Joystim VR C: Conventional therapy Duration: 30min, 3x/wk for 6wks	• Tip Pinch Power: (+exp) • Grip, Palmar Pinch, Lateral Pinch: (-) • Modified Ashworth Scale • Elbow Flexion: (-)

TPS= Chronic		• Elbow Extension: (-) • Wrist Extension: (-) • Manual Muscle Test • Flexion: (-) • Extension: (-) • Wrist: (-) • Elbow: (-) • Finger: (-) • Shoulder: (-) • Fugl-Meyers Assessment Upper Extremity: (-) • Shoulder/Elbow: (-) • Wrist: (-) • Hand: (-) • Coordination: (-) • Box and Block Test: (-) • Nine Hole Peg Test: (-)
Rogers et al. (2019) RCT (6) N_{start}= 21 N_{end}= 21 TPS= Acute	E: VR C: Conventional therapy Duration: 3hrs/d rehab, 30-40min 3x/wk, 4wks of VR (elements)	• Box and Block Test: (+exp) • Neurobehavioral Functional Inventory • Motor (+exp) • Cognitive (+exp) • Depression (-) • Somatic (-) • Communication (+exp) • Aggression (-)
Yacoby et al. (2019) RCT (5) N_{start}=24 N_{end}=20 TPS=Chronic	E: VR (kinect or PS eyetoy) C: Graded Repetitive Arm Supplementary Program (GRASP) Duration: ~ 4hrs/wk for 5wks	• Adherence: (+con) • Satisfaction: (-) • Enjoyment: (-)
Asfar et al. (2018) RCT (4) N_{Start}= 42 N_{End}=35 TPS= Subacute	E: Virtual Reality (Xbox kinict 30min/5x/4wk + conventional therapy) C: Sham Duration: 60min, 5x/wk for 4k	• Fugl–Meyer Assessment Upper Extremity: (-) • Box and Block Test: (+exp) • Functional Independence Measure Self Care: (-)
Askin et al. (2018) RCT (6) N_{Start}=40 N_{End}=38 TPS=Chronic	E: Xbox Kinect-based virtual reality training + physical therapy C: Physical therapy Duration: 1h/d, 5d/wk for 4wks	• Fugl-Meyer Assessment (+exp) • Motricity Index (+exp) • Active range of motion (+exp) • Brunnstrom Recovery Stages (-) • Modified Ashworth Scale (-) • Box and Block Test (-)
Faria et al. (2018) RCT (4) N_{Start} =32 N_{End} =24 TPS=Chronic	E: Virtual reality (Reh@Task) C: Time-matched standard occupational therapy Duration: 45min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Chedoke Arm and Hand Activity Inventory (-) • Barthel Index (-) • Motricity Index (-) • Modified Ashworth Scale (-)
Kim et al. (2018) RCT (8) N_{Start} =23 N_{End} =19 TPS=Chronic	E: Kinect-based virtual reality C: Sham virtual reality Duration: 30min/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (-) • Brunnstrom Stage: Arm and Hand (-) • Box and Block Test (-) • Korean Modified Barthel Index (-) •
Kiper et al. (2018) RCT (7) N_{Start} =139 N_{End} =136 TPS=Subacute	E: Reinforced feedback in virtual environment + conventional rehabilitation C: Conventional rehabilitation Duration: 1h/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Functional Independence Measure (+exp) • National Institute of Health Stroke Scale (+exp)
Lee et al. (2018) RCT (6) N_{Start} =31	E: Virtual reality canoe paddle training + conventional therapy C: Conventional therapy	• Manual Function Test (+exp)

N_{End} =30 TPS=Subacute	Duration: 30min/d, 3d/wk for 5wk	
Adie et al. (2017) RCT (7) N_{Start} =235 N_{End} =209 TPS=Chronic	E: Wii arm exercises C: Home-based arm exercises Duration: 45min/d for 6wk	• Action Research Arm Test (-) • Stroke Impact Questionnaire (-) • Canadian Occupational Performance Measure (-) • Motor Activity Log (-)
Ballester et al. (2017) RCT (5) N_{Start} =39 N_{End} =35 TPS=Chronic	E: Home-based virtual reality C: Home-based occupational therapy Duration: 30min/d, 5d/wk, 3wk	• Fugl-Meyer Assessment (-) • Chedoke Arm and Hand Activity Inventory (+exp) • Barthel Index (-) • Medical Research Council Scale (-) • Ashworth Scale (-) • Grip force (-)
Brunner et al. (2017) RCT (5) N_{Start} =120 N_{End} =102 TPS=Subacute	E: Virtual reality training C: Conventional training Duration: 60min/d, 4-5d/wk for 4wk	• Action Research Arm Test (-) • Box and Block Test (-) • Functional Independence Measure (-)
Rand et al. (2017) RCT (7) N_{Start} =24 N_{End}=21 TPS=Chronic	E: Video games self-training C: Traditional self-training Duration: 60min/d, 6d/wk for 5wk	• Action Research Arm Test (-) • Motor Activity Log (-) • Box and Block Test (-)
Standen et al. (2017) RCT (6) N_{Start} =27 N_{End} =18 TPS=Subacute	E: Home-based virtual reality C: Conventional therapy Duration: up to 60min/d, 7d/wk for 8wk	• Motor Activity Log (+exp) • Wolf Motor Function Test (-) • Wolf Grip Strength (+exp) • Nine-Hole Peg Test (-) • Nottingham Extended Activities of Daily Living (-)
Stockley et al. (2017) RCT (7) N_{start}= 12 N_{end}= 12 TPS= Chronic	E: VR (YOUgrabber) C: Gym Duration: 30min, 18x/ 12wks	• Motor Activity Log Amount of Use: (-) • Motor Activity Log Quality of Use: (-) • Box and Block Test: (-) • Fatigue severity scale: (-)
Turkbey et al. (2017) RCT (7) N_{Start} =20 N_{End} =19 TPS=Subacute	E: Xbox Kinect virtual reality training + conventional rehabilitation C: Conventional rehabilitation Duration: 60min/d, 5d/wk for 4wk	• Box and Block Test (+exp) • Wolf Motor Function Test (+exp) • Brunnstrom Motor Recovery Stage (+exp) • Functional Independence Measure (-)

Wang et al. (2017)
RCT (6)
N_{start}=26
N_{end}=26
TPS=Subacute
	E: VR (leap motion)
	C: Conventional rehabilitation
	Duration: 45min, 5d/wk, 4wks (conventional and experimental add on)
		• Wolf Motor Function Test:
		  • Score: (+exp)
		  • Time: (+exp)

Choi et al. (2016) RCT (6) N_{Start}=24 N_{End}=24	E: Virtual reality rehabilitation program + conventional occupational therapy C: Conventional occupational therapy Duration: 30min/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (+exp) • Brunnstrom Stage (+exp) • Manual Muscle Test (+exp) • Modified Barthel Index (-)
Givon et al. (2016) RCT (6) N_{Start} =47 N_{End} =43 TPS=Chronic	E: Virtual reality video game therapy C: Traditional therapy Duration: 60min/d, 2d/wk for 12wk	• Action Research Arm Test (-) • Grip strength (-)
Kong et al. (2016) RCT (7) N_{Start} =105 N_{End} =97 TPS=Acute	E: Nintendo Wii virtual reality training C: Conventional therapy Duration: 60min/d, 4d/wk for 3wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Stroke Impact Scale (-) • Functional Independence Measure (-)

Lee et al. (2016a) RCT (7) N_{Start} =26 N_{End} =26 TPS=Chronic	E: Virtual reality-based rehabilitation C: Group-based rehabilitation Duration: 30min/d, 3d/wk for 8wk	• Fugl-Meyer Assessment (+exp) • Manual Function Test (+exp) • Box and Block Test (-) • Modified Barthel Index (-)
Lee et al. (2016c) RCT (5) N_{Start} =14 N_{End} =10 TPS=Acute	E: Canoe game-based virtual reality training + conventional rehabilitation C: Conventional rehabilitation Duration: 30min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (+exp)
Saposnik et al. (2016) RCT (6) N_{Start} =141 N_{End} =121 TPS=Acute	E: Virtual reality training using Nintendo Wii C: Recreational activities Duration: 60min/d, 5d/wk for 2wk	• Wolf Motor Function Test (-) • Box and Block Test (+con) • Stroke Impact Scale (-) • Barthel Index (-) • Functional Independence Measure (-) • Grip Strength (-)

Bower et al. (2015)
RCT (7)
N_{start}=16
N_{end}= 16
TPS= Subacute
	E: VR motion-controlled games - 3D depth camera (similar to xbox kinect)
	C: Conventional therapy
	Duration: VR (40min/2x/4wk) and conv rehab (length unspecified)
		• Functional Independence Measure
		  • Transfers: (-)
		  • Mobility: (-)
		  • Stairs: (-)
		• Motor Assessment Scale: (-)

da Silva Ribeiro et al. (2015) RCT (7) N_{Start}=30 N_{End}=30 TPS=Chronic	E: Virtual reality training using Nintendo Wii C: Conventional physical therapy Duration: 20min/d, 3d/wk for 12wk	• Fugl-Meyer Assessment (-)
Shin et al. (2015) RCT (6) N_{Start}=35 N_{End}=32 TPS=Chronic	E: Virtual reality + conventional occupational therapy C: Conventional occupational therapy Duration: 30min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (-)
Şimşek al. (2015) RCT (7) N_{start}= 44 N_{end}= 22 TPS= Subacute	E: VR (wii) C: Bobath NDT Duration: 45-60min 3d/wk, 10wks	• Functional Independence Measure, all subscales: (-) • Satisfaction (+exp)
Choi et al. (2014) RCT (8) N_{Start}=20 N_{End}=20 TPS=Chronic	E: Virtual reality therapy using Nintendo Wii C: Conventional occupational therapy Duration: 30min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (-) • Box and Block Test (-) • Manual Function Test (-) • Grip strength (-) • Modified Barthel Index (-)
Fan et al. (2014) RCT (7) N_{Start}=27 N_{End}=20 TPS=Chronic	E1: Virtual reality E2: Conventional therapy E3: Placebo board game C: No treatment Duration: 60min/d, 3d/wk for 3wk	E1 vs E2 vs E3 vs C • Jebsen-Taylor Hand Function Test (-) • Stroke Impact Scale (-)
Kiper et al. (2014) RCT (6) N_{Start}=46 N_{End}=44 TPS=Chronic	E: Reinforced feedback in virtual environment + traditional rehabilitation C: Traditional rehabilitation Duration: 2h/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Functional Independence Measure (+exp)
Shin et al. (2014) RCT (5) N_{Start}=16 N_{End}=16 TPS=Chronic	E: Virtual reality training + conventional occupational therapy C: Occupational therapy Duration: 30min/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (-) • Modified Barthel Index (-) • Medical Research Council Score (-) • Range of Motion (-)

Thielbar et al. (2014) RCT (6) N_{Start}=14 N_{End}=14 TPS=Chronic	E: Virtual reality keypad/glove C: Occupational therapy Duration: 18h/d, 3d/wk for 6wk	• Action Research Arm Test (+exp) • Jebsen-Taylor Hand Function Test (-) • Fugl-Meyer Assessment (-) • Grip Strength (-) • Pinch Strength (-)
Duff et al. (2013) RCT (5) N_{Start}=25 N_{End}=21 TPS=Chronic	E: Adaptive mixed reality rehabilitation C: Traditional therapy Duration: 60min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (+con) • Wolf Motor Function Test (-) • Stroke Impact Scale (-) • Motor Activity Log (-)
Lee et al. (2013) RCT (6) N_{Start}=14 N_{End}=14 TPS=Chronic	E: Xbox Kinect-based virtual reality + conventional occupational therapy C: Conventional occupational therapy Duration: 60min/d, 3d/wk for 6wk	• Manual Muscle Test (-) • Modified Ashworth Scale (-) • Functional Independence Measure (-)
Sin & Lee (2013) RCT (5) N_{Start}=40 N_{End}=35 TPS=Chronic	E: Xbox Kinect-based virtual reality training + conventional occupational therapy C: Conventional occupational therapy Duration: 30min/d, 3d/wk for 6wk	• Range of Motion (+exp) • Fugl-Meyer Assessment (+exp) • Box and Block Test (+exp)
Crosbie et al. (2012) RCT (8) N_{start}=18 N_{end}=17 TPS=Chronic	E: Virtual reality training C: Conventional physiotherapy Duration: 30-45min/d, 3d/wk for 3wk	• Motricity Index (-) • Action Research Arm Test (-)

da Silva et al. (2011)
RCT (5)
N_{start}= 25
N_{end}= 15
TPS= Acute
	E: VR gloves
	C1: Conventional Occupational therapy
	C2: Non-specific games
	Duration: 20min, 3x/wk for 12wks
		E Vs C1
		• Barthel's Index: (-)
		• Motricity Index (-)
		• Fugl Meyers Assessment Upper Extremity: (-)
		    • Arm: (+exp)
		    • Wrist/Hand: (-)
		• Chedoke Arm and Hand Activity Inventory: (+exp)
		E Vs C2
		• Barthel's Index: (-)
		• Motricity Index (-)
		• Fugl Meyers Assessment Upper Extremity: (-)
		    • Arm: (+exp)
		    • Wrist/Hand: (-)
		• Chedoke Arm and Hand Activity Inventory: (+exp)

Kiper et al. (2011) RCT (6) N_{start}= 80 N_{end}= 80 TPS= Chronic	E: Reinforced feedback in virtual environment therapy (PC and Virtual Reality Rehabilitation System) with traditional neuromotor rehabilitation (TNR) C: TNR only Duration: 2 hr (exp group: 1 hr RFVE and 1 hr TNR, con group: 2 hr TNR programme), 5x/wk for 4wks	• Fugl-Meyers Assessment Upper Extremity: (+exp) • Modified Ashworth Scale: (-) • Functional Independence Measure: (+exp)
Piron et al. 2010 RCT (8) N_{start}= 57 N_{end}= 50 TPS= Chronic	E: Visual and knowledge of results feedback in VR environment C: Bobath approach Duration: 1hr, 5days/week for 4 weeks	• Fugl-Meyers Assessment (+exp)
Saposnik et al. (2010) RCT (7) N_{start}=22	E: Virtual reality training using Nintendo Wii C: Recreational therapy	• Wolf Motor Function Test (+exp) • Grip strength (-) • Box and Block Test (-)

N_{end}=16 TPS=Acute	Duration: 60min/d, 4d/wk for 2wk	• Stroke Impact Scale (-)
Yavuzer et al. (2008) RCT (6) N_{start}=20 N_{end}=20 TPS=Subacute	E: Playstation EyeToy games + conventional therapy C: Sham therapy + conventional therapy Duration: 30min/d, 5d/wk for 4wk	• Brunnstrom Recovery Stages (-) • Functional Independence Measure (+exp)
Jang et al. (2005) RCT (5) N_{start}=10 N_{end}= 10 TPS=Chronic	E: Virtual reality training C: No treatment Duration: 60min/d, 5d/wk for 4wk	• Box and Block test (+exp) • Fugl-Meyer Assessment (+exp) • Manual Function Test (+exp) •
Virtual reality with bilateral arm training compared to bilateral arm training		
Lee et al. (2016b) RCT (6) N_{Start}=20 N_{End}=18 TPS=Chronic	E: Virtual reality-based bilateral arm training C: Bilateral arm training Duration: 60min/d, 5d/wk for 4wk	• Jebsen Taylor Hand Function Test (+exp) • Box and Block Test (+exp) • Grooved Pegboard Test (+exp) • Digital Manual Muscle Test (+exp)
Virtual reality with FES compared to FES		
Lee et al. (2018) RCT (7) N_{Start}=48 N_{End}=41 TPS=Chronic	E: Virtual reality + functional electrical stimulation C: Functional electrical stimulation Duration: 30min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (-) • Box and Block Test (-) • Jebsen-Taylor Hand Function Test (-) • Stroke Impact Scale (-)
Virtual reality compared to and combined with cathodal tDCS		
Lee & Chun (2014) RCT (7) N_{Start}=64 N_{End}=59 TPS=Subacute	E1: Cathodal transcranial direct current stimulation (tDCS) E2: Virtual reality E3: Cathodal tDCS + virtual reality Duration: 30min/d, 5d/wk for 3wk	E3 vs E2/E1 • Manual Function Test (+exp_3) • Fugl-Meyer Assessment (+exp_3) • Manual Muscle Test (-) • Box and Block Test (-) • Modified Ashworth Scale (-) • Modified Barthel Index (-) E2 vs E1 • Manual Function Test (+exp_2) • Fugl-Meyer Assessment (+exp_2) • Manual Muscle Test (-) • Box and Block Test (-) • Modified Ashworth Scale (-) • Modified Barthel Index (-)
Virtual reality with a hand orthosis compared to conventional therapy		
Nijenhuis et al. (2017) RCT (6) N_{Start} =20 N_{End} =19 TPS=Chronic	E: Hand orthosis + computerised gaming exercises C: Conventional exercise Duration: 30min/d, 6d/wk for 6wk	• Action Research Arm Test (-) • Fugl-Meyer Assessment (-) • Grip Strength (-) • Box and Block Test (-) • Motor Activity Log (-) • Stroke Impact Scale (-)
Virtual reality compared to mCIMT		
McNulty et al. (2015) RCT (7) N_{Start}=41 N_{End}=40 TPS=Chronic	E: Nintendo Wii-based movement therapy C: Modified constraint-induced movement therapy Duration: 60min/d, 5d/wk for 2wk	• Wolf Motor Function Test (-) • Motor Activity Log (-) • Fugl-Meyer Assessment (-) • Modified Ashworth Scale (-) • Box and Block Test (-) • Grooved Pegboard Test (-) • Range of motion (-)
Asymmetric training with virtual reality compared to symmetric training		
Lee et al. (2014) RCT (5)	E: Asymmetric training using virtual reality + conventional physical therapy	• Fugl-Meyer Assessment (+exp) • Box and Block test (+exp) • Grip strength (+exp)

N_{Start}=30 N_{End}=24 TPS=Chronic	C: Symmetric training + conventional physical therapy Duration: 60min/d, 5d/wk for 4wk	• Modified Ashworth Scale (-) • Range of motion (+exp)
Virtual Reality combined with Mirror Therapy		
Choi et al. (2019) RCT (7) N_{start}= 36 N_{end}= 36 TPS= Chronic	E1: Leap motion VR + mirror therapy E2: Mirror therapy (conventional) C: Sham Duration: 30min, 3x/wk for 5wks	E1 Vs C • Manual Function Test: (+exp1) E2 Vs C • Manual Function Test: (+exp2) E1 Vs E2 • Manual Function Test: (+exp1)
VR combined with stretching compared to VR or stretching		

Dos Santos Junior et al. (2019)
RCT (6)
N_{start}= 48
N_{end}= 40
TPS= Chronic
	E: Proprioceptive Neuromuscular Facilitation (PNF) + VR
	C1: PNF
	C2: VR (Wii)
	Duration: 50min, 2x/wk, 2mo
		• Fugl-Meyers Assessment: (-)
		  • Passive Motion and Pain: (-)
		  • Sensory: (-)
		  • Upper Extremity: (-)
		  • Lower Extremity: (-)
		  • Balance: (-)

Multiuser versus single user VR		
Thielbar et al. (2020) crossover RCT (4) N_{start}=21 N_{end}=20 TPS=Chronic	E: Multi user VR C: Single user VR Duration: 4hrs, 4/wk, 2wks/condition	• Fugl Meyer Assessment Upper Extremity: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Virtual Reality

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Virtual reality** may not have a difference in efficacy when compared to **conventional care** for improving motor function.	39	Laffont et al. 2020; Henrique et al. 2019; Hung et al. 2019; Norouzi-Gheidari et al. 2019; Ogun et al. 2019; Oh et al. 2019; Asfar et al. 2018; Askin et al. 2018; Faria et al. 2018; Kim et al. 2018; Kiper et al. 2018; Lee et al. 2018; Adie et al. 2017; Ballester et al. 2017; Brunner et al. 2017; Rand et al. 2017; Standen et al. 2017; Stockley et al. 2017; Turkbey et al. 2017; Choi et al. 2016; Givon et al. 2016; Kong et al. 2016; Lee et al. 2016; Lee et al. 2016a; Saposnik et al. 2016; Bower et al. 2015; Da Silva Riberio et al. 2015; Simsek et al. 2015; Shin et al. 2015; Choi et al. 2014; Fan et al. 2014; Kiper et al. 2014; Shin et al. 2014; Thielbar et al. 2014; Duff et al. 2013; Lee et al. 2013; Crosbie et al. 2012; Da Silva et al. 2011; Kiper et al. 2011; Piron et al. 2010; Saposnik et al. 2010; Yavuzer et al. 2008; Jang et al. 2005
1b	**Virtual reality bilateral arm training** may produce greater improvements in motor function than **bilateral arm training**.	1	Lee et al. 2016b
1b	**Virtual reality interventions combined with FES** may not have a difference in efficacy when compared to **FES alone** for improving motor function.	1	Lee et al. 2018

1b	**Virtual reality interventions on their own or combined with cathodal tDCS** may produce greater improvements in motor function than **cathodal tDCS**.	1	Lee and Chun, 2014
1b	**Virtual reality training with a hand orthosis** may not have a difference in efficacy when compared to **conventional therapy** for improving motor function.	1	Nijenhuis et al. 2017
1b	**Virtual reality training** may not have a difference in efficacy when compared to **mCIMT** for improving motor function.	1	McNulty et al. 2015
2	**Asymmetric virtual reality training** may produce greater improvements in motor function than **symmetric conventional training**.	1	Lee at al. 2014
2	**Virtual reality training** may produce greater improvements in motor function than **no training**.	1	Jang at al. 2005
1b	**Virtual reality with mirror therapy** may produce greater improvements in motor function than **mirror therapy alone.**	1	Choi et al 2019
1b	**Virtual reality training with peripheral nerve facilitation** may not have a difference in efficacy when compared to **virtual reality or peripheral nerve facilitation** for improving motor function.	1	Dos Santos et al. 2019
1b	**Multi-user virtual reality** may not have a difference in efficacy when compared to **single-user virtual reality** for improving motor function.	1	Thielbar et al. 2020

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References
1b	**Virtual reality interventions** may produce greater improvements on measures of stroke severity than **conventional therapy**.	1	Kiper et al. 2018

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
2	There is conflicting evidence about the effect of **virtual reality interventions** to improve range of motion when compared to **conventional therapy, recreational therapy or sham interventions**.	2	Shin et al. 2014; Sin and Lee, 2013
1b	**Virtual reality training** may not have a difference in efficacy when compared to **mCIMT** for improving range of motion.	1	McNulty et al. 2015
2	**Asymmetric virtual reality training** may produce greater improvements in range of motion than **symmetric conventional training**.	1	Lee at al. 2014

DEXTERITY

LoE	Conclusion Statement	RCTs	References

1a	**Virtual reality interventions** may not have a difference in efficacy when compared to **conventional therapy, recreational therapy or sham interventions** for improving dexterity.	10	Laffont et al. 2020; Norouzi-Gheidari et al. 2019; Oh et al. 2019; Rodgers et al. 2019; Asfar et al. 2018; Askin et al. 2018; Kim et al. 2018; Brunner et al. 2017; Rand et al. 2017; Standen et al. 2017; Stockley et al. 2017; Turkbey et al. 2017; Lee et al. 2016a; Saposnik et al. 2016; Choi et al. 2014; Sin and Lee, 2013; Saposnik et al. 2010; Jang et al. 2005
1b	**Virtual reality bilateral arm training** may produce greater improvements in dexterity than **bilateral arm training**.	1	Lee et al. 2016b
1b	**Virtual reality interventions combined with FES** may not have a difference in efficacy when compared to **FES alone** for improving dexterity.	1	Lee et al. 2018
1b	**Virtual reality interventions on their own or combined with cathodal tDCS** may not have a difference in efficacy when compared to **cathodal tDCS** for improving dexterity.	1	Lee and Chun, 2014
1b	**Virtual reality training with a hand orthosis** may not have a difference in efficacy when compared to **conventional therapy** for improving dexterity.	1	Nijenhuis et al. 2017
1b	**Virtual reality training** may not have a difference in efficacy when compared to **mCIMT** for improving dexterity.	1	McNulty et al. 2015
2	**Asymmetric virtual reality training** may produce greater improvements in dexterity than **symmetric conventional training**.	1	Lee at al. 2014
2	**Virtual reality training** may produce greater improvements in dexterity than **no training**.	1	Jang at al. 2005

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1a	**Virtual reality interventions** may not have a difference in efficacy when compared to **conventional therapy, recreational therapy or sham interventions** for improving spasticity.	6	Oh et al. 2019; Askin et al. 2018; Faria et al. 2018; Ballester et al. 2017; Lee et al. 2013; Kiper et al. 2011
1b	**Virtual reality interventions on their own or combined with cathodal tDCS** may not have a difference in efficacy when compared to **cathodal tDCS** for improving spasticity.	1	Lee and Chun, 2014
1b	**Virtual reality training** may not have a difference in efficacy when compared to **mCIMT** for improving spasticity.	1	McNulty et al. 2015
2	**Asymmetric virtual reality training** may not have a difference in efficacy when compared to **symmetric conventional training** for improving spasticity.	1	Lee at al. 2014

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Virtual reality interventions** may not have a difference in efficacy when compared to **conventional therapy, recreational therapy or sham interventions** for improving muscle strength.	12	Lin et al. 2020; Oh et al. 2019; Askin et al. 2018; Faria et al. 2018; Ballester et al. 2017; Standen et al. 2017; Choi et al. 2016; Givon et al. 2016; Saposnik et al. 2016; Choi et al. 2014; Shin et al. 2014; Lee et al. 2013; Crosbie et al. 2012; Da Silva et al. 2011; Saposnik et al. 2010
1b	**Virtual reality bilateral arm training** may produce greater improvements in muscle strength than **bilateral arm training**.	1	Lee et al. 2016b
1b	**Virtual reality interventions on their own or combined with cathodal tDCS** may not have a difference in efficacy when compared to **cathodal tDCS** for improving muscle strength.	1	Lee and Chun, 2014
1b	**Virtual reality training with a hand orthosis** may not have a difference in efficacy when compared to **conventional therapy** for improving muscle strength.	1	Nijenhuis et al. 2017
2	**Asymmetric virtual reality training** may produce greater improvements in muscle strength than **symmetric conventional training**.	1	Lee at al. 2014

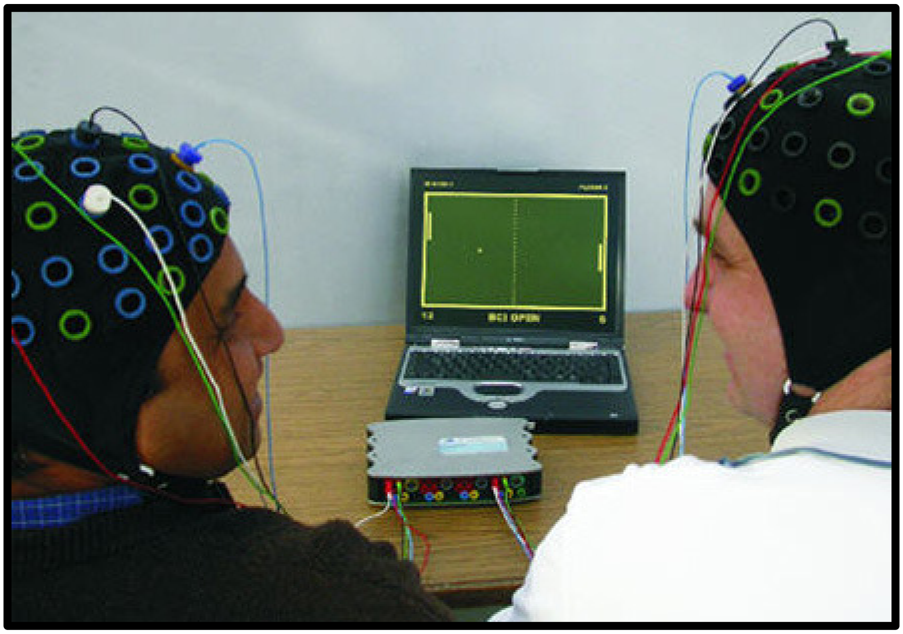
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Virtual reality** may not have a difference in efficacy when compared to **conventional care** for improving performance of activities of daily living.	32	Laffont et al. 2020; Lin et al. 2020; Hung et al. 2019; Norouzi-Gheidari et al. 2019; Ogun et al. 2019; Asfar et al. 2018; Faria et al. 2018; Kim et al. 2018; Kiper et al. 2018; Adie et al. 2017; Ballester et al. 2017; Brunner et al. 2017; Rand et al. 2017; Standen et al. 2017; Stockley et al. 2017; Turkbey et al. 2017; Choi et al. 2016; Kong et al. 2016; Lee et al. 2016; Saposnik et al. 2016; Bower et al. 2015; Simsek et al. 2015; Choi et al. 2014; Fan et al. 2014; Kiper et al. 2014; Shin et al. 2014; Duff et al. 2013; Lee et al. 2013; Da Silva et al. 2011; Kiper et al. 2011; Saposnik et al. 2010; Yavuzer et al. 2008
1b	**Virtual reality interventions combined with FES** may not have a difference in efficacy when compared to **FES alone** for improving performance of activities of daily living.	1	Lee et al. 2018
1b	**Virtual reality interventions on their own or combined with cathodal tDCS** may not have a difference in efficacy when compared to **cathodal tDCS** for improving performance of activities of daily living.	1	Lee and Chun, 2014
1b	**Virtual reality training with a hand orthosis** may not have a difference in efficacy when compared to **conventional therapy** for improving performance of activities of daily living.	1	Nijenhuis et al. 2017

1b	**Virtual reality training** may not have a difference in efficacy when compared to **mCIMT** for improving performance of activities of daily living.	1	McNulty et al. 2015

Key points

> Virtual therapy alone may not be more beneficial than conventional therapy for upper limb rehabilitation following stroke, however it may be beneficial for certain aspects of upper limb function when used in combination with conventional or other therapy approaches.

Brain Computer Interfaces



Adopted from: http://www.tech-faq.com/brain-computer-interface.html

Brain-computer interface (BCI) technology has only recently emerged as a potential rehabilitative treatment option following stroke. BCI records and decodes local brain activity during the performance of a motor movement (Van Dokkum et al. 2015). The decoded brain signals can be configured into visual, auditory or haptic feedback, and even for the control of external devices to help facilitate movement (Van Dokkum et al. 2015). BCI promotes the recruitment of brain areas involved in motor planning and execution and facilitates neural plasticity of neural networks using these areas, helping patients learn to generate normal brain activity or use brain activity to operate training devices (Van Dokkum et al. 2015). The evidence base for this intervention is still however in its infancy.

13 RCTs were inditified that examined brain computer interfaces for upper extremity motor rehabilitation poststroke.

One RCT examined a BCI combined with tDCS (Mane et al. 2019). One RCT examined a BCI combined with virtual reality (Lin et al. 2018). One RCT examined a BCI combined with motor imagery (Pichiorri et al. 2015). Three RCTs examined a BCI combined with FES (Young et al. 2016; Kim et al. 2016; Li et al. 2014). Six RCTs examined a BCI combined with robotics (Cheng et la. 2020; Wang et al. 2018; Ang et al. 2015; Curado et al. 2015; Ang et al. 2014; Ramos-Murguialday et al. 2013). One RCT compared a BCI with limb restraint or without (Mugler et al. 2019).

The methodological details and results of 13 RCTs evaluating BCI for the upper extremity motor rehabilitation in chronic stroke survivors are presented in Table 20.

Table 20. RCTs Evaluating Brain Computer Interfaces Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
BCI combined with tDCS		
Mane et al. (2019) RCT (8) N_{start}= 19 N_{end}= 19 TPS= Chronic	E: Brain-Computer Interface (BCI) + tDCS (dual (anode ipsilateral) (20min) C: BCI + sham Duration: 1hr, 5d/wk, 2wks	• Fugle-Meyers Assessment Upper Extremity: (-)
BCI combined with Virutal Reality		
Lin et al. (2018) RCT (6) N_{Start} =15 N_{End} =15 TPS=Chronic	E1: Motion tracking device+ VR game E2: Motion tracking device + brain-computer interface attention-monitoring electroencephalogram device + VR game C: Conventional therapy Duration: 35min/d, 3d/wk for 4wk	E1 vs E2 • Fugl-Meyer Assessment (exp2) E2 vs C • Fugl-Meyer Assessment (exp2) E1 vs C • Fugl-Meyer Assessment (-)
BCI combined with motor imagery		
Pichiorri et al. (2015) RCT (6) N_{start}=32 N_{end}=28 TPS=Subacute	E: Brain-computer interface + motor imagery C: Motor imagery Duration: 30min, 3x/wk, 4wks	• Fugl Meyer Assessment: (+exp) • Medical Research Council Scale: (+exp) National Institute of Health Stroke Scale: (+exp)
BCI combined with FES		
Young et al. (2016) RCT (5) N_{Start}=19 N_{End}=10 TPS=Chronic	E: Brain computer interface training + FES C: No training Duration: 120min/d for 9-15d	• Stroke Impact Scale (-) • Action Research Arm Test (-) • 9 Hole Peg Test (-)
Kim et al. (2016) RCT (7) N_{Start} =34 N_{End} =30 TPS=Chronic	E: FES with Action observation training and brain computer interface C: Conventional training Duration: 30min, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp) • Modified Barthel Index (+exp) • Wrist Flexion (+exp)
Li et al. (2014) RCT (6) N_{start}= 15 N_{end}= 14 TPS= Subacute	E: Brain-computer Interface (BCI) + Functional Electrical Stimulation (FES) C: Conventional therapy + FES Duration: 1-1.5hrs, 3x/wk, (rehab 5x/wk, 8wkS)	• Action Research Arm Test: (+exp) • Fugle-Meyers Assessment Upper Extremity: (-)
BCI Combined with Robotics versus Robotics		
Cheng et al. (2020) RCT (6) N_{start}= 11 N_{end}= 10 TPS= Chronic	E: EEG Motor Imagery Brain Computer Interface assisted Exo-glove C: Robot exo-glove only Duration: 30min standard, 90min, 3x/wk, 6wks	• Fugl Meyers Upper Extremity: (-) • Action Research Arm Test: (-)
Wang et al. (2018) RCT (6) N_{start}=24 N_{end}=24 TPS=Chronic	E: Action observation with EEG guided robot (hand exo) C: Robot (hand exo) Duration: 20x, 3-5x/wk, 5-7wks	• Fugl Meyer Assessment Upper Extremity: (-)
Ang et al. (2015) RCT (7) N_{Start}=26	E: Brain computer interface + MIT-Manus robotic training C: MIT-Manus robotic training	• Fugl-Meyer Assessment (-)

N_{End}=25 TPS=Chronic	Duration: 90min/d, 3d/wk for 4wk	
Curado et al. (2015) RCT (4) N_{start}= 32 N_{end}= Not reported TPS= Chronic	E: Brain Machine Interface + robotic orthosis C: Sham + robot Duration: 1hr, 5x/wk for 4wks	• EMG facilitation (-)
Ang et al. (2014) RCT (8) N_{Start}=22 N_{End}=21 TPS=Chronic	E1: Brain-computer interface + haptic knob (HK) robot E2: HK robot C: Standard Arm Therapy (SAT) Duration: 90min/d, 3d/wk for 6wk	E1 vs C • Fugl-Meyer Assessment (-) E2 vs C • Fugl-Meyer Assessment (-) E1 vs E2 • Fugl-Meyer Assessment (-)
Ramos-Murguialday et al. (2013) RCT (8) N_{Start}=32 N_{End}=30 TPS=Chronic	E: Brain machine interface (BMI) + arm and hand orthosis C: Sham BMI Duration: 5d/wk for 4wk	• Fugl Meyer Assessment (+exp) • Motor Activity Log (-) • Ashworth Scale (-)
BCI with limb restraint or not		

Mugler et al. (2019)
RCT (6)
N_{start}= 35
N_{end}= 32
TPS= Chronic
	E: Isometric myoelectric computer interface (60 or 90)
	C: Non-restrained myoelectric computer Interface (90)
	Duration: 60 or 90 min 3x/wk, for 6wks
		• Fugl-Meyers Assessment Upper Extremity: (-)
		• Wolf Motor Function Test - Time: (-)
		• Motor Activity Log
		  • Amount of Use: (-)
		  • Quality of Movement: (-)
		• Modified Ashworth Scale: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Brain Computer Interfaces

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Brain computer interface combined with tDCS** may not have a difference in efficacy compared to **BCI alone** for improving motor function.	1	Mane et al. 2019
1b	**Brain computer interfaces combined with virtual reality** may produce greater improvements in motor function than **virtual reality alone or conventional care**.	1	Lin et al. 2018
1b	**Brain computer interfaces combined motor imagery** may produce greater improvements in motor function than **motor imagery alone.**	1	Pichiorri et al.2015
1a	There is conflicting evidence about the effect of **brain computer interface combined with FES** to improve motor function when compared to **conventional care or FES**	3	Kim et al. 2016; Young et al 2016; Li et al. 2014
1a	**Brain computer interfaces combined with robotics** may not have a difference in efficacy compared to **robotics alone** for improving motor function.	4	Cheng et al. 2020; Ang et al. 2015; Ang et al. 2014; Ramos-

			Murguialday et al. 2013
1b	**Brain computer interfaces with limb restraint** may not have a difference in efficacy compared to **brain computer interfaces without limb restraint** for improving motor function.	1	Mugler et al. 2019

DEXTERITY

LoE	Conclusion Statement	RCTs	References
2	**Brain computer interface combined with FES** may not have a difference in efficacy compared to **conventional care or FES** for improving dexterity.	1	Young et al. 2016

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1b	**Brain computer interfaces combined with robotics** may not have a difference in efficacy compared to **robotics alone** for improving spasticity.	1	Ramos-Murguialday et al. 2013
1b	**Brain computer interfaces with limb restraint** may not have a difference in efficacy compared to **brain computer interfaces without limb restraint** for improving spasticity.	1	Mugler et al. 2019

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
1b	**Brain computer interfaces combined with FES** may produce greater improvements in range of motion than **conventional care of FES.**	1	Kim et al. 2016

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
1b	There is conflicting evidence about the effect of **brain computer interface combined with FES** to improve performance on activities of daily living when compared to **conventional care or FES**	2	Kim et al. 2016; Young et al 2016
1b	**Brain computer interfaces combined with robotics** may not have a difference in efficacy compared to **robotics alone** for improving activities of daily living.	1	Ramos-Murguialday et al. 2013
1b	**Brain computer interfaces with limb restraint** may not have a difference in efficacy compared to **brain computer interfaces without limb restraint** for improving performance on activities of daily living.	1	Mugler et al. 2019

STROKE SEVERITY

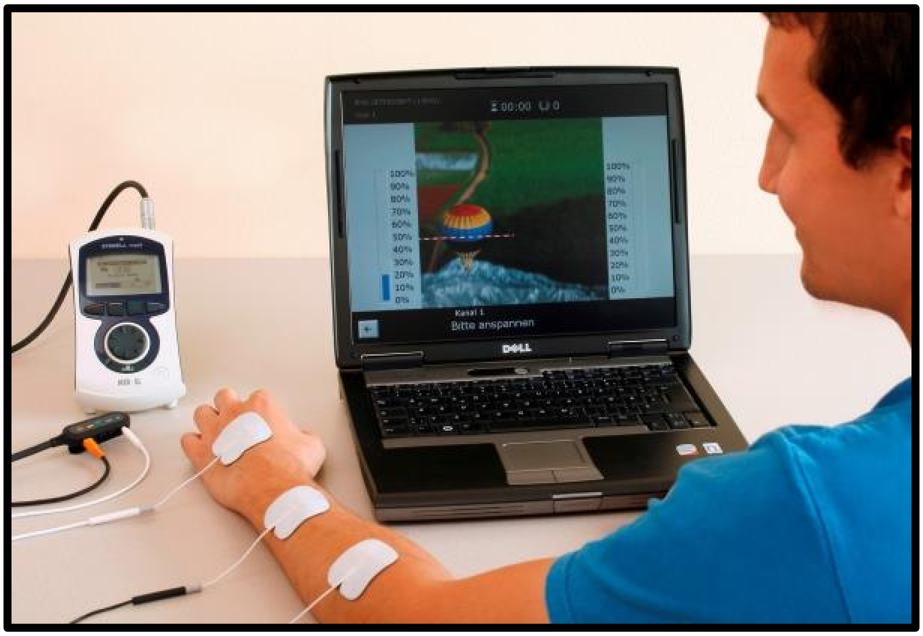
LoE	Conclusion Statement	RCTs	References
1b	**Brain computer interfaces combined motor imagery** may produce greater improvements in outcomes of stroke severity than **motor imagery alone.**	1	Pichiorri et al.2015

MUSCLE STRENGTH			
LoE	Conclusion Statement	RCTs	References
1b	**Brain computer interfaces combined motor imagery** may produce greater improvements in muscle strength than **motor imagery alone.**	1	Pichiorri et al.2015

Key points

The literature is mixed regarding brain-computer interface technology for upper limb motor rehabilitation following stroke, either on its own or combined with other therapies, but it may not be beneficial alone for other aspects of upper limb function.

EMG Biofeedback



Adopted from: http://www.udbhavphysiotherapy.com/services/emg-biofeedback/10

EMG biofeedback for the treatment of hemiparesis after stroke is performed through the application of electrodes onto specific muscle groups important for a desired motor movement to monitor electrical activity during muscle contraction (Nelson, 2007). It then provides feedback of muscle activity back to the patient by conversion of myoelectrical activity into visual and/or auditory information to increase patient awareness and facilitate motor movement (Sturma et al. 2018). EMG biofeedback is particularly useful for small muscle contractions that are otherwise unnoticeable kinaesthetically or visually in the earlier stages of stroke recovery or in cases of severe paresis (Nelson, 2007)

17 RCTs were inditified that examined EMG biofeedback for upper extremity motor rehabilitation poststroke.

15 RCTs were found comparing EMG-biofeedback to sham or conventional therapy (Kim et al. 2017; Garrido-Montenegro et al. 2016; Rayegani et al. 2014; Dogan-Aslan et al. 2012; Amagan et al. 2003; Wolf et al. 1994; Crow et al. 1989; Basmajian et al. 1987; Inglis et al. 2984; Basmajian et al. 1982; Prevo et al. 1982; Greenberg & Fowler, 1980; Hurd et al. 1980; Mroczek et al. 1978; Lee et al. 1976). Two RCTs examined EMG-biofeedback combined with an additional intervention (Cordo et al. 2013; Hemmen & Seelen, 2007).

The methodological details and results of 17 RCTs evaluating EMG biofeedback for the upper extremity motor rehabilitation are presented in Table 21.

Table 21. RCTs Evaluating EMG Biofeedback Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Kim et al. (2017) RCT (2) N_{Start} =30 N_{End} =30 TPS=Chronic	E: EMG Biofeedback and Conventional Therapy C: Conventional Therapy	• Fugl-Meyer Assessment (-) • Manual Function Test (-) • Functional Independence Measure (-)
Garrido-Montenegro et al. (2016) RCT (8) N_{Start} =14 N_{End} =14 TPS=Chronic	E: EMG/Biofeedback + conventional occupational therapy C: Occupational therapy Duration: 1 hr/d, 4d/wk for 4wk	• Barthel Index (+exp) • Instrumental Activities of Daily Living (+exp) • Action Research Arm Test (+exp) • Motor Activity Log (+exp)
Rayegani et al. (2014) RCT (5) N_{Start}=46 N_{End}=30 TPS=Chronic	E: OT + EMG + biofeedback E2: OT + neurofeedback C: OT Duration: 40 min/d, 5d/wk for 2wk	• Jebsen Taylor Hand Test (-)
Doğan-Aslan et al. (2012) RCT (5) N_{start}= 61 N_{end}= 40 TPS= Subacute/Chronic	E: Electromyographic feedback C: Conventional therapy Duration: 20min, 5x/wk, 3wks	• Upper Extremity Function Test: (-) • Fugl-Meyer Scale - wrist and hand subsections (+exp) • Wrist Extension-Active Range of Motion: (-) • Barthel Index: (+exp) • Brunstromm stage: (+exp) • Modified Ashworth Scale: (+exp)
Armagan et al.(2003) RCT (7) N_{start}=27 N_{end}=27 TPS=Subacute	E: EMG/Biofeedback Therapy C: Sham EMG/biofeedback Duration: 45 min/d, 2d/wk for 5wk	• Active range of motion (+exp) • Changes in EMG surface potentials (+exp) • Brunnstrom stages (-) • Complex movement (-)
Wolf et al. (1994) RCT (6) N_{start}=16 N_{end}=16 TPS=Chronic	E: EMG biofeedback C: Conventional Therapy Duration: 25min, 10x over 6wks, 2-4/wk	• Active Range of Motion: (-) • Passive Range of Motion: (-) • Reaching task: (-)
Crow et al. (1989) RCT (8) N_{start}=40 N_{end}=40 TPS=Subacute	E: EMG/Biofeedback Therapy C: Sham EMG/biofeedback Duration: *Not Specified*	• Action Research Arm test (+exp)
Basmajian et al. (1987) RCT (6) N_{start}=30 N_{end}=29 TPS=Chronic	E: EMG/Biofeedback Therapy C: Physical Therapy using neuro-facilitatory Duration: *Not Specified*	• Upper extremity function test (-) • Finger Oscillation test (-)
Inglis et al. (1984) RCT (5) N_{start}=30 N_{end}=30 TPS=Chronic	E: EMG/Biofeedback+ physiotherapy C: Physiotherapy Duration: *Not Specified*	• Active range of motion (+exp) • Brunnstrom (+exp) • Muscle strength (+exp)
Basmajian et al.(1982) RCT (6) N_{start}=37 N_{end}=37 TPS=Chronic	E: EMG/Biofeedback Therapy C: Physical Therapy using neuro-physiological approach Duration: *Not Specified*	• Upper extremity function test (-) • Min rate of manipulation test (-) • 9-hole peg test (-)

Prevo et al. (1982) RCT (3) N_{start}=28 N_{end}=18 TPS=Subacute	E: EMG/Biofeedback Therapy C: Conventional Therapy Duration: 30 min/d, 2d/wk for 6wk	• Proximal and distal agonists (-)
Greenberg & Fowler (1980) RCT (5) N_{start}=20 N_{end}=20 TPS=Acute	E: EMG/Biofeedback Therapy C: Conventional Occupational Therapy Duration: *Not Specified*	• Active elbow extension (-)
Hurd et al. (1980) RCT (6) N_{start}=24 N_{end}=24 TPS=Chronic	E: Actual myofeedback C: Simulated myofeedback Duration: *Not Specified*	• Active range of motion (-) • Muscle activity (-)
Mroczek et al. (1978) RCT (5) N_{start}=9 N_{end}=9 TPS=Chronic	E: EMG biofeedback C: Physical therapy Duration: *Not Specified*	• Range of Motion (-)
Lee et al. (1976) RCT (4) N_{start}=18 N_{end}=18 TPS=Acute	E1: True myofeedback E2: Placebo myofeedback C: No myofeedback with conventional training. Duration: *Not Specified*	• Peak amplitude (-)
EMG biofeedback combined with additional interventions		
Cordo et al. (2013) RCT (6) N_{Start}=46 N_{End}=43 TPS=Chronic	E1: AMES robot + torque biofeedback E2: AMES robot + EMG biofeedback Duration: 30 min/d, 3d/wk for 10 wk	• Fugl Meyer Score (-) • Flexion torque strength (+exp) • Extension strength (-) • Box and Block Test (-) • Stroke Impact Scale (-)
Hemmen & Seelen (2007) RCT (7) N_{start}=27 N_{end}=27 TPS=Subacute	E: EMG biofeedback + mental practice C: Conventional electrostimulation Duration: 30 min/d, 5d/wk for 3 mo	• Fugl-Meyer Score (-) • Action Research Arm test (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about EMG Biofeedback

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**EMG biofeedback** may not have a difference in efficacy when compared to **sham feedback or conventional therapy** for improving motor function.	9	Thielbar et al. 2017; Kim et al. 2017; Garrido-Montenegro et al. 2016; Rayegani et al. 2014; Dogan-Aslan et al. 2012; Wolf et al. 2994; Crow et al. 1989; Basmajian et al. 1987; Basmajian et al. 1982
1b	**EMG biofeedback combined with arm robotics** may not have a difference in efficacy when compared to **torque biofeedback combined with arm robotics** for improving motor function.	1	Cordo et al. 2013

1b	**EMG biofeedback combined with mental practice** may not have a difference in efficacy when compared to **conventional electrostimulation** for improving motor function.	1	Hemmen and Seelen, 2007

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**EMG biofeedback** may not have a difference in efficacy when compared to **sham feedback or conventional therapy** for improving dexterity.	1	Basmajian et al. 1982
1b	**EMG biofeedback combined with arm robotics** may not have a difference in efficacy when compared to **torque biofeedback combined with arm robotics** for improving dexterity.	1	Cordo et al. 2013

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**EMG biofeedback** may not have a difference in efficacy compared to **sham feedback or conventional therapy** for improving spasticity.	3	Dogan-Aslan et al. 2012; Prevo et al.1982; Greenberg and Fowler, 1980

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**EMG biofeedback** may not have a difference in efficacy when compared to **sham feedback or conventional therapy** for improving range of motion.	7	Dogan-Aslan et al. 2012; Armagan et al. 2003; Wolf et al. 1994; Inglis et al. 1984; Greenberg and Fowler, 1980; Hurd et al. 1980; Mroczek et al. 1978

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **EMG biofeedback** to improve performance on measures of stroke severity when compared to **sham feedback or conventional therapy**.	2	Armagan et al. 2003; Inglis et al. 1984

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**EMG biofeedback** may produce greater improvements in performance of activities of daily living than **sham feedback or conventional therapy**.	4	Kim et al. 2017; Thielbar et a. 2017; Garrido-Montenegro et al. 2016; Dogan-Aslan et al. 2012
1b	**EMG biofeedback combined with arm robotics** may not have a difference in efficacy when compared to	1	Cordo et al. 2013

	torque biofeedback combined with arm robotics to improve performance of activities of daily living.		

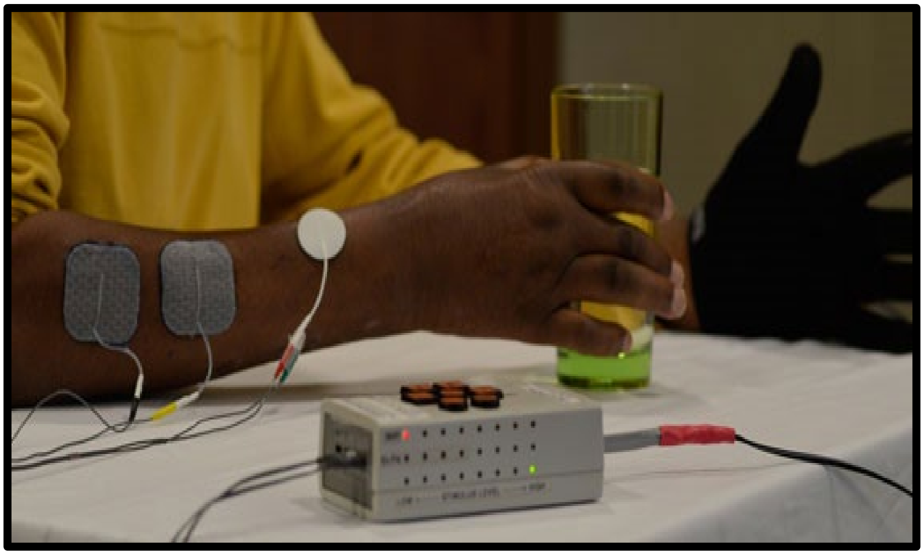
MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **EMG biofeedback** to improve muscle strength when compared to **sham feedback or conventional therapy**.	2	Thielbar et al. 2017; Inglis et al. 1984
1b	There is conflicting evidence about the effect of **torque biofeedback combined with arm robotics** to improve muscle strength when compared to **EMG biofeedback combined with arm robotics**.	1	Cordo et al. 2013

Key points

EMG biofeedback either alone or in combination with other therapies, may not be beneficial for upper limb rehabilitation following stroke.

Sensorimotor stimulation

Neuromuscular Electrical Stimulation (NMES)



Adopted from: http://fescenter.org/patient-resources/current-clinical-trials/stroke-programs/hand-function-control-2/hand-function-control/

Neuromuscular electrical stimulation (NMES) is a technique used to generate muscle contractions in regions affected by hemiparesis by stimulating lower motor neurons involved in muscle movement through transcutaneous application of electrical currents (Monte-Silva et al. 2019; Allen & Goodman 2014). Three forms of NMES are available:

1. Cyclic NMES in which a muscle is repetitively stimulated at near maximum contraction on a pre-set schedule and patient participation is passive (Nascimento et al. 2013);
2. Electromyography (EMG) triggered NMES, a target muscle is directly controlled or triggered by volitional EMG activity from the target or a different muscle to elicit a desired stimulation (Monte-Silva at al. 2019);
3. Functional electrical stimulation (FES), which refers to the application of NMES to assist voluntary during a functional task (Eraifej et al. 2017).

A total of 83 unique RCTs were found for using NMES to enhance upper extremity motor rehabilitation.

Interventions in eight RCTs were cyclic NMES compared to sham stimulation or conventional rehabilitation (Tilkici et al. 2017; Baygutalp et al. 2014; De Jong et al. 2013; Malhotra et al. 2013; Sahin et al. 2012; Lin and Yan, 2011; Mann et al. 2005; Powell et al. 1999; Chae et al. 1998; King et al. 1996; Faghri et al. 1994).

Three RCTs looked at NMES and stretching compared to these interentions alone (De jong et al. 2013; Sahin et al. 2012; King et al. 1996)

Four RCTs also looked at the combination of cyclic NMES with: robotics (Barker et al. 2017; Miyasaka et al. 2016; Lee et al. 2015; Hayward et al. 2013), and one with repetitive task training (Gharib et al. 2014).

12 RCTs looked at EMG-triggered NMES to sham stimulation or conventional rehabilitation (Kirac-Unal et al. 2019; Kwakkel et al. 2016; Dorsch et al. 2014; Shin et al. 2008; Bhatt et al. 2007; Gabr et al. 2005; Kimberley et al. 2004; Cauraugh and Kim, 2003; Cauraugh et al. 2000; Francisco et al. 1998; Heckman et al. 1997; Bowman et al. 1979).

Three RCTs looked at the combination of EMG-triggered NMES with: robotics (et al. (Qian et al. 2017; Hu et al. 2015; Barker et al. 2008), two RCTs looked at mirror therapy (Schick et al. 2017; Kojima et al. 2014), or one at a splint (Shindo et al. 2011).

14 RCTs looked at the effects of FES compared to sham stimulation or conventional rehabilitation (Demir et al. 2018; Pan et al. 2018; Carda et al. 2017; Marquez-Chin et al. 2017; Yuzer et al. 2017; Shimodozono et al. 2014; Karakus et al. 2013; Mangold et al. 2009; Hara et al. 2008; Thrasher et al. 2008; Hara et al. 2006; Ring and Rosenthal, 2005; Popovic et al. 2003; Faghri and Rodgers, 1997).

Ten RCTs looked at the combination of FES with: robotics (Daly et al. 2019), cycling Fes (Karaahmet et al. 2019), physical therapy (Khan et al. 2019) mirror therapy (Mathieson et al. 2018; Kim et al. 2015), botulinum toxin (Weber et al. 2010), action observation paired with brain computer interface (Kim et al. 2016), bilateral arm training (Chan et al. 2009), and task-oriented therapy (Jonsdottir et al. 2017; Alon et al. 2007).

Fourteen RCTs looked at the effect of different NMES techniques compared to each other (Knutson et al. 2019; Zheng et al. 2019; Cunning ham et al. 2018; Jeon et al. 2017; Knutson et al. 2016; Wilson et al. 2016; Boyaci et al. 2013; You et al. 2013; Knutson et al. 2012; Chae et al. 2009; De Kroon and Ijzerman, 2008; Hemmen and Seelen, 2007; Cauruahg et al. 2005; Cauruahg et al. 2003)

Three RCTs looked at differing intensity of NMES (Page et al. 2012; Hsu et al. 2010; Kowalczewski et al. 2007), high versus low frequency cyclic NMES (Doucet and Griffin, 2013), and early versus delayed FES (Popovic et al. 2004).

One study looked at NMES combined with thermal stimulation (Chen et al. 2019), bilateral arm training (Cauruagh et al. 2011), mental practice (Park et al. 2019). One study looked at cNMES comared to EMG bridging (Zhou et al. 2017)

Two studies examined the combination of FES and brain computer interface (Young et al. 2016; Li et al. 2014).

The methodological details and results of all 67 RCTs are presented in table 22.

Table 22. Summary of RCTs Evaluating NMES for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Cyclic NMES versus conventional therapy		
Tilkici et al. (2017) RCT (6) N_{Start} =40 N_{End} =40 TPS=Chronic	E: Neuromuscular Electrical Stimulation C: Conventional Therapy Duration: 30min/d, 5d/wk for 3wk	• Modified Ashworth Scale (+exp) • Wrist Extension (+exp) • Brunnstrom's Recovery Stages (-) • Modified Ashworth Scale (-) • Fugl-Meyer Assessment (-) • Duruoz Hand Index (-) • Functional Independence Measure (-)
Baygutalp et al. (2014) RCT (5) N_{Start}=30 N_{End}=30 TPS=Chronic	E: NMES + conventional therapy C: Conventional therapy Duration: 60min/d, 5d/wk for 3wk	• Modified Ashworth Scale (-) • Barthel Index (-) • Brunnstrom's Recovery Stages (-)
Malhotra et al. (2013) RCT (5) N_{Start}=90 N_{End}=65 TPS=Acute	E: NMES C: Conventional therapy Duration: 30 min (2x/d), 5d/wk for 6 wk	• Passive Range of Motion (-)
Lin & Yan (2011) RCT (6) N_{stat}=46 N_{end}=37 TPS=Acute	E: Cyclic NMES + standard rehabilitation C: Standard rehabilitation Duration: 30 min/d, 5d/wk for 3 wk	• Fugl-Meyer Assessment (+exp) • Barthel Index (+exp)
Mann et al. (2005) 5 (RCT) N_{start}=22 N_{end}=22 TPS=Chronic	E: Neuromuscular Electrical Stimulation C: Passive Extension Exercises Duration: 10-30min (2x per day) for 12wk	• Action Research Arm Test (+exp)
Powell et al. (1999) RCT (7) N_{start}=60 N_{end}=48 TPS=Subacute	E: Cyclic electrical stimulation + standard rehabilitation C: Standard rehabilitation Duration: 30 min (3x per day), 3d/wk for 8 wk	• Action Research Arm test (+exp)
Chae et al. (1998) RCT (6) N_{start}=46 N_{end}=28 TPS=Subacute	E: Cyclic NMES C: Sham stimulation + routine rehabilitation Duration: 1 hr/d, 5d/wk for 3 wk	• Fugl-Meyer Assessment (+exp)
Faghri et al. (1994) RCT (4) N_{start}=26 N_{end}=NR TPS=NR	E: Cyclic NMES + conventional therapy C: Conventional Therapy Duration: 1.5-6h/d for 6wk	• Arm tone (+exp)
NMES and NMES combined with stretching versus stretching alone or sham		
De Jong et al. (2013) RCT (8) N_{start}=46 N_{end}=46 TPS=Subacute	E: Arm stretch positioning + NMES C: Sham stretch positioning + Sham NMES Duration: 45 min (2x/d), 5d/wk, for 8 wk	• Modified Ashworth Scale (-)
Sahin et al. (2012) RCT (5) N_{start}=42 N_{end}=38	E: Stretching + NMES C: Stretching Duration: 5d/wk for 4wk	• Modified Ashworth Scale (+exp)

TPS=Chronic		
King et al. (1996) RCT (4) N_{start}=21 N_{end}=NR TPS=Chronic	E: NMES C: Passive stretch Duration: *Not reported*	• Tone reduction (+exp)
Cyclic NMES combined with robotics		
Barker et al. (2017) RCT (7) N_{Start} =50 N_{End} =38 TPS=Subacute	E1: SMART Arm Training + Outcome-Triggered Electrical Stimulation + Conventional Therapy E2: SMART Arm Training + Conventional Therapy C: Conventional Therapy Duration: 60min/d, 5d/wk for 4wk	E1 vs E2 vs C • Motor Assessment Scale (-) • Modified Ashworth Scale (-) • Triceps Strength (-)
Miyasaka et al. (2016) RCT (5) N_{Start}=30 N_{End}=30 TPS=Subacute	E: NMES + robotic training C: Robotic training Duration: 1 hr/d, 5d/wk for 2 wk	• Fugl-Meyer Assessment (-) • Range of Motion (-)
Lee et al. (2015) RCT (8) N_{Start}=39 N_{End}=39 TPS=Chronic	E: NMES + robotic therapy C: Sham NMES + robotic therapy Duration: 90-100min/d, 5d/wk for 4wk	• Modified Ashworth Scale (+exp) • Wolf Motor Function Test (+exp) • Stroke Impairment Scale (+exp) • Fugl-Meyer Assessment (-) • Motor Activity Log (-)
Hayward et al. (2013) RCT (6) N_{start}=8 N_{end}=8 TPS=Acute	E: SensoriMotor Active Rehabilitation Training (SMART) with outcome trigger electrical stimulation (OT-stim) C: SensoriMotor Active Rehabilitation Training (SMART) Duration: 1 hr/d, 5d/wk for 4 wk	• Motor Assessment Scale (-) • Upper Arm Function (-)
Cyclic NMES with repetitive task training		
Gharib et al. (2014) RCT (9) N_{Start}=40 N_{End}=40 TPS=Chronic	E: Cyclic NMES (20Hz) + repetitive task training C: Sham electrical stimulation + repetitive task practice Duration: 1 hr/d, 4d/wk for 8 wk	• Modified Ashworth Scale (+exp) • Jebsen Taylor Hand Function Test (+exp) • Range of Motion (+exp)
EMG-triggered NMES compared to sham stimulation		

Kirac-Unal et al. (2019)
RCT (7)
N_{start}= 27
N_{end}= 23
TPS= Acute/Subacute
	E: Task oriented
	EMG-triggered ES therapy (Nu-Tek Maxi plus 2 Dual Channel EMG ETS device) with conventional physical therapy
	C: Conventional therapy
	Duration: 1 hr 15 min/session (exp) 1 hr/ session (con). 5x/wk for 4 wk for 3 months.
		• Action Research Arm Test:
		  • Grasp: (+exp)
		  • Grip: (+exp)
		  • Pinch: (+exp)
		  • Gross movement: (-)
		• Functional Independence Measure: (-)
		• Brunnstrom Recovery Stages
		  • Upper Extremity: (-)
		  • Hand: (+exp)
		• Grip Strength: (+exp)
		• Stroke Impact Scale
		  • Strength: (-)
		  • Activities of Daily Living: (-)
		  • Hand Function: (-)

Kwakkel et al. (2016) RCT (7) N_{Start}=159 N_{End}=159 TPS=Acute	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	E1 vs C1 • Action Research Arm Test: (-) • Fugl-Meyer Assessment: (-) • Motricity Index: (-) • Stroke Impact Scale: (-) • Wolf Motor Function Test: (-) • Motor Activity Log: (-) E2 vs C2 • Action Research Arm Test: (+exp$_2$)

	extension early after stroke (received usual care) Duration: 1 hr/d, 3d/wk for 3 wk	• Fugl-Meyer Assessment: (-) • Motricity Index: (-) • Stroke Impact Scale: (+exp2) • Wolf Motor Function Test: (-) • Motor Activity Log: (-)
Dorsch et al. (2014) RCT (7) N_{Start}=33 N_{End}=30 TPS=Acute	E: EMG-triggered NMES C: Usual therapy Duration: 30 min/d, 6d/wk for 8wk	• Modified Ashworth Scale (-) • Manual Muscle Test (-)
Shin et al. (2008) RCT (4) N_{start}= 14 N_{end}= 14 TPS= Chronic	E: EMG-NMES C: Conventional control Duration: 30min, 5x/wk, 10wks	• Box and Block Test (+exp) • Strength (+exp) • Accuracy (+exp) • Delay in onset and offset (+exp, +exp)
Bhatt et al. (2007) RCT (3) N_{start}=20 N_{end}=18 TPS=Chronic	E1: EMG-triggered NMES E2: Tracking training E3: EMG-triggered NMES + tracking training Duration: 1 hr/d, 5d/wk, for 2 wk	E1 vs E2 vs E3 • Jebson Taylor Hand Function Test (-) • Box & Block Test (-)
Gabr et al. (2005) RCT (4) N_{start}=12 N_{end}=12 TPS=Chronic	E: EMG-triggered NMES C: Home exercise Duration: 45 min/d, 3d/wk for 4 wk	• Fugl Meyer Score (+exp) • Action Research Arm Test (-)
Kimberley et al. (2004) RCT (7) N_{start}=16 N_{end}= 16 TPS=Chronic	E: EMG-triggered NMES C: Sham Duration: 3hr/d, 5d/wk for 3 wk	• Box & Block test (+exp) • Motor Activity Log (+exp) • Jebsen Taylor Hand Function Test (+exp)
Cauraugh and Kim (2003) RCT (5) N_{start}=34 N_{end}=31 TPS=Chronic	E1: EMG-triggered NMES + blocked practice E2: EMG-triggered NMES + random practice C: Conventional therapy Duration : 90 min/d, 2d/wk (24hr in between) for 2 wk	E1/E2 vs C • Box and Block Test (+exp1, +exp2) • Sustained wrist/finger contraction (+exp1, +exp2) E1 vs E2 • Box and Block Test (-) • Sustained wrist/finger contraction (-)
Cauraugh et al. (2000) RCT (4) N_{start}=11 N_{end}=11 TPS=Chronic	E: EMG-triggered NMES + passive range of motion + stretching exercises C: Passive range of motion + stretching exercises Duration: 30 min/d, 4d/wk, for 3 wk	• Box and Block test (+exp) • Motor Assessment scale (-) • Fugl-Meyer upper extremity (-)
Francisco et al. (1998) RCT (3) N_{start}=9 N_{end}=9 TPS=Acute	E: EMG-triggered NMES + standard therapy C: Conventional Therapy Duration: 30 min (2x per day), 5d/wk for 4 wk	• Fugl-Meyer Assessment (+exp) • Functional Independence Measure (+exp)
Heckman et al. (1997) RCT(4) N_{start}=28 N_{end}=28 TPS=Subacute	E: EMG-triggered ES + standard therapy C: Standard therapy Duration: 5d/wk for 4wk	• Hand extension (+exp) • Muscle tone (+exp)
Bowman et al. (1979) RCT (3) N_{start}=30 N_{end}=NR TPS=NR	E: Conventional therapy + positional feedback electrical stimulation therapy C: Conventional Therapy Duration: 30min (2x per day), 5d/wk for 4wk	• Range of motion (+exp)
EMG-triggered NMES combined with robotics		

Qian et al. (2017) RCT (6) N_{Start} =24 N_{End} =24 TPS=Acute-Subacute	E: Electromyography-Driven Neuromuscular Electrical Stimulation-Robot Arm C: Conventional Therapy Duration: 40min, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Modified Ashworth Scale (+exp) • Action Research Arm Test (-) • Functional Independence Measure (-)
Hu et al. (2015) RCT (6) N_{Start}=26 N_{End}=26 TPS=Chronic	E: EMG-driven NMES robot C: EMG-driven robot Duration: 30 min/d, 4d/wk for 5 wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (+exp) • Modified Ashworth Scale (-)
Barker et al. (2008) RCT (7) N_{start}=33 N_{end}=30 TPS=Chronic	E1: SMART Arm + EMG-triggered NMES E2: SMART Arm C: Conventional therapy Duration: 1 hr/d, 3d/wk for 4 wk	E1/E2 vs C • Modified Ashworth Scale: (+exp_1, +exp_2)
EMG-triggered NMES with mirror therapy		
Schick et al. (2017) RCT (7) N_{Start} =33 N_{End} =32 TPS=Subacute	E: Bilateral Electromyography-Neuromuscular Electrical Stimulation with Mirror Therapy C: Electromyography-Neuromuscular Electrical Stimulation Duration: 30min/d, 5d/wk for 3wk	• Fugl-Meyer Assessment (-) • Rivermead Assessment of Somatosensory Performance (-) • Box and Block Test (-) • Barthel Index (-)
Kojima et al. (2014) RCT crossover (7) N_{Start}=13 N_{End}=13 TPS=Subacute	E: Mirror therapy + EMG-triggered NMES first C: Mirror therapy + EMG-triggered NMES delayed Duration: 30 min/d, 4d/wk for 8 wk	• Fugl-Meyer Assessment (+exp) • Hand range of Motion (+exp)
EMG-triggered NMES with splint		
Shindo et al. (2011) RCT (6) N_{start}=24 N_{end}=20 TPS=Subacute	E: EMG-triggered NMES + splint C: Splint Duration: 45 min/d, 3d/wk for 3 wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (-) • Action Research Arm Test (+exp)
FES versus conventional therapy		
Demir et al. (2018) RCT (4) N_{Start} =29 N_{End} =17 TPS=Chronic	E: Functional Electrical Stimulation and Conventional Physiotherapy C: Conventional Physiotherapy Duration: 15-45min (2x per day), 5d/wk for 8wks	• Fugl-Meyer Assessment (-) • Modified Ashworth Scale (-) • Motor Activity Log-28 (-) • Jebsen-Taylor Hand Function Test (-)
Pan et al. (2018) RCT (6) N_{Start} =12 N_{End} =12 TPS=Subacute	E: Fuinctional Electrical Stimulation C: Sham Electrical Stimulation Duration: 40min/d, 2d/wk for 8wk	• Fugl-Meyer Assessment (-)
Carda et al. (2017) RCT-Crossover (7) N_{Start} =11 N_{End} =11 TPS=Chronic	E: Functional Electrical Stimulation C: Conventional Therapy Duration: 90min/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp) • Wolf Motor Function Test (-) • Resistance to Passive Movement Scale (-)
Marquez-Chin et al. (2017) RCT (7) Secondary Analysis N_{Start} =21 N_{End} =21 TPS=Subacute	E: Functional Electrical Stimulation C: Conventional Therapy Duration: 1h/d, 5d/wk for 8wk	• Functional Independence Measure (+exp) • Fugl-Meyer Assessment (+exp)
Yuzer at al. (2017) RCT (6) N_{Start} =30 N_{End} =30 TPS=Subacute	E: Functional Electrical Stimulation and Conventional Therapy C: Conventional Therapy Duration: 30min/d, 5d/wk for 4wk	• Barthel Index (+exp) • Brunnstrom Stages (-) • Upper Extremity Performance Test (-)

Shimodozono et al. (2014) RCT (8) N_{Start}=27 N_{End}=24 TPS= Subacute	E1: Continuous NMES + repetitive facilitative exercise E2 Repetitive facilitative exercise C: Conventional therapy Duration: 40 min/d, 5d/wk for 4 wk	• Fugl-Meyer Assessment (+exp_2) • Elbow extension (+exp_2) • Shoulder flexion (-) • Wrist flexion (-)
Karakus et al. (2013) RCT (8) N_{Start}=28 N_{End}=28 TPS= Subacute	E: FES + standard rehabilitation C: Standard rehabilitation Duration: 30min/d, 5d/wk for 2wk	• Brunnstrom recovery stages (+exp) • Motricity Index (+exp) • Modified Ashworth Scale (-)
Mangold et al. (2009) RCT (5) N_{start}=23 N_{end}=23 TPS=Subacute	E: FES C: Conventional therapy Duration: 1 hr/d, 3d/wk for 4 wk	• Barthel Index (-) • Chedoke McMaster Stroke Assessment (-)
Hara et al. (2008) RCT (5) N_{start}=20 N_{end}=20 TPS=Chronic	E: FES C: Conventional therapy Duration: 45 min/d, 6d/wk for 4 wk	• Range of motion (+exp) • Modified Ashworth Scale (+exp)
Thrasher et al. (2008) RCT (5) N_{start}=21 N_{end}=19 TPS=Subacute	E: FES + conventional therapy C: Conventional therapy Duration: 30 min/d, 4d/wk for 12 wk	• Rehabilitation Engineering Laboratory Hand Function Test (+exp)
Hara et al. (2006) RCT (4) N_{start}=14 N_{end}=14 TPS=Chronic	E: FES C: Conventional therapy Duration: 1 hr/d, 2d/wk for 4 mo	• Modified Ashworth Scale (-) • Range of Motion (+exp)
Ring & Rosenthal (2005) RCT(6) N_{start}=22 N_{end}=NR TPS=Subacute	E: Neuroprosthetic FES C: Conventional therapy Duration: 25 min/d, 3d/wk for 5 wk	• Modified Ashworth Scores (+exp) • Box & Block test (+exp) • Jebsen Taylor Hand Function test (+exp)
Popovic et al. (2003) RCT (6) N_{start}=28 N_{end}=28 TPS=Subacute	E: FES C: Standard therapy Duration: 30 min/d, 7d/wk for 3 wk	• Upper extremity performance test (+exp)
Faghri & Rodgers (1997) RCT (4) N_{start}=26 N_{end}=26 TPS=Acute	E: FES + conventional therapy C: Conventional therapy Duration: 6 hr/d, 6d/wk for 6 wk	• Range of motion (+exp) • Shoulder muscle tone (+exp)
FES Techniques vs Eachother		
de Kroon et al. (2004) RCT (6) N_{start}= 30 N_{end}= 27 TPS= Chronic	E: Electrical stimulation of flexors and extensors C: Electrical stimulation of extensors only Duration: 20-60min increased over time, 3x/d, 6wks	• Action Arm Research test: (-) • Grip strength hand ratio: (-) • Motricity index: (-) • Ashworth Scale: (-) • Active Range of Motion, Wrist: (-)
FES combined with additional therapies		

Daly et al. (2019)
RCT (5)
N_{start}= 38
N_{end}= 31
TPS= Chronic
	E1: Distal (wrist/hand Functional Electrical Stimulation)
	E2: Proximal (Shoulder/elbow) (Functional Electrical Stimulation + inMotion robot)
	C: Whole arm
	Duration: 1.5hrs, 5x/wk, 12wks
		E1 Vs C
		• Fugl Meyers Assessment Upper Extremity: (-)
		• Arm Motor Assessment Test
		  • Time: (-)
		  • Function (-)
		E2 Vs C
		• Fugl Meyers Assessment Upper Extremity: (-)

		• Arm Motor Assessment Test
		  • Time: (-)
		  • Function (-)
		E1 Vs E2
		• Fugl Meyers Assessment Upper Extremity: (-)
		• Arm Motor Assessment Test
		  • Time: (-)
		  • Function (-)

Karaahmet et al. (2019) RCT (5) N_{start}= 30 N_{end}= 21 TPS= Subacute	E: Cycling Functional electrical stimulation C: Conventional care Duration: Rehab 30min, 5x/wk for 4wks	• Acromiohumeral Distance: (-) • Brunnstrom: (-) • Fugle-Meyers Assessment Upper Extremity: (-) • Frenchay Arm Test: (-) • Functional Independence Measure: (-)
Khan et al. (2019) RCT (8) N_{start}= 60 N_{end}= 60 TPS= Chronic	E: Theta Burst Stimulation (TBS) + Physical therapy (PT) E2: Functional Electrical Stimulation (FES) + Physical therapy (PT) C: Physical Therapy (PT) Duration: 4wks, 3x stimulation plus 5x physical therapy for 30min	E1 Vs C • Fugle-Meyers Assessment: (+exp1) • Modified Rankin Scale: (+exp1) • Barthel Index: (+exp1) • National Institute of Health Stroke Scale: (+exp1) E2 Vs C • Fugle-Meyers Assessment: (+exp2) • Modified Rankin Scale: (+exp2) • Barthel Index: (+exp2) • National Institute of Health Stroke Scale: (+exp2) E1 Vs E2 • Fugle-Meyers Assessment: (-) • Modified Rankin Scale: (-) • Barthel Index: (-) • National Institute of Health Stroke Scale: (-)
Mathieson et al. (2018) RCT (8) N_{Start} =50 N_{End} =47 TPS=Acute	E1: Functional Electrical Stimulation E2: Mirror Therapy E3: Functional Electrical Stimulation with Mirror Therapy Duration: 30min (2x per day), 5d/wk for 3wk	E1 vs E2 • Action Research Arm Test (+exp) • Fugl-Meyer Assessment (+exp) • Nottingham Extended Activities of Daily Living Test (- • Functional Independence Measure (-)
Jonsdottir et al. (2017) RCT (5) N_{Start} =82 N_{End} =45 TPS=Subacute	E: Myoelectric Continuous Control of Functional Electrical Stimulation Task-Oriented Therapy C: Task Oriented Therapy Duration: 45min/d, 5d/wk for 5-6wk	• Action Research Arm Test (-) • Fugl-Meyer Assessment (-) • Disability of the Arm, Shoulder, and Hand Questionnaire (-)
Kim et al. (2016) RCT (7) N_{Start} =34 N_{End} =30 TPS=Chronic	E: FES with Action observation training and brain computer interface C: Conventional training Duration: 30min, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp) • Modified Barthel Index (+exp) • Wrist Flexion (+exp)
Kim et al. (2015) RCT (5) N_{Start}=33 N_{End}=29 TPS=Chronic	E1: FES with biofeedback + mirror therapy E2: FES + mirror therapy C: Conventional rehabilitation Duration: 30 min/d, 5d/wk for 4 wk	E1 vs C • Functional Independence Measure (+exp) • Jebsen Taylor Hand test (+exp) • Manual Muscle Test (+exp) • Box and Block Test (+exp) • Wrist Extension (+exp) • Grip strength (-) • Modified Ashworth Scale (-) E1 vs E2 • Functional Independence Measure (-) • Jebsen Taylor Hand test (+exp) • Manual Muscle Test (+exp) • Box and Block Test (+exp) • Wrist Extension (+exp) • Grip strength (+exp)

		• Modified Ashworth Scale (-)
Weber et al. (2010) RCT (7) N_{start}=23 N_{end}=23 TPS=Chronic	E: FES + botulinum toxin-A + home based exercise program C: Botulinum toxin-A + home-based exercise program Duration: 1 hr/d, 5d/wk for 4 wk	• Motor Activity Log (-) • Action Research Arm Test (-)
Chan et al. (2009) RCT (7) N_{start}=20 N_{end}=20 TPS=Chronic	E: Bilateral arm training + FES C: Bilateral arm training + sham FES Duration: 70 min/d, 3d/wk for 5 wk	• Fugl-Meyer Assessment (+exp) • Functional test for the Hemiplegic Upper Extremity (+exp) • Modified Ashworth Scale (-)
Alon et al. (2007) RCT (5) N_{start}=15 N_{end}=15 TPS=Subacute	E: FES + task specific training C: Task specific training Duration: 30 min(2x/d), 5d/wk for 12 wk	• Box and Block Test (+exp) • Jebsen-Taylor light object lift (+exp) • Fugl-Meyer Assessment (+exp)
Electrical Stimulation techniques versus each other		
Knutson et al. (2020) RCT (5) N_{start}= 67 N_{end}= 53 TPS= <2yr (chronic?)	E1: Arm + Hand Contralaterally Controlled Functional Electrical Stimulation (CCFES) E2: Hand CCFES E3: Arm + Hand cyclic neuromuscular electrical stimulation. Duration: i) A + H cNMES: 60 mins/session for 10 sessions ii) CCFES groups: 46 mins/session for 10 sessions +70 mins FTP for 2 FTP sessions = 10 hrs/wk for 12wks. 36 wks total (12wk therapy, 24 wk post-intervention)	E1 Vs C • Box and Block Test: (-) • Fugle-Meyers Assessment Upper Extremity: (+exp) • Stroke Upper Limb Capacity Scale: (-) • Arm Motors Abilities Test: (-) • Reachable Workspace: (+exp1) E2 Vs C • Box and Block Test: (-) • Fugle-Meyers Assessment Upper Extremity: (-) • Stroke Upper Limb Capacity Scale: (-) • Arm Motors Abilities Test: (-) • Reachable Workspace: (-) E3 Vs C • Box and Block Test: (-) • Fugle-Meyers Assessment Upper Extremity: (-) • Stroke Upper Limb Capacity Scale: (-) • Arm Motors Abilities Test: (-) • Reachable Workspace: (-) E1 Vs E2 Vs E3 • Box and Block Test: (-) • Fugle-Meyers Assessment Upper Extremity: (+exp1) • Stroke Upper Limb Capacity Scale: (-) • Arm Motors Abilities Test: (-) • Reachable Workspace: (+exp1)
Zheng et al. (2019) RCT (5) N_{start}=50 N_{end}=41 TPS=Acute	E: Functional Electrical Stimulation (FES) C: Cyclic NMES Duration: 30min, 5x over 2wks	• Fugl Meyer Upper Extremity: (+exp) • Manual Muscle Testing: (+exp) • Modified Barthel Index: (+exp) • Active wrist Range of Motion: (+exp)
Cunningham et al. (2018) RCT (6) N_{start}= 15 N_{end}= TPS= Chronic Crossover	E: Cyclic Neuromuscular Electrical Stimulation cNMES C: Controlled Functional Electrical stimulation CCFES (bilateral controlled) Duration: 1hr, 1x/condition, over 1 week washout	• Improved interhemispheric inhibition (+con)
Jeon et al. (2017) RCT (5) N_{Start} =20 N_{End} =20 TPS=Subacute	E: EMG-triggered NMES C: FES Duration: 30min, 5d/wk for 4wk	• Fugl-Meyer Assessment (-)
Knutson et al. (2016)	E1: Functional Electrical Stimulation E2: Cyclic NMES Duration: 2hrs, 7d/wk for 6 wk	• Fugl-Meyer Assessment (-) • Arm Motor Abilities Test (-) • Box and Block Test (+exp)

RCT (5) N_{Start} =80 N_{End} =64 TPS=Chronic		
Wilson et al. (2016) RCT (6) N_{Start} =122 N_{End} =96 TPS=Subacute	E1: Cyclic Neuromuscular Electrical Stimulation E2: Electromyographically-triggered Neuromuscular Electrical Stimulation E3: Sensory Stimulation Duration: 40 min (2x/d), 5d/wk for 8 wk	• Fugl-Meyer Assessment (-) • Modified Arm Motor Ability Task (-)
Boyaci et al. (2013) RCT (7) N_{Start}=31 N_{End}=31 TPS=Chronic	E1: EMG-triggered NMES E2: Cyclic NMES C: Control Duration: 45 min/d, 5d/wk for 3 wk	E1 vs C • Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp) • Spasticity in wrist flexor (-) • Spasticity in finger flexor (-) • Range of Motion in active wrist extension (+exp) • Range of Motion in active metacarpophalangeal joint extension (+exp) • Grip strength (+exp) E2 vs C • Fugl-Meyer Assessment (+exp_2) • Motor Activity Log (-) • Spasticity in wrist flexor (+exp_2) • Spasticity in finger flexor (-) • Range of Motion in active wrist extension (+exp_2) • Range of Motion in active metacarpophalangeal joint extension (-) • Grip strength (-) E1 vs E2 • Fugl-Meyer Assessment (-) • Motor Activity Log (-) • Spasticity in wrist flexor (-) • Spasticity in finger flexor (-) • Range of Motion in active wrist extension (-) • Range of Motion in active metacarpophalangeal joint extension (-) • Grip strength (-)
You et al. (2013) RCT (7) N_{Start}=18 N_{End}=16 TPS=Chronic	E: Mental training + EMG stimulation C: FES Duration: 40 min/d, 2d/wk for 4wk	• Range of Motion (-) • Modified Ashworth Scale (-) • Fugl-Meyer Assessment (+exp) • Motor Activity Log (-) • Barthel Index (-)
Knutson et al. (2012) RCT (6) N_{start}=21 N_{end}=21 TPS=Subacute	E1: Contralaterally controlled FES E2: Cyclic NMES Duration: 90 min/d, 3d/wk for 4 wk	• Maximum finger extension angle (-) • Tracking error (% of AROM) (-) • Fugl-Meyer Assessment (-) • Box and Block Test (-) • Arm Motor Abilities Test Score (-)
Chae et al. (2009) RCT (8) N_{start}=26 N_{end}=26 TPS=Chronic	E1: EMG-triggered NMES E2: Cyclic NMES Duration: 1 hr/d, 7d/wk for 6 wk	• Arm Motor Ability Test (-)
De Kroon & Ijzerman (2008) RCT (7) N_{start}=22 N_{end}=22 TPS=Chronic	E1: EMG-triggered NMES E2: Cyclic NMES Duration: 30 min/d, 3d/wk for 6 wk	• Action Research Arm test (-) • Grip Strength (-) • Fugl-Meyer Score (-) • Motricity Index (-)
Hemmen & Seelen (2007) RCT (7) N_{start}=27	E1: EMG-triggered NMES E2: Cyclic NMES Duration: 30 min/d, 5d/wk for 3mo	• Fugl-Meyer Assessment (-) • Action Research Arm test (-)

N_{end}=27 TPS=Subacute		

Cauraugh et al. (2005)
RCT (4)
N_{start}= 21
N_{end}= 21
TPS= Chronic
	E1: NMES bilateral (impaired arm stimulation)
	E2: NMES bilateral (unimpaired moving)
	C: NMES unilateral stimulation
	Duration: 90min, 4d over 2wks
		E1 Vs C
		• Reaction time (-)
		• Movement time: (+exp)
		• Velocity:
		  • Unidirectional: (+con)
		  • Bidirectional (+exp)
		  • Deceleration time: (+exp)
		E2 Vs C
		• Reaction time: (-)
		• Movement time: (+exp)
		• Velocity:
		  • Unidirectional: (+con)
		  • Bidirectional (+exp)
		  • Deceleration time: (+exp)
		E1 vs E2
		• Reaction time: (-)
		• Movement time: (-)
		• Velocity:
		  • Unidirectional (-)
		  • Bidirectional (-)
		  • Deceleration time: (-)

Cauraugh et al. (2003) RCT (6) N_{start}= 28 N_{end}= 28 TPS= Chronic	E1: Blocked NMES training E2: Random NMES training C: No stimulation control Duration: 90min, 4d over 2wks	E1 Vs C • Box and Block Test: (+exp) E2 Vs C • Box and Block Test: (+exp) E1 vs E2 • Box and Block Test: (-)
Low versus high intensity NMES studies		
Page et al. (2012) RCT (7) N_{start}=32 N_{end}=32 TPS=Chronic	E1: 30 minutes of electrical stimulation therapy with repetitive task specific practice E2: 60 minutes of electrical stimulation therapy with repetitive task specific practice E3: 120 minutes of electrical stimulation therapy with repetitive task specific practice Duration: 30 min OR 60 min OR 120 min, 5d/wk for 8 wk.	E3 vs. E2/E1 • Fugl-Meyer Assessment ($+exp_3$) • Arm Motor Ability Test ($+exp_3$) • Action Research Arm Test ($+exp_3$)
Hsu et al. (2010) RCT (6) N_{start}=66 N_{end}=66 TPS=Acute	E1: High intensity cyclic NMES (60 min) E2: Low intensity cyclic NMES (30 min) C: No treatment Duration: 30/60 min, 5d/wk for 4 wk	E1/E2 vs C • Fugl Meyer Assessment ($+exp_1$, $+exp_2$) • Action Research Arm Test ($+exp_1$, $+exp_2$) • Grasp ($+exp_1$, $+exp_2$) • Grip ($+exp_1$, $+exp_2$) • Pinch ($+exp_1$, $+exp_2$) • Gross Movement ($+exp_1$, $+exp_2$) E1 vs E2 • Fugl Meyer Assessment (-) • Action Research Arm Test (-) • Grasp (-) • Grip (-) • Pinch (-) • Gross Movement (-)
Kowalczewski et al. (2007) RCT (6) N_{start}=19 N_{end}=18 TPS=Subacute	E1: High intensity FES exercise therapy (60 min) E2: Low intensity FES exercise therapy (15 min) Duration: 15/60 min, 5d/wk for 3 wk	• Wolf Motor Function Test ($+exp_1$) • Motor Activity Log (-) • Fugl-Meyer Assessment (-)

High versus low frequency cyclic NMES		
Doucet and Griffin (2013) RCT (5) N_{Start}=16 N_{End}=16 TPS=Chronic	E1: High frequency cyclic NMES (40Hz) E2: Low frequency cyclic NMES (20Hz) Duration: 1 hr/d, 4d/wk for 4 wk	• Lateral pinch strength (+exp) • Minnesota Manual Dexterity Test (+exp) • Endurance of thumb adduction (+exp)
NMES combined with Thermal Stimulation		
Chen et al. (2019) RCT (6) N_{start}= 43 N_{end}= 38 TPS= Chronic	E: NMES + thermal stimulation (15/15min hybrid) C: NMES or thermal stimulation (30min) Duration: 3x/wk, 8wks	• Fugl-Meyers Upper Extremity: (-) • Motricity Index: (-) • Modified Ashworth Scale: (-) • Barthel's Index: (-)
NMES + Bilateral Arm Training		
Cauraugh et al. (2011) RCT (6) N_{start}= 18 N_{end}= 18 TPS= Chronic	E: Long term care (BAT +NMES) (10mo) C: Short term care (BAT +NMES) (4wks) Duration: 90min, 1x/wk, (16mo follow-up retention test)	• Box and Block Test: (+exp) • Reaction time: (+exp) • Force produced: (+exp)
NMES combined with Mental Imagery		
Park et al. (2019) RCT (8) N_{start}=68 N_{end}=68 TPS=Chronic	E: Mental imagery + electromyogram-triggered neuromuscular electrical stimulation (EMG-NMES) C: Electromyogram-triggered neuromuscular electrical stimulation Duration: 30min, 5d/wk, 6wks	• Action Research Arm Test: (-) • Fugl-Meyer upper extremity: (-) • Korean version of Modified Barthel Index: (-)
Early versus delayed FES		
Popovic et al. (2004) RCT (6) N_{start}=41 N_{end}=32 TPS=Acute	E: Early (acute) FES C: Delayed (chronic) FES Duration: 30 min/d, 7d/wk for 3 wk	• Upper extremity performance test (+exp)
EMG Bridge versus cNMES		
Zhou et al. (2017) RCT (6) N_{start}=42 N_{end}=36 TPS=Subacute	E: Electromyogrpahical bridge C: Cyclic NMES Duration: 2 sessions over 4 wks	• Brunnstrom stage: (+exp) • Fugl Meyer Upper Extremity: (+exp) • Motor Status Scale: (+exp)
FES combined with BCI		
Li et al. (2014) RCT (6) N_{start}= 15 N_{end}= 14 TPS= Subacute	E: Brain-computer Interface (BCI) + Functional Electrical Stimulation (FES) C: Conventional therapy + FES Duration: 1-1.5hrs, 3x/wk, (rehab 5x/wk, 8wkS)	• Action Research Arm Test: (+exp) • Fugle-Meyers Assessment Upper Extremity: (-)
Young et al. (2016) RCT (5) N_{Start}=19 N_{End}=10 TPS=Chronic	E: Brain computer interface training C: No training Duration: 120min/d for 9-15d	• Stroke Impact Scale (-) • Action Research Arm Test (-) • 9 Hole Peg Test (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp₂ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about NMES

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **Cyclic NMES** to produce greater improvements in motor function than **sham stimulation or conventional therapy**.	6	Tilkici et al. 2017; Baygutalp et al. 2014; Lin and Yan 2011; Mann et al. 2005; Powell et al. 1999; Chae et al. 1998
1a	**Cyclic NMES combined with arm robotics** may not have a difference in efficacy when compared to **arm robotics on their own or conventional therapy** for improving motor function.	3	Miyasaka et al. 2016; Lee et al. 2015; Hayward et al. 2013
1b	**Cyclic NMES combined with repetitive task training** may produce greater improvements in motor function than **repetitive task training alone**.	1	Gharib et al. 2014
1a	**EMG-triggered NMES** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving motor function.	9	Kirac-Unal et al. 2019; Park et al. 2017; Kwakkel et al. 2016; Shin etl al. 2008; Bhatt et al. 2007; Gabr et al. 2005; Kimberley et al. 2004; Cauraugh et al. 2000; Francisco et al. 1998
1a	**EMG-triggered NMES combined with arm robotics** may produce greater improvements in motor function than **arm robotics on their own or conventional therapy**.	2	Qian et al. 2017;
1b	**EMG-triggered NMES combined with arm robotics** may produce greater improvements in motor function than **EMG combined with arm robotics alone.**	1	Hu et al. 2015
1a	There is conflicting evidence about the effect of **EMG-triggered NMES combined with mirror therapy** to improve motor function when compared to **mirror therapy on its own**.	2	Schick et al. 2017; Kojima et al. 2014
1b	**EMG-triggered NMES combined with splints** may produce greater improvements in motor function than **splints on their own**.	1	Shindo et al. 2011
1a	There is conflicting evidence about the effect of **FES** to improve motor function when compared to **sham stimulation or conventional therapy**.	7	Pan et al. 2018; Carda et al. 2017; Maquez-Chin et al. 2017; Yuzer et al. 2017; Mangold et al. 2009; Thrasher et al. 2008; Ring and Rosenthal, 2005; Popovic et al. 2003
1b	**FES of extensors and flexors** may not have a difference in efficacy when compared to **FES of extensors only** for improving motor function.	1	De Kroon et al. 2004
1b	**FES** may produce greater improvements in motor function than **mirror therapy**.	1	Mathieson et al. 2018
2	There is conflicting evidence about the effect of **FES combined with task-specific training or myoelectrical control** to improve motor function when compared to **task-specific training**.	2	Jonsdottir et al. 2017; Alon et al. 2007

1b	**FES combined with action observation and brain computer interface** may produce greater improvements in motor function than **conventional therapy.**	1	Kim et al, 2016
2	**FES combined with biofeedback and mirror therapy** may produce greater improvements in motor function than **FES combined with mirror therapy or conventional therapy**.	1	Kim et al. 2015
1b	**FES combined with botulinum toxin A and a home exercise program** may not have a difference in efficacy when compared to **botulinum toxin A combined with a home exercise program** for improving motor function.	1	Weber et al. 2010
1b	**Bilateral arm training combined with FES** may produce greater improvements in motor function than **bilateral arm training combined with sham FES**.	1	Chan et al. 2009
2	**Distal FES combined with robotics** may not have a difference in efficacy when compared to **proximal** or **whole arm FES** for improving motor function.	1	Daly et al. 2109
2	**FES combined with cycling ergometry** may not have a difference in efficacy when compared to **conventional care alone** for improving motor function.	1	Karaahmet et al 2109
1b	**FES combined physical therapy** may produce greater improvements in motor function than **physical therapy alone.**	1	Khan et al. 2019
1a	**EMG-triggered NMES** may not have a difference in efficacy when compared to **cyclic NMES** for improving motor function.	3	Wilson et al. 2016; Boyaci et al. 2013; De Kroon et al. 2008; Hemmen et al. 2007
2	**EMG-triggered NMES** may not have a difference in efficacy when compared to **FES** for improving motor function.	1	Jeon et al. 2017
1b	**CCFES or FES** may not have a difference in efficacy when compared to **cyclic NMES or EMG triggered NMES** for motor function.	3	Zheng et al. 2019; Knutson et al. 2016; Knutson et al. 2012
2	There is conflicting evidence about the effect of **CCFES on the hand and arm** when compared to **arm and hand NMES** for improving motor function**.**	1	Knutson et al. 2020
1a	**High intensity NMES** may produce greater improvements in motor function when compared to **low intensity NMES.**	3	Page et al. 2012; Hsu et al. 2020; Kowalczewski et al. 2007
1b	**NMES combined with thermal stimulation** may not have a difference in efficacy when compared to **NMES or thermal stimulation alone** for improving motor function.	1	Chen et al. 2019
1b	**Long term NMES combined with bilateral arm training** may produce greater improvements in motor function than **short term NMES combined with bilateral arm training.**	1	Cauraugh et al. 2011

1b	**EMG-NMES combined with mental imagery** may not have a difference in efficacy when compared to cyclic **EMG-NMES** for improving motor function.	1	Park et al. 2019
1b	**Early FES** may produce greater improvements in motor function than **delayed FES**.	1	Popovic et al. 2004
1b	**EMG bridging techniques** may produce greater improvements in motor function than **cyclic NMES**	1	Zhou et al. 2017
1b	**FES combined with BCI** may not have a difference in efficacy compared to **FES and conventional therapy or non-BCI training** alone for improving dexterity.	2	Young et al. 2016; Li et al. 2014

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1b	**EMG-triggered NMES** may produce greater improvements in dexterity than **sham stimulation or conventional therapy**.	5	Shin et al. 2008; Bhatt et al. 2007; Kimberley et al. 2004; Cauraugh and Kim 2003; Cauraugh et al. 2000
1b	**EMG-triggered NMES combined with mirror therapy** may not have a difference in efficacy when compared to **mirror therapy on its own** for improving dexterity.	1	Schick et al. 2017
1b	**FES** may produce greater improvements in dexterity than **sham stimulation or conventional therapy**.	1	Demir et al. 2018; Ring and Rosenthal, 2005
2	**FES combined with task-specific training** may produce greater improvements in dexterity than **task-specific training**.	1	Alon et al. 2007
2	**FES combined with biofeedback and mirror therapy** may produce greater improvements in dexterity than **FES combined with mirror therapy or conventional therapy**.	1	Kim et al. 2015
1b	There is conflicting evidence about the effect of **FES** to improve dexterity when compared to **cyclic NMES**.	2	Knutson et al. 2016; Knutson et al. 2012
2	**CCFES on the hand and arm** may not have a difference in efficacy when compared to **arm and hand NMES** for improving dexterity.	1	Knutson et al. 2020
1b	**Blocked NMES training** may not have a difference in efficacy when compared to **random NMES training** for improving dexterity.	1	Cauraugh et al. 2003
2	**High frequency NMES (40hz)** may produce greater improvements dexterity than **low frequency NMES (20hz).**	1	Doucet and Griffin
1b	**Long term NMES combined with bilateral arm training** may produce greater improvements in dexterity than **short term NMES combined with bilateral arm training.**	1	Cauraugh et al. 2011

2	**FES combined with BCI** may not have a difference in efficacy compared to **non-BCI training** alone for improving dexterity.	1	Young et al. 2016

PROPRIOCEPTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**EMG-triggered NMES combined with mirror therapy** may not have a difference in efficacy when compared to **mirror therapy on its own** for improving proprioception.	1	Schick et al. 2017

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **cyclic NMES** to improve spasticity when compared to **sham stimulation or conventional therapy**.	3	Tilkici et al. 2017; Baygutalp et al. 2014; 1996; Faghri et al. 1994
1b	**NMES combined with** stretching may produce greater improvements in spasticiy then **NMES alone, stretching alone, or sham.**	3	Dejong et al. 2013; Sahin et al. 2012; King et al. 1996
1a	There is conflicting evidence about the effect of **cyclic NMES combined with arm robotics** to improve spasticity when compared to **arm robotics on their own or conventional therapy**.	2	Barker et al. 2017; Lee et al. 2015
1b	**Cyclic NMES combined with repetitive task training** may produce greater improvements in spasticity than **repetitive task training alone**.	1	Gharib et al. 2014
1b	**EMG-triggered NMES** may produce greater improvements in spasticity than **sham stimulation or conventional therapy**.	1	Dosch et al. 2014; Cauraugh and Kim, 2003; Heckman et al. 1997
1a	of **EMG-triggered NMES combined with arm robotics** may produce greater improvements in spasticity than **arm robotics on their own or conventional therapy**.	2	Qian et al. 2017; Barker et al. 2008
1b	**EMG-triggered NMES combined with arm robotics** may not have a difference in efficacy when compared to **EMG combined with arm robotics alone** for improving spasticity.	1	Hu et al. 2015
1a	**FES** may not have a difference in efficacy when compared **sham stimulation or conventional therapy** for improving spasticity.	8	Demir et al. 2018; Carda et al. 2017; Yuzer et al. 2017; Karakus et al. 2013; Hara et al. 2008; Hara et al. 2006; Ring and Rosenthal, 2005; Faghri and Rodgers, 1997
2	**FES combined with biofeedback and mirror therapy** may not have a difference in efficacy when compared to **FES combined with mirror therapy or conventional therapy** for improving spasticity.	1	Kim et al. 2015

1a	**EMG-triggered NMES** may not have a difference in efficacy when compared to **cyclic NMES** for improving spasticity.	1	Boyaci et al. 2013
1b	**NMES combined with thermal stimulation** may not have a difference in efficacy when compared to **NMES or thermal stimulation alone** for improving spasticity.	1	Chen et al. 2019

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **cyclic NMES** to improve range of motion when compared to **sham stimulation or conventional therapy**.	2	Tilkici et al. 2017; Malhotra et al. 2013
2	**Cyclic NMES combined with arm robotics** may not have a difference in efficacy when compared to **arm robotics on their own or conventional therapy** for improving range of motion.	1	Miyasaka et al. 2016
1b	**Cyclic NMES combined with repetitive task training** may produce greater improvements in range of motion than **repetitive task training alone**.	1	Gharib et al. 2014
2	**EMG-triggered NMES** may produce greater improvements in range of motion than **sham stimulation or conventional therapy**.	2	Heckman et al. 1997; Bowman et al. 1979
1b	**EMG-triggered NMES combined with mirror therapy** may produce greater improvements in range of motion than **mirror therapy on its own**.	1	Kojima et al. 2014
2	**FES** may produce greater improvements in range of motion when compared to **sham stimulation or conventional therapy**.	3	Hara et al. 2008; Hara et al. 2006; Faghri and Rodgers, 1997
1a	**EMG-triggered NMES** may not have a difference in efficacy when compared to **cyclic NMES** for improving range of motion.	1	Boyaci et al. 2013
1b	**FES of extensors and flexors** may not have a difference in efficacy when compared to **FES of extensors only** for range of motion.	1	De Kroon et al. 2004
1b	**FES combined with action observation and brain computer interface** may produce greater improvements in motor function than **conventional therapy.**	1	Kim et al, 2016
1b	**FES or CCFES** may not have a difference in efficacy when compared to **cyclic NMES or EMG NMES** for improving range of motion.	3	Zheng et al. 2019; Knutson et al. 2016; Knutson et al. 2012
2	**CCFES on the hand and arm** may produce greater improvments in range of motion when compared to **arm and hand NMES.**	1	Knutson et al. 2020
2	**FES combined with cycling ergometry** may not have a difference in efficacy when compared to **conventional care alone** for range of motion.	1	Karaahmet et al 2109

2	**High frequency NMES (40hz)** may produce greater improvements range of motion than **low frequency NMES (20hz).**	1	Doucet and Griffin

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References
1a	**Cyclic NMES** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving performance of activities of daily living.	3	Tilkici et al. 2017; Baygutalp et al. 2014; Lin and Yan 2011
1a	**Cyclic NMES combined with arm robotics** may not have a difference in efficacy when **compared to arm robotics on their own or conventional therapy** for improving performance of activities of daily living.	3	Barker et al. 2017; Lee et al. 2015; Hayward et al. 2013
1a	**EMG-triggered NMES** may not improve performance of activities of daily living when compared to **sham stimulation or conventional therapy**.	5	Kirac-Unal et al. 2019; Kwakkel et al. 2016; Kimberely et al. 2004; Cauraugh et al. 2000; Francisco et al. 1998
1b	**EMG-triggered NMES combined with splints** may not have a difference in efficacy when compared **to splints on their own** for improving performance of activities of daily living.	1	Shindo et al. 2011
1a	There is conflicting evidence about the effect of **FES** to improve performance of activities of daily living when compared to **sham stimulation or conventional therapy**.	5	Demir et al. 2018; Carda et al. 2017; Marquez-Chin et al. 2017; Yuzer et al. 2017; Mangold et al. 2009
1b	**FES** may not have a difference in efficacy when compared to **mirror therapy** for improving performance of activities of daily living.	1	Mathieson et al. 2018
1b	**FES combined with action observation and brain computer interface** may produce greater improvements in motor function than **conventional therapy.**	1	Kim et al, 2016
2	**FES combined with biofeedback and mirror therapy** may produce greater improvements in performance of activities of daily living than **FES combined with mirror therapy or conventional therapy**.	1	Kim et al. 2015
1b	**FES combined with biofeedback and mirror therapy** may not have a difference in efficacy when compared to **FES combined with mirror therapy or conventional therapy** for improving performance of activities of daily living.	1	Kim et al. 2015
1b	**FES combined with botulinum toxin A and a home exercise program** may not have a difference in efficacy when compared to **botulinum toxin A combined with a home exercise program** for improving performance on activities of daily living.	1	Weber et al. 2010

1b	**Bilateral arm training combined with FES** may not have a difference in efficacy when compared to **bilateral arm training combined with sham FES** for improving performance of activities of daily living.	1	Chan et al. 2009
2	**FES combined with cycling ergometry** may not have a difference in efficacy when compared to **conventional care alone** for activities of daily living.	1	Karaahmet et al 2109
1b	**FES combined physical therapy** may produce greater improvements in motor function than **physical therapy alone.**	1	Khan et al. 2019
1a	**EMG-triggered NMES** may not have a difference in efficacy when compared to **cyclic NMES** for improving performance of activities of daily living.	3	Wilson et al. 2016; Boyaci et al. 2013; Chae et al. 2009
1b	**High intensity NMES** may not have a difference in effiacy when compared to **low intensity NMES** for improving performance in activities of daily living.	1	Kowalczewski et al. 2007
1b	**NMES combined with thermal stimulation** may not have a difference in efficacy when compared to **NMES or thermal stimulation alone** for improving performance of activities of daily living.	1	Chen et al. 2019
1b	**CCFES or FES** may not have a difference in efficacy when compared to **cyclic NMES or EMG NMES** for improving performance on activities of daily living.	3	Zheng et al. 2019; Knutson et al. 2016; Knutson et al. 2012
1b	**EMG-NMES combined with mental imagery** may not have a difference in efficacy when compared to cyclic **EMG-NMES** for improving performance of activities of daily living.	1	Park et al. 2019

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	**EMG-triggered NMES** improve muscle strength when compared to **sham stimulation or conventional therapy.**	3	Kirac-Unal et al. 2019; Kwakkel et al. 2016; Shin et al. 2008
1b	**EMG-triggered NMES combined with arm robotics** may not have a difference in efficacy when compared to **arm robotics on their own or conventional therapy** for improving muscle strength.	1	Barker et al. 2017
1n	**FES of extensors and flexors** may not have a difference in efficacy when compared to **FES of extensors only** for improving muscle strength.	1	De Kroon et al. 2004
2	There is conflicting evidence about the effect of **FES combined with biofeedback and mirror therapy** to improve muscle strength when compared to **FES combined with mirror therapy or conventional therapy**.	1	Kim et al. 2015
1a	**EMG-triggered NMES** may not have a difference in efficacy when compared to **cyclic NMES** for improving muscle strength.	2	Boyaci et al. 2013; De Kroon et al. 2008

2	**FES** may produce greater improvemnts in mucle strenght when compared to **cyclic NMES.**	1	Zheng et al. 2019
1b	**High intensity NMES** may produce greater improvements in muscle strength when compared to **low intensity NMES.**	1	Hsu et al. 2020;
2	**High frequency NMES (40hz)** may produce greater improvements muscle strength than **low frequency NMES (20hz).**	1	Doucet and Griffin
1b	**Long term NMES combined with bilateral arm training** may produce greater improvements in muscle strength than **short term NMES combined with bilateral arm training.**	1	Cauraugh et al. 2011

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **FES** to improve stroke severity when compared to **conventional therapy**.	2	Yuzer et al. 2017; Karakus et al. 2013
1b	**FES combined with physical therapy** may produce greater improvements on measures of stroke severity than **physical therapy alone.**	1	Khan et al. 2019
2	**CCFES on the hand and arm** may not have a difference in efficacy when compared to **arm and hand NMES** for stoke severity.	1	Knutson et al. 2020
1b	**EMG bridging techniques** may produce greater improvements in stroke severity than **cyclic NMES**	1	Zhou et al. 2017
1b	**FES combined with BCI** may not have a difference in efficacy compared to **non-BCI training** alone.	1	Young et al. 2016

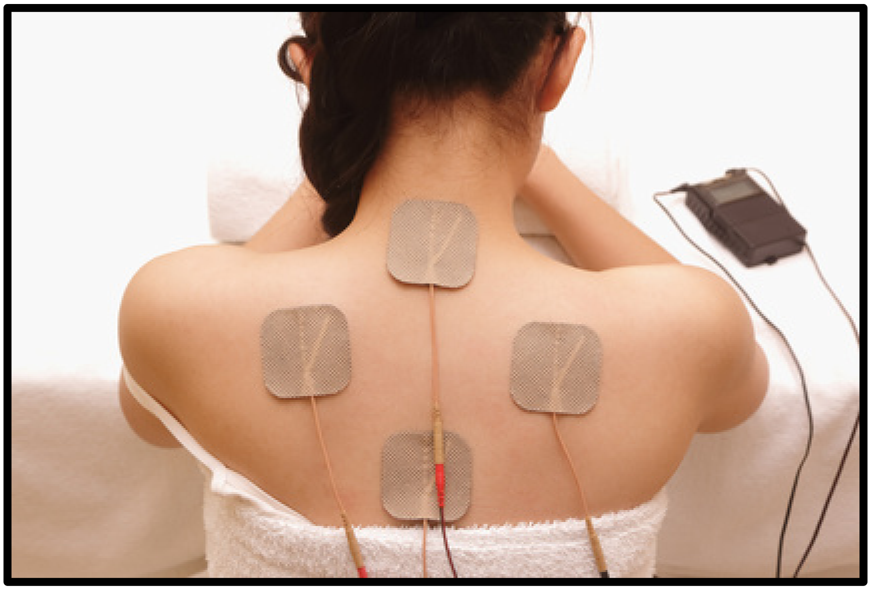
Key points

The literature is mixed regrading cyclic and EMG-triggered neuromuscular electrical stimulation types, as well as functional electrical stimulation, alone or combined with other therapy approaches, for upper limb rehabilitation following stroke.

The literature is mixed regrading combinations of neuromuscular electrical stimulation with other therapies for upper limb rehabilitation following stroke.

The various types of neuromuscular electrical stimulation may not be more beneficial compared to one another.

Transcutaneous Electrical Nerve Stimulation (TENS)



Adopted from: http://www.massageprocedures.com/complementary-modalities/tens/

Transcutaneous electrical nerve stimulation (TENS) involves the application of electrical current through surface electrodes on the skin to facilitate activation of nerves (Teoli et al. 2019). Stimulation can be applied at a low frequency (<10Hz) to produce muscle contractions or at a high (>50Hz) frequency primarily used to produce paresthesia without muscle contractions (Teoli et al. 2019). TENS units are often small, portable, battery-operated devices (Teoli et al. 2019). The application of afferent electrical stimulation at the sensory level may help to enhance neuroplasticity of the brain, through increased activation and recruitment of cortical networks involving contralesional primary sensory cortex, supplementary motor area, dorsal premotor cortex, posterior parietal cortex, and secondary sensory cortices (Veldman et al. 2015; Sonde et al.1998).

A total of 21 RCTs were found that evaluated the use of TENS for upper extremity motor rehabilitation poststroke.

19 RCTs compared TENS to conventional care or sham (Chatterjee et al. 2019; Ertzgaard et al. 2018; Kattenstroth et al. 2018; Kimberley et al. 2018; Jung et al. 2017; Liu et al. 2017; Carrico et al. 2016; Fleming et al. 2015; Dos Santos-Fontes et al. 2013; Kim et al. 2013a; Ikuno et al. 2012; Klaiput et al. 2009; Celnik et al. 2007; McDonnell et al. 2007; Wu et al. 2006; Conforto et al. 2002; Sonde et al. 1998; Tekeoglu et al. 1998; Butefisch et al. 1995). One RCT compared EMG-TENS to EMG-NMES (Chuang et al. 2017), and one RCT compared high to low dose stimulation (Ghaziani et al. 2018).

The methodological details and results of all 21 RCTs are presented in Table 23.

Table 23. RCTs Evaluating TENS Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Chatterjee et al. (2019) RCT (7) N_{start}= 40 N_{end}= 39	E: Sensory stimulation glove C: Conventional Therapy (not time matched) Duration: 45min, 7x/wk for 2wks	• Action Research Arm Test: (-) • Fugl Meyers Upper Extremity: (-) • Nine Hole Peg Test: (-)
Ertzgaard et al. (2018) RCT (10) N_{start}= 31 N_{end}= 27 TPS= Chronic	E: Transcutaneous Electrical Nerve Stimulation (TENS) C: Sham Duration: 60min, 4x/wk, 6wks (no washout)	• Action Research Arm Test: (-) • Modified Ashworth Scale: (-) • Wolf Motor Function Test: (-)
Kattenstroth et al. (2018) RCT (4) N_{Start} =71 N_{End} =48 TPS= Acute	E: Repetitive Sensory Stimulation C: Sham Repetitive Sensory Stimulation Duration: 45min/d, 5d/wk for 2wk	• Tactile Discrimination (+exp) • Grating Orientation Task (+exp) • Grip Strength (+exp) • 9 Hole Peg Test (-) • Jebsen Taylor Hand Function Test (-) • Joint Position Sense Test (-)

Kimberley et al. (2018)
RCT (9)
N_{start}= 17
N_{end}= 17
TPS= Chronic
	E: Active (0.8 mA) VNS w/ rehab
	C: Sham VNS w/ rehab
	Duration: 3x/wk for 6 wks in clinic rehab + 90 days at home therapy, then crossover and repeat
		• Fugle-Meyers Assessment Upper Extremity: (-)
		• Wolf Motor Function Test
		  • Functional: (+exp)
		  • Time: (-)
		• Box and Block Test: (-)
		• Nine Hole Peg Test: (-)
		• Stroke Impact Scale: (-)
		• Motor Activity Log: (-)

Jung et al. (2017) RCT (7) N_{Start} =46 N_{End} =46 TPS= Chronic	E: Transcutaneous Electrical Nerve Stimulation and Task-Related Training C: Sham Transcutaneous Electrical Nerve Stimulation and Task-Related Training Duration: 1h, 5d/wk for 4wk	• Manual muscle test (+exp) • Active Range of Motion (+exp) • Fugl-Meyer Assessment (+exp
Liu et al. (2017) RCT crossover (7) N_{start}= 32 N_{end}= 32 TPS= Chronic	E: Peripheral nerve electrical stimulation C: Sham Duration: 1hr, 1x, 1wk washout	• Pinch Strength: (-) • Purdue Dexterity Score: (+exp)
Carrico et al. (2016) RCT (7) N_{start}= 36 N_{end}= 31 TPS= Chronic	E: Peripheral nerve stimulation C: Sham Duration: 2hrs stim, 4hrs trianing, 5d/wk, 2wks	• Fugl Meyer Assessment Upper Extremity: (+exp) • Wolf Motor Function Test (time): (+exp) • Action Research Arm Test: (+exp)
Fleming et al. (2015) RCT (7) N_{Start}=33 N_{End}=30 TPS=Chronic	E: Active Somatosensory Stimulation C: Sham Somatosensory Stimulation Duration: 30min/d, 3d/wk for 4wk	• Action Research Arm Test (+exp) • Fugl-Meyer Assessment (-) • Motor Activity Log (-)
dos Santos-Fontes et al. (2013) RCT (8) N_{Start}=20 N_{End}=20 TPS=Chronic	E: Peripheral nerve stimulation C: Sham nerve stimulation Duration: 2h/d, 7d/wk for 4wk	• Jebsen Taylor Hand Function Test (+exp)

Kim et al. (2013a) RCT (7) N_{Start}=34 N_{End}=30 TPS=Chronic	E: TENS + task related training C: Placebo + Task related training Duration: 30 min, 5d/wk, for 4 wk	• Fugl-Meyer Assessment (+exp) • Manual Function Test (+exp) • Box and Block Test (+exp) • Modified Ashworth Scale (-)
Ikuno et al. (2012) RCT (8) N_{start}=22 N_{end}=22 TPS=Subacute	E: Peripheral sensory nerve stimulation + task-specific therapy C: Task-specific therapy Duration: 6d/wk for 2wk	• Wolf Motor Function Test (-) • Box and Block Test (-) • Pinch Strength (-) • Grip Strength (-)
Klaiput et al. (2009) RCT (8) N_{start}=20 N_{end}=20 TPS=Subacute	E: Peripheral nerve stimulation C: Sham stimulation Duration: 2h session	• Pinch Strength (+exp)
Celnik et al. (2007) RCT (6) N_{start}=9 N_{end}=9 TPS=Chronic	E1: Single session of peripheral nerve stimulation E2: No stimulation C: Asynchronous nerve stimulation Duration: 2h session	E1 vs E2/C • Jebsen-Taylor Hand Function Test (+exp)
McDonnell et al. (2007) RCT (7) N_{start}=20 N_{end}=20 TPS=Subacute	E: Task-specific training with TENS C: Task-specific training without TENS Duration: 1h/d, 3d/wk for 3wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Grip lift task (+exp)
Wu et al. (2006) RCT (6) N_{start}=9 N_{end}=9 TPS=Chronic	E: Single session of peripheral nerve (somatosensory) stimulation C: No stimulation Duration: 2h session	• Jebsen Taylor Hand Function Test (+exp)
Conforto et al. (2002) RCT (6) N_{start}=8 N_{end}=8 TPS=Chronic	E: Single session of medial nerve (somatosensory) stimulation C: Sham stimulation Duration: 2h session	• Pinch muscle strength (+exp)
Sonde et al. (1998) RCT (5) N_{start}=44 N_{end}=44 TPS=Chronic	E: TENS + physiotherapy C: Physiotherapy Duration: 60min/d, 5d/wk for 12wk	• Fugl-Meyer Assessment (+exp) • Barthel Index (-)
Tekeoglu et al. (1998) RCT (6) N_{start}=60 N_{end}=60 TPS=Subacute	E: Rehabilitation + TENS C: Rehabilitation Duration: 30min/d, 5d/wk for 8wk	• Barthel Index (+exp)
Bütefisch et al. (1995) RCT (3) N_{start}=27 N_{end}=24 TPS=Subacute	E: Enhanced specific therapy + TENS C: Enhanced non-specific therapy Duration: 15min (2x per day) for 2wk	• Grip strength (-)
EMG-triggered NMES with BAT versus EMG-TENS with BAT		
Chuang et al. (2017) RCT (7) N_{Start}=38 N_{End}=38	E: Electromyography-Neuromuscular Electric Stimulation with Bilateral Arm Training	• Fugl-Meyer Assessment (-)

TPS=Chronic	C: Electromyography-Transcutaneous Electrical Nerve Stimulation with Bilateral Arm Training Duration: 40min, 3d/wk for 4wk	
High versus Low Dose Electircal Somatosensory Stimulation		
Ghaziani et al. (2018) RCT (7) N_{start}= 102 N_{end}= 88 TPS= Acute Ch11	E: High dose electrical somatosensory stimulation C: Low dose electrical somatosensory stimulation Duration: 1hr, 7d/wk up to 4wks post-stroke	• Box and Block Test: (-) • Fugle-Meyers Assessment Upper Extremity: (-) • Perceptual Threshold Touch: (-) • Hand Grip Strength: (-) • Palmer Pinch Strength: (-) • Key Pinch: (-) • Tip Pinch Strength: (-) • Modified Rankin Scale: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about TENS

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **TENS** to improve motor function when compared to **sham stimulation, task-specific therapy or conventional therapy**.	14	Ertzgaard et al. 2018; Kattenstroth et al. 2018; Kimberley et al. 2018; Capone et al. 2017; Jung et al. 2017; Carrico et al. 2016; Fleming et al. 2015; dos Santos-Fontes et al. 2013; Kim et al. 2013; Ikuno et al. 2012; Celnik et al. 2007; McDonnell et al. 2007; Wu et al. 2006; Sonde et al. 1998
1b	**TENS combined with EMG and bilateral training** may not have a difference in efficacy when compared to **EMG-triggered NMES and bilateral training** for improving motor function.	1	Chuang et al. 2017
1b	**High dose TENS** may not have a difference in efficacy when compared to **low dose TENS** for improving motor function.	1	Ghaziani et al. 2018

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **TENS** to improve muscle strength when compared to **sham stimulation, task-specific therapy or conventional therapy**.	6	Jung et al. 2017; Liu et al. 2017; Ikuno et al. 2012; Klaliput et al. 2009; Conforto et al. 2002; Butefisch et al. 1995
1b	**High dose TENS** may not have a difference in efficacy when compared to **low dose TENS** for improving muscle strength.	1	Ghaziani et al. 2018

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **TENS** to improve dexterity when compared to **sham stimulation and task-specific therapy**.	6	Kimberley et al. 2018; Liu et al. 2017; Kim et al. 2013; Ikuno et al. 2012; McDonnel et al. 2007
1b	**High dose TENS** may not have a difference in efficacy when compared to **low dose TENS** for improving dexterity.	1	Ghaziani et al. 2018

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**TENS** may not have a difference in efficacy when compared to **sham stimulation and task-specific therapy** for improving spasticity.	3	Ertzgaard et al. 2018; Kattenstroth et al. 2018; Kim et al. 2013

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**TENS** may not have a difference in efficacy when compared to **sham stimulation and task-specific therapy** for improving activities of daily living.	4	Kimberley et al. 2018; Fleming et al. 2015; Sonde et al. 1998; Tekeoglu et al. 1998

Key points

The literature is mixed regarding the benefits of transcutaneous electrical nerve stimulation for some aspects of upper limb function following stroke.

Thermal Stimulation

Adopted from: https://beautisecrets.com/paraffin-waxtreatment

Thermal stimulation is another method used to facilitate sensorimotor function, thermal stimulation applied either in a noxious or innocuous form have different effects on sensory receptors in the body (Lin et al. 2017). The perception of pain from nociceptors produced by noxious heat (>43°C) and cold (<8°C) activates brain regions such as the second somatosensory cortex, posterior insular cortex and the premotor area that would not be activated by warm and cold receptors from innocuous heat (40-43°C) and cold (20-28°C) temperatures (Lin et al. 2017). Innocuous thermal stimulation has also been found to induce greater corticomotor excitability, and as such has been suggested to influence cortical reorganization and neuroplasticity (Lin et al. 2017).

A total of five RCTs were found that evaluated the use of thermal stimulation for upper extremity motor rehabilitation poststroke.

Noxious thermal stimulation was used in three RCTs with comparator groups including innocuous thermal stimulation (Lin et al. 2017), thermal stimulation on the lower extremities (Wu et al. 2010a), and conventional rehabilitation (Chen et al. 2005). Innocuous thermal stimulation through paraffin wax compared to a placebo wax was used in a single study (Wang et al. 2017). One RCT compared thermal stimulation combined with vibration (Law et al. 2018).

The methodological details and results of all five RCTs are presented in Table 24.

Table 24. RCTs Evaluating Thermal Stimulation Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Noxious versus innocuous thermal stimulation, lower extremity thermal stimulation and conventional rehabilitation		
Lin et al. (2017) RCT (7) N_{Start} =79 N_{End} =61 TPS= Acute	E: Noxious thermal stimulation (Heat: 46-47°C; cold: 7-8°C) C: Innocuous thermal stimulation (Heat: 40-41°C; cold: 20-21°C) Duration: 30min/d, for a total of 20-24 sessions	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Motricity Index (-) • Barthel Index (-) • Modified Ashworth Scale (-)
Wu et al. (2010a) RCT (6) N_{start}=23 N_{end}=23 TPS=Subacute	E: Thermal stimulation on upper extremity (Heat: 46-47°C; cold: 7-8°C) C: Thermal stimulation on lower extremity (Heat: 46-47°C; cold: 7-8°C)	• Stroke Rehabilitation Assessment of Movement (+exp) • Action Research Arm Test (+exp)
Chen et al. (2005) RCT (7) N_{Start}=46 N_{End}=29 TPS=Acute	E: Thermal stimulation (Heat: 46-47°C; cold: 7-8°C) C: Conventional rehabilitation	• Brunnstrom Recovery Stages (+exp) • Modified Ashworth Scale (-) • Grasping (-)
Innocuous thermal stimulation versus placebo		
Wang et al. (2017) RCT (8) N_{Start} =52 N_{End} =52 TPS= Subacute	E: Paraffin wax thermal stimulation (Heat: 40-42°C) C: Placebo paraffin thermal stimulation	• Modified Ashworth Scale (+exp) • Brunnstrom Recovery Stages (-)
Thermal Stimulation combined with Additional Therapy		
Law et al. (2018) RCT (7) N_{start}= 12 N_{end}= 12 TPS= Subacute	E: Multisensory stimulation (thermal + vibration) C: Conventional therapy Duration: 90min, 2x/wk, 12wks	• Fugle-Meyers Assessment: (+exp) • Manual Muscle Testing: (+exp) • Function Test for the Hemiplegic Upper Extremity-HK: (+exp) • Modified Barthel Index: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Thermal Stimulation

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**

1a	There is conflicting evidence about the effect of **Noxious thermal stimulation** to improve motor function when compared to **innocuous thermal stimulation, thermal stimulation on the lower extremities and conventional rehabilitation.**	3	Lin et al. 2017; Wu et al. 2010; Chen et al. 2005
1b	**Thermal stimulation in combination with muscle vibration** may produce greater improvements in motor function than **conventional control**	1	Law et al. 2018

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Noxious thermal stimulation** may not have a difference in efficacy when compared to **innocuous thermal stimulation** for improving muscle strength.	1	Lin et al. 2017
1b	**Thermal stimulation in combination with muscle vibration** may produce greater improvements in muscle strength than **conventional control**	1	Law et al. 2018

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Thermal stimulation with muscle vibration** may not have a difference in efficacy when compared to **conventional care** for improving activities of daily living.	1	Law et al. 2018

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Noxious thermal stimulation** may not have a difference in efficacy when compared to **innocuous thermal stimulation, and conventional rehabilitation** for improving spasticity.	2	Lin et al. 2017; Chen et al. 2005
1b	**Innocuous thermal stimulation** may produce greater improvements on spasticity than **placebo**.	1	Wang et al. 2017

Key points

Noxious thermal stimulation may not be beneficial for upper limb rehabilitation following stroke, whereas innocuous thermal stimulation may improve some aspects of upper limb function.

Muscle Vibration

Adopted from: https://www.humanlocomotion.org/products/focal-vibration-motors

Various forms of muscle vibration applications exist including: focal muscle vibration, whole body vibration, and stochastic resonance stimulation. Whole body vibration involves standing, sitting, or performing various tasks/movements on a vibration platform with the purpose of improving muscle strength and function (Liao et al. 2015; Park et al. 2018). Focal muscle vibration is a new therapeutic approach that involves the application of low-amplitude/high-frequency vibratory stimulation to a specific muscle through small portable devices (Celletti et al. 2017).

A total of 15 RCTs were found that evaluated the use of muscle vibration therapies for upper extremity motor rehabilitation poststroke.

Nine RCTs compared focal or segmental muscle vibration to conventional therapy or sham (Amino et al .2019; Toscano et al. 2019; Calabro et al. 2017; Costantino et al. 2017; Casale et al. 2014; Paoloni et al. 2014; Tavernese et al. 2013; Caliandro et al. 2012; Noma et al. 2012). Two RCTs examined whole body vibration (Ahn et al. 2019; Lee et al. 2016). Two RCTs compared different muscle vibration techniques (Li et al. 2020; Yoon et al. 2017). One RCT examined muscle vibration combined with mirror therapy (Guo et al. 2019). One RCT compared muscle vibration to botox (Wu et al. 2018).

The methodological details and results of all 15 RCTs are presented in Table 25.

Table 25. RCTs Evaluating Muscle Vibration Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Focal/Segmental Vibration Therapy vs Sham or Convetional Care		
Amino et al. (2019) RCT (6) N_{start}= 37 N_{end}= 34 TPS= Not reported Ch11	E: Segmental muscle vibration C: Conventional physical therapy Duration: 30min 3x/wk for 8wks	• Barthel Index: (-) • Elbow Range of Motion: (-) • Elbow Tone: (+exp) • Elbow Flexor/Extensor Strength: (-)
Toscano et al. (2019) RCT (7) N_{start}=22 N_{end}=22 TPS=Acute Ch11	E: Repetitive focal muscle vibrations C: Sham Duration: Rehab 1hr/d, vibratiom 30min/d, 3ds	• Fugl Meyer Assessment: (+exp) • Motricity index: (+exp) • National Institutes of Health Stroke Scale: (+exp) • Modified Ashworth Scale: (-)
Calabro et al. (2017) RCT (7) N_{Start}=20 N_{End}=19 TPS=Subacute-Chronic	E: Focal Muscle Vibration C: Sham Muscle Vibration Duration: 30min/d, 5d/wk for 6wk	• Modified Ashworth Scale (+exp) • Functional Independence Measure (+exp) • Fugl-Meyer Assessment (+exp)
Costantino et al. (2017) RCT (7) N_{Start}=32 N_{End}=32 TPS=Chronic	E: 300 Hz vibrations on the upper limbs C: Sham vibrations Duration: 30min/d, 3d/wk for 4wk	• Hand Grip Strength (+exp) • Modified Ashworth Scale (+exp) • Disabilities of the Arm, Shoulder and Hand Score (+exp) • Functional Independence Measure (+exp) • Fugl-Meyer Assessment (+exp) • Jebsen Taylor Hand Function Test (+exp)

Casale et al. (2014)
RCT (7)
N_{start}= 30
N_{end}= 30
TPS= Chronic
	E: Muscle vibration
	C: Sham
	Duration: (60min physio + 30min stimulation, 5d/wk, 2wks
		• Motor Assessment Scale: (+exp)
		• Motor Task:
		  • Completed (+exp)
		  • Time (+exp)
		  • Trajectory error (-)

Paoloni et al. (2014) RCT (8) N_{Start}=22 N_{End}=22 TPS=Chronic	E: Segmental muscle vibration + conventional therapy C: Conventional therapy Duration: 30min/d, 5d/wk for 2wk	• Muscle modulation of anterior deltoid (+exp) • Muscle modulation of biceps brachii (+exp)
Tavernese et al. (2013) RCT (8) N_{Start}=44 N_{End}=44 TPS=Chronic	E: Segmental muscle vibration + standard therapy C: Standard therapy Duration: 30min/d, 5d/wk for 2wk	• Angular velocity at shoulder (+exp) • Movement duration (+exp) • Normalized jerk (+exp) • Elbow angle (-) • Shoulder angle (-) • Shoulder abduction (-)
Caliandro et al. (2012) RCT (7) N_{Start}=49 N_{End}=36 TPS=Chronic	E: Focal muscle vibration C: Sham Duration: 30min/d, for 3d	• Wolf Motor Function Test (+exp)

Noma et al. (2012)
RCT (7)
N_{start}= 36
N_{end}= 36
TPS= Subacute
Chap 11
	E: Muscle vibration
	C: Stretch control
	C2: Rest control
	Duration: 1x, 5min
		E Vs C1
		• Modified Ashworth Scale
		  • Elbow flex: (+exp)
		  • Wrist flex: (+exp)
		E VS C2
		• Modified Ashworth Scale

		• Elbow flex: (+exp) • Wrist flex: (+exp) C1 Vs C2 • Modified Ashworth Scale • Elbow flex: (-) • Wrist flex: (-)
Whole Body Vibration vs Conventional Care		
Ahn et al. (2019) RCT (6) N_{start}= 60 N_{end}=60 TPS= Not reported	E: Whole body vibration C: Conventional therapy Duration: Exp/sham (30min/5x/3wk); conv (60-120min/5x/3wk)	• Motor Function Test: (+exp) • Grip strength: (+exp)
Lee et al. (2016) RCT (6) N_{Start}=45 N_{End}=45 TPS=Chronic	E1: Whole-body vibration and task-related training E2: Whole-body vibration C: Conventional Therapy Duration: 30min/d, 3d/wk for 4wk	E1/E2 vs C • Fugl-Meyer Assessment (+exp, +exp_2) • Grip Strength (+exp, +exp_2) E1 vs E2 • Grip Strength (+exp, +exp_2) • E1 vs E2/C • Wolf Motor Function Test (+exp1) • Modified Ashworth Scale (+exp1)
Muscle Vibrations Against Eachother		
Li et al. (2020) RCT (7) N_{start}= 86 N_{end}= 82 TPS= Subacute Ch11	E: Radial extraoral shockwave (rEWST) agonist muscle E2: rEWST Antagonist muscle C: Conventional therapy Duration: 6x/wk, 3wks rehab + 5x every 4d shockwave	E1 Vs C • Modified Ashworth Scale: (+exp1) • Modified Tardieu Scale (R1, R2): (+exp1) • Fugle-Meyers Assessment Upper Extremity: (-) E2 Vs C • Modified Ashworth Scale: (+exp2) • Modified Tardieu Scale (R1, R2): (+exp2) • Fugle-Meyers Assessment Upper Extremity: (-) E1 Vs C • Modified Ashworth Scale: (-) • Modified Tardieu Scale (R1, R2): (+exp2) • Fugle-Meyers Assessment Upper Extremity: (-)
Yoon et al. (2017) RCT (5) N_{start}=138 N_{end}=124 TPS=Chronic Ch11	E1: Extracorpeal shockwave on muscle belly E2: Extracorpeal shockwave on myotendinous junction C: sham Duration: 1x/wk for 3wks	E1 vs C • Modified Ashworth Scale: (+exp1) • Modified Tardieu Scale: (+exp1) E2 vs C • Modified Ashworth Scale: (+exp2) • Modified Tardieu Scale: (+exp2)
Vibration Combined with Mirror therapy		
Guo et al. (2019) RCT (6) N_{start}= 120 N_{end}= 120 TPS=Chronic	E1: Mirror therapy + extracorporeal shock E2: Mirror therapy E3: Shockwave alone C: Conventional therapy Duration: 30min 5d/wk, 4wks conv + 20min 5d/wk, 4wks additional	E1 Vs C • Fugl-Meyer Upper Extremity Assessment: (+exp1) • Modified Ashworth Scale: (+exp1) E2 Vs C • Fugl-Meyer Upper Extremity Assessment: (+exp2) • Modified Ashworth Scale: (-) E3 Vs C • Fugl-Meyer Upper Extremity Assessment: (+exp3) • Modified Ashworth Scale: (+exp3) E1 vs E2 Vs E3 • Fugl-Meyer Upper Extremity Assessment: (+exp1) • Modified Ashworth Scale: (+exp1)
Muscle vibration versus Botox		
Wu et al. (2018) RCT (8) N_{start}=42	E: Extracorpeal shockwave C: Botox Duration: 1x/wk, 3wks	At 8wks • Modified Ashworth Scale- wrist (-) • Modified Ashworth Scale- elbow (-)

N_{end}=40 TPS=Chronic Ch11		• Tardieu wrist: (-) • Tardieu elbow: (-) • Fugl Meyer Upper Extremity: (+exp) • Passive Range of Motion (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Muscle Vibration

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Muscle vibration therapies** may produce greater improvements in motor function than **sham vibration or conventional therapy**.	6	Guo et al. 2019; Toscano et al. 2019; Calabro et al. 2017; Costantino et al. 2017; Casale et al. 2014; Caliandro et al. 2012
1b	**Vibration of antagonist muscles** may not have a difference in efficacy when compared to **agonist muscles** improving motor function.	1	Li et al. 2020
1b	**Mirror therapy in combination with shockwave therapy** may produce greater improvements in motor function than **shockwave alone, or conventional control**	1	Guo et al. 2019
1b	**Thermal stimulation in combination with muscle vibration** may produce greater improvements in motor function than **conventional control**	1	Law et al. 2018
1b	**Muscle vibration** may produce greater improvements in motor function than **botox.**	1	Wu et al. 2018

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Muscle vibration therapies** may produce greater improvements in muscle strength than **sham vibration or conventional therapy**.	4	Amino et al. 2019; Toscano et al. 2019; Costantino et al. 2017; Paoloni et al. 2014
1a	**Whole body vibration therapies** may produce greater improvements in muscle strength than **sham vibration or conventional therapy**.	2	Ahn et al. 2019; Lee et al. 2016
1b	**Thermal stimulation in combination with muscle vibration** may produce greater improvements in muscle strength than **conventional control**	1	Law et al. 2018

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**

1a	**Muscle vibration therapies** may produce greater improvements in performance on activites of dailing living than **sham vibration or conventional therapy**.	3	Amino et al. 2019; Calabro et al. 2017; Costantino et al. 2017;
1b	**Thermal stimulation with muscle vibration** may not have a difference in efficacy when compared to **conventional care** for improving performance on activites of dailing living.	1	Law et al. 2018

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Muscle vibration therapies** may produce greater improvements in spasticity than **sham vibration or conventional therapy**.	7	Amino et al. 2019; Guo et al. 2019; Tuscano et al. 2019; Calabro et al. 2017; Constantino et al. 2017; Yoon et al. 2017; Noma et al. 2012
1b	There is conflicting evidence about the effect of **vibration of antagonist muscles** to improve spasticity when compared to **vibration of agonist muscles**.	1	Li et al. 2020
1b	**Mirror therapy in combination with shockwave therapy** may produce greater improvements in spasticity than **shockwave alone, or conventional control**	1	Guo et al. 2019
1b	**Muscle vibration** may not have a difference in efficacy when compared to **botox** for improving spasticity.	1	Wu et al. 2018

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **muscle vibration therapies** to improve range of motion when compared to **sham vibration or conventional therapy**.	2	Amino et al. 2019; Tavernese et al. 2013
1b	**Muscle vibration** may produce greater improvements in range of motion than **botox.**	1	Wu et al. 2018

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Muscle vibration therapies** may produce greater improvements in outcomes of stroke severity than **sham vibration or conventional therapy**.	1	Toscano et al. 2019

Key points

Muscle vibration may be beneficial for improving upper limb function following stroke.

Additional Afferent and Peripheral Stimulation Methods

Adopted from: https://www.saebo.com/saebostim-micro/

Additional sensory stimulation methods evaluated for motor rehabilitation included short wave therapy, repetitive peripheral magnetic stimulation, intermittent pneumatic compression and other sensory stimulation techniques. Short-wave therapy is a non-invasive intervention in which electromagnetic radiation is applied to the region of the body typically at 27.12MHz in a continuous or pulse fashion (Wang et al. 2017). In repetitive peripheral magnetic stimulation coils are placed over paralysed muscles that generates a magnetic field that passes through the skin, and in turn can depolarize neurons to allow a muscle contraction (Momosaki et al. 2017). Repetitive peripheral magnetic stimulation can stimulate painlessly deep muscle structures that are out of range of traditional electrical stimulation (Momosaki et al. 2017). Intermittent pneumatic compression is the application of inflatable splints where pressure is applied intermittently to increase sensory input (Cambier et al. 2003).

A total of Nine RCTs were found that evaluated the use of afferent and peripheral stimulation for upper extremity motor rehabilitation poststroke.

Five RCTs examined tactile sensory stimulation (Seo et al. 2019; Law et al. 2018; Hunter et al. 2011; Stein et al. 2010; Cambier et al. 2003). One RCT examined proprioceptive ‘rocking chair’ stimulation (Feys et al. 1998). One RCT examined repetitive peripheral magnetic stimulation (Krewer et al. 2014). One RCT examined and sensory specific training regime (Carey et al. 2011). One RCT examined sensory stimulation combined with tDCS (Menezes et al. 2018).

The methodological details and results of all Nine RCTs are presented in Table 26.

Table 26. RCTs Evaluating Afferent and Peripheral Stimulation Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Tactile sensory stimulation compared to conventional care or sham		
Seo et al. (2019) RCT (9) N_{start}= 12 N_{end}= 12 TPS= Chronic	E: Sensory stimulation vibration bracelet C: Sham Duration: 2hrs, 3x/wk, 2wks	• Sensory Detection Threshold: (-) • Box and Block Test: (+exp) • Wolf Motor Function Test: (-)
Law et al. (2018) RCT (7) N_{start}= 12 N_{end}= 12 TPS= Subacute	E: Multisensory stimulation (thermal + vibration) C: Conventional therapy Duration: 90min, 2x/wk, 12wks	• Fugle-Meyers Assessment: (+exp) • Manual Muscle Testing: (+exp) • Function Test for the Hemiplegic Upper Extremity-HK: (+exp) • Modified Barthel Index: (-)
Hunter et al. (2011) RCT (7) N_{start}=76 N_{end}=75 TPS= Acute	E: Mobilization and Tactile Stimulation (3 dose levels) C: Conventional therapy Duration: 30-120min (3x per day), 5d/wk for 2wk	• Motricity Index (-) • Action Research Arm Test (-)
Stein et al. (2010) RCT (10) N_{start}=30 N_{end}=30 TPS=Chronic	E: Stochastic resonance stimulation (combination of subthreshold electrical stimulation and vibration) C: Sham stimulation Duration: 3d/wk for 4wk	• Fugl-Meyer Assessment (-) • Motor Activity Log (-) • Action Research Arm Test (-)
Cambier et al. (2003) RCT (7) N_{start}=23 N_{end}=23 TPS=Subacute	E: Intermittent pneumatic compression C: Sham Duration: 30min/d, 5d/wk for 4wk	• Nottingham Sensory Assessment (+exp) • Fugl-Meyer Assessment (+exp) • Ashworth Scale (-)
Rocking Chair Proprioceptive Stimulation vs Sham		
Feys et al. (1998) RCT (6) N_{start}=100 N_{end}=100 TPS=Acute	E: Rocking chair movement (proprioceptive stimulation) C: Sham stimulation Duration: 30min/d, 5d/wk for 6wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Barthel Index (-)
Repetitive Peripheral Magnetic Stimulaition vs Sham		
Krewer et al. (2014) RCT (9) N_{Start}=63 N_{End}=44 TPS=Chronic	E: Repetitive peripheral magnetic stimulation C: Sham stimulation Duration: 20min/d, 2d/wk for 2wk	• Modified Tardieu Scale (-) • Fugl-Meyer Assessment (-) • Barthel Index (-)
Sensory Discrimination Training vs Sham		

Carey et al. (2011)
RCT (8)
N_{start}= 50
N_{end}= 48
TPS= Chronic
	E: Sensory discrimination training
	C: Sham
	Duration: 60min, 3x/wk, 10 sessions (3-4wks)
		• Standardized sensory deficit index
		  • Fabric match test: (+exp)
		  • Wrist position sense test: (+exp)
		  • Finger position sense test: (+exp)
		  • Function tactile object recognition test): (+exp)

Sensory Stimulation Combined with tDCS		
Menezes et al. (2018) RCT (8) N_{start}= 22 N_{end}= 20	E: Active repetitive peripheral nerve sensory stimulation (RPPS) + sham tDCS E2: Sham RRPS + active tDCS E3: Active RRPS + active tDCS	E1 Vs C • Wrist Range of Motion (Flexion, Extension): (-) • Grip, Pinch Strength: (-) E2 Vs C

TPS= Chronic	C: Sham RRPS + sham tDCS Duration: 1 (2hrs RPPS, 20min tDCS) /session, 10-15d washout	• Wrist Range of Motion (Flexion, Extension): (-) • Grip, Pinch Strength: (-) E3 Vs C • Wrist Range of Motion (Flexion, Extension): (-) • Grip, Pinch Strength: (-) E1 Vs E2 Vs E3 • Wrist Range of Motion (Flexion, Extension): (-) • Grip, Pinch Strength: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Additional Afferent and Peripheral Stimulation

MOTOR FUNCTION

LoE	Conclusion Statement	RCTs	References
1b	**Tactile stimulation methods** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving motor function.	5	Seo et al. 2019; Law et al. 2018; Hunter et al. 2011; Stein et al. 2010; Cambier et al. 2003
1b	**"Rocking chair" proprioceptive stimulation** may not have a difference in efficacy when compared to **sham stimulation** for improving motor function.	1	Feys et al. 1998
1b	**Repetitive peripheral magnetic stimulation** may not have a difference in efficacy when compared to **sham stimulation** for improving motor function.	1	Krewer et al. 2014
1b	**"Rocking chair" proprioceptive stimulation** may not have a difference in efficacy when compared to **sham stimulation** for improving motor function.	1	Feys et al. 1998

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **tactile stimulation methods** to improve muscle strength when compared to **sham or conventional care**.	2	Law et al. 2018; Hunter et al. 2011

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1b	**Tactile stimulation methods** may produce greater improvements in dexterity than **sham or conventional therapy**	1	Seo et al. 2019

ACTIVITIES OF DAILY LIVING

LoE	Conclusion Statement	RCTs	References

1a	**Tactile stimulation methods** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving activities of daily living.	2	Law et al. 2018; Stein et al. 2010
1b	**"Rocking chair" proprioceptive stimulation** may not have a difference in efficacy when compared to **sham stimulation** for improving activities of daily living.	1	Feys et al. 1998
1b	**Repetitive peripheral magnetic stimulation** may not have a difference in efficacy when compared to **sham stimulation** for improving activities of daily living.	1	Krewer et al. 2014

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Tactile stimulation methods** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving spasticity.	1	Cambier et al. 2003
1b	**"Rocking chair" proprioceptive stimulation** may not have a difference in efficacy when compared to **sham stimulation** for improving spasticity.	1	Feys et al. 1998
1b	**Repetitive peripheral magnetic stimulation** may not have a difference in efficacy when compared to **sham stimulation** for improving spasticity.	1	Krewer et al. 2014

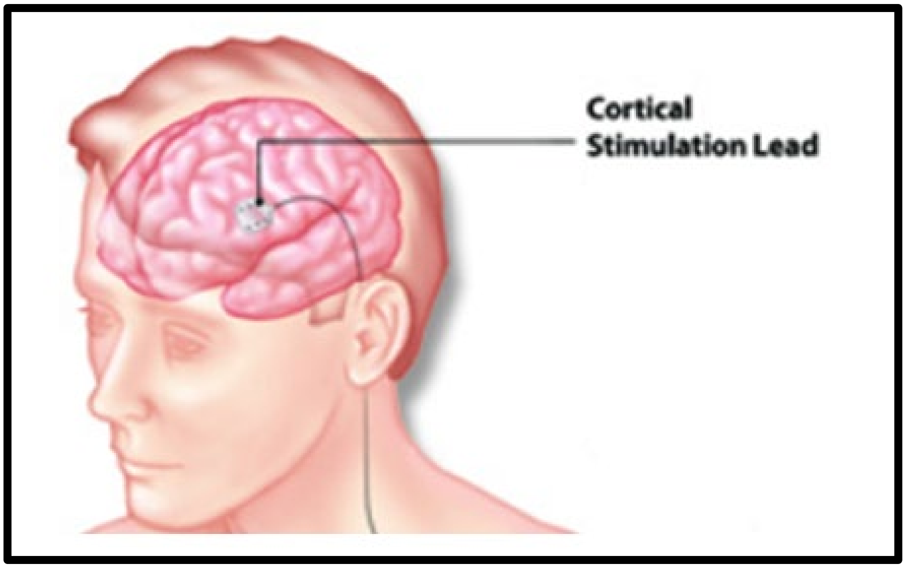
PROPRIOCEPTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **tactile stimulation methods** to improve proprioception when compared to **sham or conventional care**.	2	Seo et al. 2019; Cambier et al. 2003
1b	**Sensory discrimination training** may produce greater improvements in proprioception than **sham therapy**	1	Carey et al. 2011

Key points

Additional afferent and peripheral stimulation may not be beneficial for upper limb rehabilitation following stroke.

Invasive central nervous system stimulation

Invasive Cortical and Nerve Electrode Implant Stimulation



Adopted from: https://www.medgadget.com/2008/01/brain_stimulation_device_for_stroke_victims_fails_clinical_trial.html

Cortical stimulation in the motor cortex was traditionally used for the management of neuropathic pain, but preclinical evidence from animal models and clinical observations of pain patients showing motor improvements using this technique led to its adoption as an intervention for motor rehabilitation in stroke survivors (Levy et al. 2008; Tsubokawa et al. 1991). The neurosurgical procedure is performed through an extradural craniotomy where the stimulation electrode is placed on the dura matter of the motor cortex in a region predetermined from stereotaxic neuronavigation and functional magnetic resonance imaging (Levy et al. 2016; Brown et al. 2006). The frequency of stimulation is typically at 50Hz, and stimulation parameters remain consistent for the length of the intervention (Levy et al. 2016; Huang et al. 2008).

However, due to the invasive nature of this procedure and potential for adverse events, RCTs mainly investigating this technique for stroke rehabiltiation were feasibility studies (Brown et al. 2006; Huang et al. 2008; Levy et al. 2008), and only recently a phase III clinical trial (Levy et al. 2016).

Vagus nerve stimulation has been shown in preclinical evidence from animal models to influence neuroplasticity, as stimulation can lead to increased acetylcholine and norepinephrine release, both of which are involved in the reorganization of cortical networks (Dawson et al. 2016). As well as pairing upper limb rehabilitation with vagus nerve stimulation has been shown to further promote plasticity in preclinical settings (Hays et al. 2016). Only one study has looked at vagus nerve stimulation with upper limb rehabilitation in stroke survivors (Dawson et al. 2016).

The methodological details and results of 5 RCTs (Levy et al. 2016; Dawson et al. 2016; Huang et al. 2008; Levy et al. 2008; Brown et al. 2006) that have evaluated the use of invasive cortical and nerve stimulation methods for improving motor function post stroke are presented in Table 27.

Table 27. RCTs Evaluating Invasive Brain Stimulation Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Motor cortex stimulation		
Levy et al. (2016) RCT (6) N_{Start}=164 N_{End}=128 TPS=Chronic	E: Cortical implant with epidural 6-contact lead perpendicular to the primary motor cortex and a pulse generator C: Conventional rehabilitation Duration: *Not Specified*	• Arm Motor Ability Test (-) • Fugl-Meyer Assessment (-)
Huang et al. (2008) RCT (5) N_{start}=24 N_{end}=24 TPS=Chronic	E1: Motor cortex stimulation (50Hz) C1: Conventional rehabilitation E2: Motor cortex stimulation (101Hz) C2: Conventional rehabilitation Duration: 2.5hr/d, 5d/wk for 4 wk	• Fugl Meyer Score (+exp, +exp$_2$) • Box and Block Test (+exp, +exp$_2$) • Stroke Impact Scale (-) • Arm Motor Ability Test (-) • Grip strength (-)
Levy et al. (2008) RCT (5) N_{start}=24 N_{end}=24 TPS=Chronic	E: Motor cortex stimulation C: Conventional rehabilitation Duration: *Not Specified*	• Fugl Meyer Score (+exp) • Arm Motor Ability Test (+exp)
Brown et al. (2006) RCT (6) N_{start}=10 N_{end}=10 TPS=Chronic	E: Motor cortex stimulation C: Conventional rehabilitation Duration: 30min/d, 5d/wk for 3 wk	• Fugl Meyer Scale (+exp) • Stroke Impact Scale (+exp)
Vagus nerve stimulation		
Dawson et al. (2016) RCT (7) N_{Start}=20 N_{End}=20 TPS=Chronic	E: Impanted vagus nerve stimulation C: Conventional rehabilitation Duration: 20min/d, 4 d/wk for 8 wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (-) • Grip Strength (-) • Nine Hole Peg Test (-) • Box and Block Test (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Invasive Cortical and Nerve Stimulation

MOTOR FUNCTION			
LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **motor cortex stimulation** to improve motor function when compared to **conventional therapy**.	4	Levy et al. 2016; Huang et al. 2008; Levy et al. 2008; Brown et al. 2006
1b	There is conflicting evidence about the effect of **vagus nerve stimulation** to improve motor function when compared to **conventional therapy**.	1	Dawson et al. 2016

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
2	**Motor cortex stimulation** may not have a difference in efficacy when compared to **conventional therapy** for improving muscle strength.	1	Huang et al. 2008
1b	**Vagus nerve stimulation** may not have a difference in efficacy when compared to **conventional therapy** for improving muscle strength.	1	Dawson et al. 2016

DEXTERITY			
LoE	Conclusion Statement	RCTs	References
2	**Motor cortex stimulation** may produce greater improvements in dexterity than **conventional therapy**.	1	Huang et al. 2008
1b	**Vagus nerve stimulation** may not have a difference in efficacy when compared to **conventional therapy** for improving dexterity.	1	Dawson et al. 2016

ACTIVITIES OF DAILY LIVING			
1a	There is conflicting evidence about the effect of **motor cortex stimulation** to improve performance of activities of daily living when compared to **conventional therapy**.	3	Levy et al. 2016; Huang et al. 2008; Brown et al. 2006

Key points

The literature is mixed regarding invasive cortical and nerve stimulation for upper limb rehabilitation following stroke.

Non-invasive brain stimulation

Repetitive Transcranial Magnetic Stimulation (rTMS)

Adopted from: https://www.rtmscentre.co.uk/rtms-treatment-in-the-uk/

Transcranial magnetic stimulation is a painless and non-invasive method of affecting neural activity through the exogenous generation of an electromagnetic field through a coil placed on the scalp, that consequently induces a change in the electrical fields of the brain (Peterchev et al. 2012). The voltage and current of the electromagnetic field generated are dependent on the parameters of the stimulation device, which is not distorted by the biological tissues in which it is applied in (Peterchev et al. 2012). The neuromodulatory effects of transcranial magnetic stimulation are attributed largely to neural membrane polarization shifts that can lead to changes in neuron activity, synaptic transmission, and activation of neural networks (Peterchev et al. 2012). Repetitive transcranial magnetic stimulation (rTMS) is the application of repetitive trains of transcranial magnetic stimulation at regular intervals.

After a stroke, interhemispheric competition is altered; with cortical excitability increasing in the unaffected hemisphere increasing and decreasing in the affected hemisphere (Zhang et al. 2017). rTMS can be used to help modulate this interhemispheric competition, with low stimulation frequencies (≤1Hz) decreasing cortical excitability and inhibiting activity of the contralesional hemisphere, while high frequency (>1Hz) stimulation increases excitability and have a facilitatory effect on activity of the ipsilesional hemisphere (Dionisio et al. 2018).

A growing number of studies have investigated the effects of rTMS on improving upper extremity motor rehabilitation after a stroke. Low frequency rTMS versus sham stimulation or conventional therapy was assessed in 36 RCTs (Dos Santos et al. 2019; Du et al. 2019; El-Tamaway et al. 2019; Cha et al. 2018; Harvey et al. 2018; Long et al. 2018; Tarri et al. 2018; Watanabe et al. 2018; Askin et al. 2017; Gu et al. 2017; Meng and Song, 2017; Ozkeskin et al. 2017; Yang et al. 2017; Du et al. 2016; Li et al. 2016; Blesneag et al. 2015; Cassidy et al. 2015; Ludermann-Podubecka et al. 2015; Matsuura et al. 2015; Abo et al. 2014; Barros Galvao et al. 2014; Rose et al. 2014; Wang et al. 2014; Etoh et al. 2013; Higgins et al. 2013; Saskai et al. 2013; Conforto et al. 2012; Seniow et al. 2012; Emara et al. 2010; Khedr et al. 2009; Takeuchi et al. 2008; Liepert et al. 2007; Pomeroy et al. 2007; Fregni et al. 2006; Mansur et al. 2005;

Takeuchi et al. 2005), while high frequency rTMS versus sham stimulation or conventional therapy was assessed in 16 RCTs (Du et al. 2019; Gu et al. 2017; Guan et al. 2017; Du et al. 2016; Hosomi et al. 2016; Li et al. 2016; Cassidy et al. 2015; Kim et al. 2014; Kwon et al. 2014; Saskai et al. 2013; Chang et al. 2010; Emara et al. 2010; Khedr et al. 2010; Khedr et al. 2009; Malcom et al. 2007; Khedr et al. 2005). RCTs looking at multimodal interventions with rTMS were limited, and combinations included bilateral stimulation (both high and low frequency rTMS; (Long et al. 2018; Takeuchi et al. 2009)), mirror therapy (Ji et al. 2014), virtual reality (Zheng et al. 2015), sensory cueing (Yang et al. 2017), cyclic NMES (Etoh et al. 2019; Tosun et al. 2017), action observation (Noh et al. 2019), mental practice (Pan et al. 2019) and tDCS (Cho et al. 2017).

The methodological details and results of all 52 RCTs evaluating rTMS for the upper extremity motor rehabilitation are presented in Table 28.

Table 28. RCTs Evaluating rTMS Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Low frequency (1Hz) rTMS vs sham stimulation or conventional therapy		
Dos Santos et al. (2019) RCT (8) N_{start}= 20 N_{end}= 18 TPS= Chronic Ch11	E: Low Frequency rTMS C: Sham Duration: 3x/wk, 10x total + 30min Physical Therapy	• Modified Ashworth Scale: (+exp)
Du et al. (2019) RCT (9) N_{start}= 60 N_{end}= 44 TPS= Acute	E1: High frequency (rTMS) E2: Low frequency rTMS C: Sham Duration: 5 consecutive days (~22min)	E1 Vs C • Fugl-Meyers Upper Extremity: (+exp1) E2 Vs C • Fugl-Meyers Upper Extremity: (+exp2) E1 Vs E2 • Fugl-Meyers Upper Extremity: (-)
El-Tamaway et al. (2019) RCT (5) N_{start}= 40 N_{end}= Not reported TPS= Subacute	E: Low frequency rTMS C: Conventional therapy Duration: 20min, 5x/wk, 2wks	• Fugl-Meyer Assessment: (+exp) • Hand Grip Dynamometer: (-)
Harvey et al. (2018) RCT (8) N_{start}= 199 N_{end}= 169 TPS= Chronic	E: Navigated low frequency rTMS C: Sham Duration: 60min, 3x/wk, 6wks therapy (15min of stimulation/sham before)	• Fugl-Meyers Assessment Upper Extremity: (-) • Action Research Arm Test: (-) • Wolf Motor Function Test: (-)
Long et al. (2018) RCT (7) N_{Start} =62 N_{End} =62 TPS=Acute Multi-site	E1: Low Frequency (1Hz) combined with High Frequency (10Hz) Repetitive Transcranial Magnetic Stimulation E2: Low Frequency (1Hz) Repetitive Transcranial Magnetic Stimulation C: Sham Repetitive Transcranial Magnetic Stimulation Duration: *Not specified*	E2 vs C • Fugl-Meyer Assessment (+exp$_2$) • Wolf Motor Function Test (-)
Tarri et al. (2018) RCT (6) N_{Start} =24 N_{End} =24	E: Paired associative stimulation (electrical stimulation + low frequency (1Hz) rTMS) C: Sham Stimulation	• Fugl-Meyer Assessment (-)

TPS=Subacute	Duration: *Not specified*	
Watanabe et al. (2018) RCT (5) N_{Start} =21 N_{End} =21 TPS=Acute	E1: Intermittent Theta-Burst Stimulation E2: Low Frequency (1Hz) Repetitive Transcranial Magnetic Stimulation C: Sham Stimulation Duration: *Not specified*	E2 vs C • Fugl-Meyer Assessment: (-) • Stroke Impairment Assessment Set (-) • Modified Ashworth Scale (+exp2) • Grip Strength (-)
Askin et al. (2017) RCT (7) N_{Start} =40 N_{End} =40 TPS=Chronic	E: Low frequency (1Hz) Repetitive Transcranial Magnetic Stimulation to unaffected hemisphere C: Conventional Physical Therapy Duration: 1 hr/d, 5d/wk, for 2wk	• Box and Block Test (+exp) • Functional Independence Measure (+exp) • Brunnstrom Recovery Stages (-) • Fugl-Meyer Assessment (-) • Modified Ashworth Scale (-)
Gu et al. (2017) RCT (9) N_{start}= 24 N_{end}= 24 TPS= Chronic	E: High frequebcy rTMS C: Low frequency rTMS Duration: 5d/wk, 2wks (1000 pulses)	E1 vs E2 vs C • Motricity Index: (-) • Modified Brunnstrom Classification: (-)
Meng & Song (2017) RCT (6) N_{Start} =20 N_{End} =20 TPS=NR	E: Low Frequency (1Hz) Repetitive Transcranial Magnetic Stimulation to unaffected hemisphere C: Sham Repetitive Transcranial Magnetic Stimulation Duration: 30 min/d, 7d/wk for 2wk	• National Institute of Health Stroke Scale (+exp) • Barthel Index (+exp) • Fugl-Meyer Assessment (+exp)
Ozkeskin et al. (2017) RCT (9) N_{Start} =21 N_{End} =21 TPS=Chronic	E: Low frequency (1Hz) Repetitive Transcranial Magnetic Stimulation to unaffected hemisphere C: Sham Repetitive Transcranial Magnetic Stimulation Duration: 90 min/d, 5d/wk for 2wk	• Brunnstrom Recovery Stages (-) • Finger Touch Localization (-) • Modified Ashworth Scale (-) • Wrist Proprioceptive Evaluations (+exp)
Cha et al. (2016) RCT (9) N_{start}= 30 N_{end}= 30 TPS= Subacute	E: Low frequency rTMS C: Sham Duration: 20min rTMS, 30min conventional therapy	• Box and Block Test (+exp) • Grip strength (-)
Du et al. (2016) RCT (7) N_{Start} =69 N_{End} =59 TPS=Acute	E1: High frequency (3Hz) rTMS E2: Low frequency (1Hz) rTMS C: Sham rTMS Duration: 30min/d, 5d/wk for 1wk	E2 vs C • Fugl-Meyer Assessment (+exp2) • Medical Research Council Score (+exp2) • National Institute of Health Stroke Scale (+exp2) • Modified Rankin Scale (+exp2) • Barthel Index (+exp2)
Li et al. (2016) RCT (7) N_{Start} =127 N_{End} =127 TPS=Subacute	E1: Low frequency (1Hz) rTMS E2: High frequency (10Hz) rTMS C: Sham Duration: 40min/d, 5d/wk for 2wk	E1 vs C • Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (-)
Ludemann-Podubecka et al. (2016) RCT (7) N_{Start} =10 N_{End} =10 TPS=Subacute	E: Low frequency (1Hz) rTMS C: Sham Duration: 30min/d, 5d/wk for 6wk	• Jebsen Taylor Hand Function Test (+exp) • Box and Block Test (-)
Blesneag et al. (2015) RCT (6) N_{start}= 16 N_{end}= 16 TPS= Acute	E: Low frequency rTMS C: Sham Duration: 10 consecutive sessions (20min/5x/2wk**)**	Fugl-Meyer Assessment Upper Extremity: (-)
Cassidy et al. (2015) RCT (7) N_{Start} =11 N_{End} =11 TPS=Chronic	E1: High frequency (6Hz) rTMS E2: Low frequency (1Hz) rTMS C: Sham Duration: 1hr/d, 3d/wk for 5wk	E2 vs. C • Box and Block Test (+exp2)

Ludemann-Podubecka et al. (2015) RCT (7) N_{Start} =40 N_{End} =33 TPS=Chronic	E: Low frequency (1Hz) rTMS C: Sham Duration: 30min/d, 5d/wk for 6 wk	• Wolf Motor Function Test (+exp) • Motor Evaluation Scale (+exp) • Finger Tapping (-)
Matsuura et al. (2015) RCT (8) N_{start}= 20 N_{end}= 20 TPS= Acute	E: Low frequency rTMS C: Sham Duration: 20min/d, 5 consecutive days	• Fugl-Meyer Assessment Upper Extremity: (+exp) • Purdue Pegboard Test: (+exp) • Grip Strength: (-)
Abo et al. (2014) RCT (7) N_{Start}=66 N_{End}=66 TPS=Chronic	E: Low frequency (1Hz) rTMS + OT training (NEURO) C: CIMT Duration: 20min rTMS & 120min OT (2x/d), 6d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp)
Barros Galvao et al. (2014) RCT (8) N_{Start}=20 N_{End}=18 TPS=Chronic	E: Low frequency (1Hz) rTMS C: Sham Duration: 1hr/d, 5d/wk for 2wk	• Modified Ashworth Scale (-) • Fugl-Meyer Assessment (-) • Functional Independence Measure (-) • Wrist range of motion (-)
Rose et al. (2014) RCT (5) N_{Start}=22 N_{End}=19 TPS=Chronic	E: Low frequency (1Hz) rTMS + functional task practice (FTP) C: Sham + FTP Duration: 1.5hr/d, 4d/wk, 4wk	• Wolf Motor Function Test (-) • Pinch strength (lateral and palmar) (-) • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Modified Ashworth Scale (-) • Motor Activity Log (-)
Wang et al. (2014) RCT (9) N_{Start}=44 N_{End}=44 TPS=Chronic	E1: Low frequency (1Hz) rTMS applied to primary motor cortex E2: Low frequency (1Hz) rTMS applied to premotor area C: Sham Duration: *Not Specified*	E1 vs C • Wolf Motor Function Test (+exp) • Fugl-Meyer Assessment (+exp) • Medical Research Council Scale (+exp) E2 vs C • Wolf Motor Function Test: (+exp_2) • Fugl-Meyer Assessment: (+exp_2) • Medical Research Council Scale (+exp_2) E1 vs E2 • Wolf Motor Function Test (+exp) • Fugl-Meyer Assessment (+exp) • Medical Research Council Scale (+exp)
Etoh et al. 2013 RCT Crossover (7) N_{Start}=18 N_{End}=18 TPS=Chronic	E1: Low frequency (1Hz) rTMS C: Sham rTMS Duration: 4min, 5d/wk for 2wk	• Action Research Arm Test (+exp) • Fugl Meyer Assessment (-) • Simple test for evaluating hand function (-) • Modified Ashworth scale (-)
Higgins et al. (2013) RCT (7) N_{Start}=11 N_{End}=11 TPS=Chronic	E: Low frequency (1Hz) rTMS C: Sham Duration: 90min/d, 4d/wk for 4wk	• Box and Block Test (-) • Motor Acitivity Log (-) • Wolf Motor Function Test (-)
Sasaki et al. (2013) RCT (8) N_{Start}=29 N_{End}=29 TPS=Acute	E1: High frequency (10Hz) rTMS E2: 1Hz rTMS non-lesioned hemisphere C: Sham Duration: 45min/d, 2d/wk for 6wk	E2 vs C • Grip strength (-) • Tapping frequency (-)
Conforto et al. (2012) RCT (6) N_{start}=29 N_{end}=28 TPS=Acute	E: Low frequency (1Hz) rTMS C: Sham Duration: 25min/d, 5d/wk for 4wk	• Jebsen-Taylor Hand Function test (+exp) • Pinch Force (+exp) • Fugl-Meyer Assessment (+exp) • Modified Ashworth Scale (-)
Seniów et al. (2012) RCT (8)	E: Low frequency (1Hz) rTMS + PT C: Sham + PT	• Wolf Motor Function Test (-) • Fugl-Meyer Assessment (-)

N_{start}=40 N_{end}=33 TPS=Chronic	Duration: 75min/d, 5d/wk for 3wk	
Emara et al. (2010) RCT (7) N_{start}=60 N_{end}=60 TPS=Subacute	E1: High frequency (5Hz) rTMS E2: Low frequency (1Hz) rTMS C: Sham Duration: 30min/d, 5d/wk for 4wk	E2 vs C • Finger tapping test (+exp_2) • Frenchay Activities Index (+exp_2) • Modified Rankin Scale (+exp_2)
Khedr et al. (2009) RCT (8) N_{start}=36 N_{end}=36 TPS=Acute	E1: Low frequency (1Hz) rTMS E2: High frequency (3Hz) rTMS C: Sham Duration: 30min/d, 3d/wk for 4wk	E1 vs C • Grip strength (+exp) • Purdue Pegboard task (+exp) • Barthel Index (+exp) • NIHSS (+exp)
Takeuchi et al. (2008) RCT (7) N_{start}=20 N_{end}=20 TPS=Chronic	E: Low frequency (1Hz) rTMS + pinch force motor training C: Sham + pinch force motor training Duration: *Not Specified*	• Pinch force (+exp)
Liepert et al. (2007) RCT (7) N_{start}=12 N_{end}=12 TPS=Acute	E: Low frequency (1Hz) rTMS C: Sham Duration: 3hr/d, 3d/wk for 4wk	• Grip strength (-) • 9-hole peg test (+exp)
Pomeroy et al. (2007) RCT (8) N_{start}=27 N_{end}=24 TPS=Chronic	E1: Low frequency (0.5Hz) rTMS + voluntary muscle contraction (VMC) E2: Low frequency (0.5Hz) rTMS + placebo VMC E3: Sham rTMS + VMC C: Sham rTMS + placebo VMC Duration: *Not Specified*	• Flexion/extension torque (-) • Action Research Arm Test (-)
Fregni et al. (2006) RCT (7) N_{start}=15 N_{end}=15 TPS=Chronic	E: Low frequency (1Hz) rTMS C: Sham Duration: 20min/d, 5d/wk for 6wk	• Jebsen-Taylor Hand Function test (+exp)
Mansur et al. (2005) RCT (4) N_{start}=10 N_{end}=10 TPS=Chronic	E: Low frequency (1Hz) rTMS C: Sham Duration: *Not Specified*	• Finger tapping test (-) • Perdue Pegboard test (+exp)
Takeuchi et al. (2005) RCT (6) N_{start}=20 N_{end}=20 TPS=Chronic	E: Low frequency (1Hz) rTMS C: Sham Duration: 25min/d, 3d/wk for 5wk	• Hand and pinch force (-)
High frequency (>1Hz) rTMS vs Sham or conventional therapy		
Du et al. (2019) RCT (9) N_{start}= 60 N_{end}= 44 TPS= Acute	E1: High frequency (rTMS) E2: Low frequency rTMS C: Sham Duration: 5 consecutive days (~22min)	E1 Vs C • Fugl-Meyers Upper Extremity: (+exp1) E2 Vs C • Fugl-Meyers Upper Extremity: (+exp2) E1 Vs E2 • Fugl-Meyers Upper Extremity: (-)
Gu et al. (2017) RCT (9) N_{start}= 24 N_{end}= 24 TPS= Chronic	E: High frequebcy rTMS C: Low frequency rTMS Duration: 5d/wk, 2wks (1000 pulses)	E1 vs E2 vs C • Motricity Index: (-) • Modified Brunnstrom Classification: (-)

Guan et al. (2017) RCT (5) N_{Start} =42 N_{End} =27 TPS=Acute	E: High frequency (5Hz) Repetitive Transcranial Magnetic Stimulation C: Sham Repetitive Transcranial Magnetic Stimulation Duration: 25 min/d, 4d/wk for 6wk	• National Institutes of Health Stroke Scale (+exp) • Barthel Index (+exp) • Fugl-Meyer Assessment (+exp) • Modified Rankin Score (-)
Du et al. (2016) RCT (7) N_{Start} =69 N_{End} =55 TPS=Acute	E1: High frequency (3Hz) rTMS E2: Low frequency (1Hz) rTMS C: Sham rTMS Duration: 30min/d, 5d/wk for 1wk	E1 vs C • Fugl-Meyer Assessment (-) • Medical Research Council Score (-) • National Institute of Health Stroke Scale (+exp) • Modified Rankin Scale (+exp) • Barthel Index (+exp)
Hosomi et al. (2016) RCT (8) N_{Start} =41 N_{End} =39 TPS=Subacute	E: High frequency (5Hz) rTMS C: Sham Duration: 1hr/d, 5d/wk for 2wk	• Brunnstorm Recovery Stages (-) • Fugl-Meyer Assessment (-) • National institute for Health Stroke Scale (-) • Grip Power (-)
Li et al. (2016) RCT (7) N_{Start} =127 N_{End} =127 TPS=Subacute	E1: Low frequency (1Hz) rTMS E2: High frequency (10Hz) rTMS C: Sham Duration: 40min/d, 5d/wk for 2wk	E2 vs C • Fugl-Meyer Assessment (+exp_2) • Wolf Motor Function Test (-)
Kim (2014) RCT (6) N_{Start}=31 N_{End}=31 TPS=Chronic	E: High frequency (10Hz) rTMS C: Sham Duration: 10min/d, 5d/wk for 4wk	• Manual Function Test (+exp)
Kwon et al. (2014) RCT (7) N_{start}= 14 N_{end}= 14 TPS= Chronic	E: 10 Hz (high freq) rTMS and Interleaved combination method (ICM) motor training E2: 10 Hz (high freq) rTMS and Preconditioned combination method (PCM) motor training (standard) C: N/A Duration: 20 min/session, 2 sessions total; 1 session per condition (washout period 48 hours	E1 Vs C • Purdue Pegboard Test: (-) • Nine-Hole Peg Test: (-) • Movement Time (Sequential Finger Motor Task) (-) • Movement Accuracy (Sequential Finger Motor Task) (-) E2 Vs C • Purdue Pegboard Test: (-) • Nine-Hole Peg Test: (-) • Movement Time (Sequential Finger Motor Task): (+exp2) • Movement Accuracy (Sequential Finger Motor Task): (+exp2) E1 Vs E2 • Purdue Pegboard Test: (-) • Nine-Hole Peg Test: (-) • Movement Time (Sequential Finger Motor Task) (-) • Movement Accuracy (Sequential Finger Motor Task) (-)
Sasaki et al. (2013) RCT (8) N_{Start}=29 N_{End}=29 TPS=Acute	E1: 10Hz rTMS lesioned hemisphere E2: 1Hz rTMS non-lesioned hemisphere C: Sham Duration: 45min/d, 2d/wk for 6wk	E1 vs C • Grip strength (+exp) • Tapping frequency (+exp)
Chang et al. (2010) RCT (5) N_{start}=28 N_{end}=28 TPS=Subacute	E: High frequency (10Hz) rTMS C: Sham Duration: 2min, 5d/wk for 2wk	• Motricity Index (+exp) • Fugl-Meyer Assessment (-)
Emara et al. (2010) RCT (7) N_{start}=60 N_{end}=60 TPS=Subacute	E1: 5Hz rTMS E2: 1Hz rTMS C: Sham Duration: 30min/d, 5d/wk for 4wk	E1 vs C • Finger tapping test (+exp) • Frenchay Activities Index (+exp) • Modified Rankin Scale (+exp)

Khedr et al. (2010) RCT (8) N_{start}=48 N_{end}=38 TPS=Acute	E1: 3Hz rTMS E2: 10Hz rTMS C: Sham Duration: 30min/d, 3d/wk for 4wk	E1/E2 vs C • Grip strength (+exp, +exp_2) • NIHSS (+exp, +exp_2) • Modified Rankin Scale (+exp, +exp_2) E1 vs E2 • Grip strength (-) • NIHSS (-) Modified Rankin Scale (-)
Khedr et al. (2009) RCT (8) N_{start}=36 N_{end}=36 TPS=Acute	E1: 1Hz rTMS E2: 3Hz rTMS C: Sham Duration: 30min/d, 3d/wk for 4wk	E2 vs C • Grip strength (+exp_2) • Purdue Pegboard task (+exp_2) • Barthel Index (+exp_2) • NIHSS (+exp_2)
Malcolm et al. (2007) RCT (6) N_{start}=19 N_{end}=19 TPS=Chronic	E: High frequency (20Hz) rTMS C: Sham Duration: 40min/d, 6d/wk for 5wk	• Wolf Motor Function Test (-) • Motor Activity Log (-)
Khedr et al. (2005) RCT (6) N_{start}=52 N_{end}=52 TPS=Acute	E: High frequency (3Hz) rTMS C: Sham Duration: 45min/d, 5d/wk, 2wk	• Barthel Index (+exp) • NIHSS (+exp) • Scandinavian Stroke Impact Scale (+exp)
Low frequency combined with high frequency rTMS or low frequency versus high frequency rTMS		
Long et al. (2018) RCT (7) N_{Start} =62 N_{End} =62 TPS=Acute	E1: Low Frequency Combined with High Frequency Repetitive Transcranial Magnetic Stimulation E2: Low Frequency Repetitive Transcranial Magnetic Stimulation C: Sham Repetitive Transcranial Magnetic Stimulation Duration: *Not Specified*	E1 vs C • Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp) E1 vs E2 • Fugl-Meyer Assessment (-) • Wolf Motor Function Test (+exp)
Takeuchi et al. (2009) RCT (6) N_{start}=30 N_{end}=30 TPS=Chronic	E1: Bilateral (dual) rTMS (1Hz and 10Hz) E2: 10Hz rTMS E3: 1Hz rTMS Duration: 15min/d, 3d/wk for 5wk	E1 vs E2 • Pinch force (+exp) E1 vs E3 • Pinch force (+exp)
rTMS plus NMES comapared to rTMS		

Etoh et al. (2019)
RCT (8)
N_{start}= 20
N_{end}= 20
TPS= Chronic
	E: Low frequency rTMS + NMES
	C: Sham + low frequency rTMS
	Duration: 10min, 5d/wk, 4wks
		• Fugl-Meyers Assessment Upper Extremity: (-)
		• Action Research Arm Test: (-)
		• Box and Block Test: (+exp)
		• Modified Ashworth Scale:
		  • Elbow: (-)
		  • Wrist: (-)
		  • Finger: (-)

Tosun et al. (2017) RCT (7) N_{Start} =25 N_{End} =25 TPS=Subacute	E1: Low Frequency (1Hz) Repetitive Transcranial Magnetic Stimulation E2: Low Frequency Repetitive Transcranial with Cyclic NMES C: Physical Therapy Duration: 1 hr/d, 5d/wk for 4wk	E1/E2 vs C; E1 vs E2 • Fugl-Meyer Assessment (-) • Motricity Index (-) • Brunnstrom Recovery Stages (-) • Modified Ashworth Scale (-) • Barthel Index (-)
rTMS plus additional interventions		

Noh et al. (2019)
RCT (7)
N_{start}= 22
N_{end}= 22
TPS= Acute/subacute
	E: Low frequency rTMS + Action Observation
	C: Low frequency rTMS
	Duration: 20min each, 5x/wk, 2wks
		• Brunstomm Recovery Stages
		  • Proximal: (-)
		  • Distal: (-)
		• Fugl-Meyers Assessment: (-)
		• Manual Function Test (-)
		  • Proximal: (-)
		  • Distal: (-)
		• Grip Power Test: (-)

Pan et al. (2019) RCT (7) N_{start}= 44 N_{end}= 42 TPS= subacute	E: Low frequency rTMS + mental practice C: Low frequency rTMS Duration: 30min, 5d/wk, 2wks	• Wolf Motor Function Test: (+exp) • Fugl-Meyer Assessment Upper Extremity: (+exp) • Modified Barthel Index: (+exp) • Box and Block Test: (+exp)
Cho et al. (2017) RCT (6) N_{start}= 30 N_{end}= 30 TPS= Acute	E: High frequency rTMS + cathodal tCDS C: High frequency rTMS Duration: 20min, 5x/wk for 2wks	• Fugle Meyers Assessment: (+exp)
Yang et al. (2017) RCT (8) N_{Start} =60 N_{End} =60 TPS=Subacute	E1: Low frequency (1Hz) Repetitive Transcranial Magnetic Stimulation with Sensory Cueing E2: Low frequency (1Hz) Repetitive Transcranial Magnetic Stimulation C: Conventional Therapy Duration: 45 min/d, 5d/wk for 4wk	E1 vs C • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) Modified Barthel Index (-) E2 vs C • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Modified Barthel Index (-) E1 vs E2 • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Modified Barthel Index (-)
Zheng et al. (2015) RCT (7) N_{Start}=112 N_{End}=108 TPS=Chronic	E: Low frequency (1Hz) rTMS + virtual reality (VR) training C: Sham + VR training Duration: 45min/d, 6d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp) • Modified Barthel Index (+exp)
Ji et al. (2014) RCT (7) N_{Start}=35 N_{End}=35 TPS=Chronic	E1: Mirror therapy + high frequency (10Hz) rTMS E2: Mirror therapy C: Sham Duration: 15 min/d, 6d/wk for 4wk	E1 vs E2 • Fugl-Meyer Assessment (+exp) • Box and Block Test (+exp) E1 vs C • Fugl-Meyer Assessment (+exp) • Box and Block Test (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about rTMS

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Low frequency rTMS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving motor function.	27	Du et al. 2019; El-Tamaway et al. 2019; Harvey et al. 2018; Long et al. 2018; Tarri et al. 2018; Watanabe et al. 2018; Askin et al. 2017; Gu et al. 2017; Meng and Song, 2017; Ozkesin et al. 2017; Tosun et al. 2017; Yang et al. 2017; Du et al. 2016; Li et al. 2016; Blesneag et al. 2015; Ludermann-Podubecka et al. 2015; Matsuura et al. 2015; Abo et al. 2014; Barros Galvao et al. 2014; Rose et al. 2014; Wang et al. 2014; Etoh et al. 2013; Higgins et al. 2013; Conforto et al. 2012; Seniow et al. 2012; Pomeroy et al. 2007; Fregni et al. 2006

1a	**High frequency rTMS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving motor function.	9	Du et al. 2019; Gu et al. 2017; Guan et al. 2017; Du et al. 2016; Hosomi et al. 2016; Li et al. 2016; Kim et al. 2014; Chang et al. 2010; Malcom et al. 2007
1b	There is conflicting evidence about the effect of **bilateral rTMS stimulation (both high and low frequency)** to improve motor function when compared to **sham stimulation or conventional therapy**.	1	Long et al. 2018
1b	**Low frequency rTMS with sensory cueing** may not have a difference in efficacy when compared to **low frequency rTMS or sham stimulation** for improving motor function.	1	Yang et al. 2017
1b	**Low frequency rTMS combined with virtual reality training** may produce greater improvements in motor function than **virtual reality training on its own or sham stimulation combined with virtual reality**.	1	Zheng et al. 2015
1b	**Mirror therapy combined with high frequency rTMS** may produce greater improvements in motor function than **mirror therapy on its own or sham stimulation**.	1	Ji et al. 2014
1a	**Low frequency rTMS with cyclic NMES** may not have a difference in efficacy when compared to **low frequency rTMS or conventional therapy** for improving motor function.	2	Etoh et al. 2019; Tosun et al. 2017
1b	**Low frequency rTMS with Action Observation** may not have a difference in efficacy when compared to **low frequency rTMS** for improving motor function.	1	Noh et al. 2019
1b	**Mental Practice combined with low frequency rTMS** may produce greater improvements in motor function than **low frequency rTMS.**	1	Pan et al. 2019
1b	**tDCS combined with high frequency rTMS** may produce greater improvements in motor function than **high frequency rTMS**.	1	Cho et al. 2017

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **low frequency rTMS** to improve dexterity when compared to **sham stimulation or conventional therapy**.	13	Cha et al. 2018; Askin et al. 2017; Ozkeskin et al. 2017; Ludermann-Podubecka et al. 2016; Cassidy et al. 2015; Ludermann-Podubecka et al. 2015; Matsuura et al. 2015; Higgins et al. 2013; Saskai et al. 2013; Emara et al. 2010; Khedr et al. 2009; Liepert et al. 2007; Mansur et al. 2005
1a	**High frequency rTMS** may produce greater improvements in dexterity than **sham stimulation or conventional therapy**.	5	Cassidy et al. 2015; Kwon et al. 2014; Saskai et al. 2013; Emara et al. 2010; Khedr et al. 2009
1b	**Mirror therapy combined with high frequency rTMS** may produce greater improvements in dexterity than **mirror therapy on its own or sham stimulation**.	1	Ji et al. 2014

1b	**Low frequency rTMS with cyclic NMES** may not have a difference in efficacy when compared to **low frequency rTMS or conventional therapy** for improving dexterity.	1	Etoh et al. 2019

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Low frequency rTMS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving spasticity.	9	Dos Santos et al. 2019; Watanabe et al. 2018; Askin et al. 2017; Ozkeskin et al. 2017; Tosun et al. 2017; Barros Galvao et al. 2014; Rose et al. 2014; Etoh et al. 2013; Conforto et al. 2012
1a	**Low frequency rTMS with cyclic NMES** may not have a difference in efficacy when compared to **low frequency rTMS or conventional therapy** for improving spasticity.	2	Etoh et al. 2019; Tosun et al. 2017

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Low frequency rTMS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving range of motion.	2	Barros Galvao et al. 2014; Pomeroy et al. 2007

PROPRIOCEPTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Low frequency rTMS** may produce greater improvements in proprioception than **sham stimulation or conventional therapy**.	1	Ozkeskin et al. 2017

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Low frequency rTMS** may produce greater improvements on measures of stroke severity than **sham stimulation or conventional therapy**.	5	Askin et al. 2017; Meng and Song, 2017; Du et al. 2016; Emara et al. 2010; Khedr et al. 2009
1a	**High frequency rTMS** may produce greater improvements on measures of stroke severity than **sham stimulation or conventional therapy**.	6	Guan et al. 2017; Du et al. 2016; Hosomi et al. 2016; Emara et al. 2010; Khedr et al. 2010; Khedr et al. 2009
1b	**Low frequency rTMS with cyclic NMES** may not have a difference in efficacy when compared to **low frequency rTMS or conventional therapy** for improvements on measures of stroke severity.	1	Tosun et al. 2017

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **low frequency rTMS** to improve performance of activities	9	Askin et al. 2017; Meng and Song, 2017; Tosun et al. 2017; Yang et al. 2017; Du et al. 2016; Barros Galvao et al. 2014; Rose et

	of daily living when compared to **sham stimulation or conventional therapy**.		al. 2014; Higgins et al. 2013; Emara et al. 2010; Khedr et al. 2009
1a	**High frequency rTMS** may produce greater improvements in performance of activities of daily living than **sham stimulation or conventional therapy**.	6	Guan et al. 2017; Du et al. 2016; Emara et al. 2010; Khedr et al. 2009; Malcom et al. 2007; Khedr et al. 2005
1b	**Low frequency rTMS with sensory cueing** may not have a difference in efficacy when compared to **low frequency rTMS or sham stimulation** for improving performance of activities of daily living.	1	Yang et al. 2017
1b	**Low frequency rTMS combined with virtual reality training** may produce greater improvements in performance of activities of daily living than **virtual reality training on its own or sham stimulation combined with virtual reality**.	1	Zheng et al. 2015
1b	**Low frequency rTMS with cyclic NMES** may not have a difference in efficacy when compared to **low frequency rTMS or conventional therapy** for improving performance of activities of daily living.	1	Tosun et al. 2017

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	**Low frequency rTMS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving muscle strength.	15	El Tamaway et al. 2019; Cha et al. 2018; Watanabe et al. 2018; Gu et al. 2017; Tosun et al. 2017; Du et al. 2016; Matsuura et al. 2015; Rose et al. 2014; Wang et al. 2014; Saskai et al. 2013; Conforto et al. 2012; Khedr et al. 2009; Takeuchi et al. 2008; Liepert et al. 2007; Takeuchi et al. 2005
1a	There is conflicting evidence about the effect of **high frequency rTMS** to improve muscle strength when compared to **sham stimulation or conventional therapy**.	8	Gu et al. 2017; Du et al. 2016; Hosomi et al. 2016; Saskai et al. 2013; Chang et al. 2010; Khedr et al. 2010; Khedr et al. 2009
1a	**Bilateral rTMS stimulation (both high and low frequency)** may produce greater improvements in muscle strength than **low frequency rTMS**.	1	Takeuchi et al. 2009
1a	**Bilateral rTMS stimulation (both high and low frequency)** may produce greater improvements in muscle strength than **high frequency rTMS**.	1	Takeuchi et al. 2009
1b	**Low frequency rTMS with cyclic NMES** may not have a difference in efficacy when compared to **low frequency rTMS or conventional therapy** for improving muscle strength.	1	Tosun et al. 2017
1b	**Low frequency rTMS with Action Observation** may not have a difference in efficacy when compared to **low frequency rTMS** for improving muscle strength.	1	Noh et al. 2019
1b	**Mental Practice combined with low frequency rTMS** may produce greater improvements in muscle strength than **low frequency rTMS.**	1	Pan et al. 2019

Key points

There is conflicting evidence about the benefits of low -frequency rTMS for upper limb rehabilitation following stroke when compared to conventional or sham therapy.

There is conflicting evidence about the benefits of high-frequency rTMS on improving upper limb rehabilitation following stroke when compared to conventional or sham therapy.

Both low- and high-frequency rTMS combined with select other therapies may be beneficial for some aspects of upper limb rehabilitation following stroke.

Theta Burst Stimulation (TBS)

Adopted from: https://www.psychiatryadvisor.com/home/depression-advisor/intermittent-theta-burst-stimulation-for-major-depressive-disorder-treatment/

Theta Burst Stimulation (TBS) is an emerging treatment modality that is a patterned form of rTMS where stimulation pulses are delivered in triplets or bursts at a high frequency (50Hz), and in a short interval (200ms), intending to mimic naturally occurring theta brain oscillations (Schwippel et al. 2019). TBS can also be used to adjust interhemispheric rivalry after a stroke and promote motor recovery through the delivery of continuous TBS (cTBS) to reduce cortical excitability in the contralesional hemisphere (600 pulses over 40 seconds); or intermittent TBS (iTBS) to increase cortical excitability in the ipsilesional hemisphere (600 pulses over 190 seconds) (Schwippel et al. 2019; Cotoi et al. 2019).

A total of 16 RCTs were found that evaluated the use of TBS for upper extremity motor rehabilitation poststroke.

Nine RCTs evaluated the effects of iTBS (Chen et al. 2019; Khan et al. 2019; Watanabe et al. 2018; Ackerley et al. 2016; Volz et al. 2016; Kim et al. 2015; Hsu et al. 2013; Talelli et al. 2012), and five RCTs the effects of cTBS (Nicolo et al. 2018; Di Lazzaro et al. 2016; Ackerley et al. 2014; Di Lazzaro et al. 2014; Talelli et al. 2012; Ackerley et al. 2010. Additionally, two RCTs evaluated the effects of iTBS combined with low frequency rTMS compared to sham TBS/rTMS for improving upper extremity motor rehabilitation outcomes (Meng et al. 2020; Sung et al. 2013), and one RCT exmaned iTBS compared to FES (Khan et al. 2019).

The methodological details and results of all 16 RCTs are presented in Table 29.

Table 29. RCTs Evaluating TBS Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Intermittent TBS versus sham stimulation		

Chen et al. (2019)
RCT (7)
N_{start}= 23
N_{end}= 22
TPS= Chronic
	E: iTBS
	C: Sham
	Duration: ~20min, 5x/wk for 2wks
		• Modified Ashworth Scale: (+exp)
		• Fugle Meyers Assessment: (+exp)
		• Action Research Arm Test: (+exp)
		  • Gross (-)
		  • Grasp (+exp)
		  • Grip (+exp)
		  • Pinch (+exp)
		• Box and Block Test: (+exp)
		• Motor Activity Log:
		  • Amount of Use: (-)
		  • Quality of Movement: (-)

Watanabe et al. (2018) RCT (5) N_{Start} =21 N_{End} =21 TPS=Acute	E1: Intermittent Theta-Burst Stimulation E2: Low Frequency Repetitive Transcranial Magnetic Stimulation C: Sham Stimulation Duration: *Not Specified*	E1 vs C: • Fugl-Meyer Assessment (-) • Stroke Impairment Assessment Set (-) • Modified Ashworth Scale (-) • Grip Strength (-)
Ackerley et al. (2016) RCT (8) N_{Start}=18 N_{End}=18 TPS=Chronic	E: iTBS C: Sham TBS Duration: 45min/d, 5d/wk for 2wk	• Action Research Arm Test (+exp) • Fugl-Meyer Assessment (-)
Volz et al. (2016) RCT (5) N_{Start}=26 N_{End}=17 TPS=Acute	E: iTBS C: Sham TBS Duration: *Not Specified*	• Grip Strength (+exp) • Jebsen Taylor Hand Function Test (-)
Kim et al. (2015) RCT (8) N_{Start}=15 N_{End}=15 TPS=Chronic	E: iTBS C: Sham TBS Duration: 30min/d, 3d/wk for 4wk	• Modified Tardieu Scale (+exp) • Peak torque (+exp) • Modified Ashworth Scale (+exp)
Hsu et al. (2013) RCT (7) N_{start}=12 N_{end}=12 TPS=Subacute	E: iTBS C: Sham Duration: 30min/d, 3d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (-)
Talelli et al. (2012) RCT (7) N_{start}=41 N_{end}=41 TPS=Chronic	E: iTBS C: Sham iTBS Duration: 1hr/d, 5d/wk for 2wk	• Nine Hole Peg Test (-) • Jebsen Taylor Hand test (-)
Intermittent TBS combined with/versus rTMS		
Meng et al. (2020) RCT (9) N_{start}= 28 N_{end}= 28 TPS= Subacute	E: Low frequency rTMS + intermittent Theta Burst Stimulation E2: Low frequency rTMS + sham C: Sham + sham Duration: 5x/wk, 2wks	E1 Vs C • Fugl-Meyers Assessment Upper Extremity: (+exp$_1$) • Barthel Index: (+exp$_1$) E2 vs C • Fugl-Meyers Assessment Upper Extremity: (-) • Barthel Index: (-)

		E1 Vs E2 • Fugl-Meyers Assessment Upper Extremity: (+exp$_1$) • Barthel Index: (+exp$_1$)
Sung et al. (2013) RCT (6) N_{Start}=54 N_{End}=54 TPS= Chronic	E1: Low frequency (1Hz) rTMS + iTBS E2: Sham rTMS + iTBS E3: Low frequency (1Hz) rTMS + sham iTBS C: Sham rTMS + sham Itbs Duration: 45min/d, 5d/wk for 4wk	E1/E2/E3 vs C • Wolf Motor Function test (+exp, +exp$_2$, +exp$_3$) • Fugl-Meyer Assessment (+exp, +exp$_2$, +exp$_3$) • Medical Research Council Scale (+exp, +exp$_2$, +exp$_3$) • Functional Independence Measure (-) E1 vs E2 • Wolf Motor Function test (+exp) • Fugl-Meyer Assessment (+exp) • Medical Research Council Scale (+exp) • Functional Independence Measure (-) E1 vs E3 • Wolf Motor Function test (+exp) • Fugl-Meyer Assessment (-) • Medical Research Council Scale (+exp) • Functional Independence Measure (-) E2 vs E3 • Wolf Motor Function test (-) • Fugl-Meyer Assessment (+exp$_3$) • Medical Research Council Scale (+exp$_3$) • Functional Independence Measure (-)
Continuous TBS versus iTBS and/or sham stimulation		
Nicolo et al. (2018) RCT (9) N_{start}= 41 N_{end}= 41 TPS= Subacute	E1: Neuronavigated Continuous Theta Burst Stimulation (TBS) E2: Cathodal -tDCS C: Sham Duration: 30min, 3x/wk, 3wks	E1 Vs C • Fugl-Meyers Assessment Upper Extremity: (-) • Box and Block Test: (-) • Nine Hole Peg Test: (-) • Motor Activity Log-14 Quantitative Score: (-) • Jamar Dynamometer: (-) E2 Vs C • Fugl-Meyers Assessment Upper Extremity: (-) • Box and Block Test: (-) • Nine Hole Peg Test: (-) • Motor Activity Log-14 Quantitative Score: (-) • Jamar Dynamometer: (-) E1 Vs E2 • Fugl-Meyers Assessment Upper Extremity: (-) • Box and Block Test: (-) • Nine Hole Peg Test: (-) • Motor Activity Log-14 Quantitative Score: (-) • Jamar Dynamometer: (-)
Di Lazzaro et al. (2016) RCT (7) N_{Start}=20 N_{End}=17 TPS=Chronic	E: cTBS + robotic therapy C: Sham TBS + robotic therapy Duration: 1hr/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (-)
Ackerley et al. (2014) RCT (9) N_{start}= 24 N_{end}=13 TPS= Chronic	E: iTBS E2: cTBS C: Sham Duration: single session unspecified length	E1 Vs C • Griplift (-) E2 Vs C • Griplift (-) E1 Vs E2 • Griplift Kinetics (-) • Action Research Arm Test: (-)

Di Lazzaro et al. (2014) RCT (6) N_{Start}=12 N_{End}=12 TPS=Chronic	E: cTBS C: Sham Duration: 40min/d, 5d/wk for 2wk	• Action Research Arm Test (-) • Nine Hole Peg Test (-) • Jebsen Taylor hand test (-) • Grasp strength (-) • Pinch strength (-)
Talelli et al. (2012) RCT (7) N_{start}=41 N_{end}=41 TPS=Chronic	E: cTBS C: Sham cTBS Duration: 1hr/d, 5d/wk for 2wk	• Nine Hole Peg Test (-) • Jebsen Taylor Hand test (-)
Ackerley et al. (2010) RCT (7) N_{start}= 24 N_{end}= 10 TPS= Chronic	E1: iTBS E2: cTBS C: Sham Duration: single session unspecified length	E1 Vs C • Griplift (+exp1) E2 Vs C • Griplift (+exp2) E1 Vs E2 • Griplift Kinetics (-) • Action Research Arm Test: (-)
TBS compared to FES and Conventional Therapy		
Khan et al. (2019) RCT (8) N_{start}= 60 N_{end}= 60 TPS= Chronic	E: iTBS + Physical therapy E2: FES + Physical therapy C: Physical Therapy Duration: 4wks, 3x stimulation plus 5x physical therapy for 30min	E1 Vs C • Fugl-Meyer Assessment: (+exp1) • Modified Rankin Scale: (+exp1) • Barthel Index: (+exp1) • National Institute of Health Stroke Scale: (+exp1) E2 Vs C • Fugl-Meyer Assessment: (+exp2) • Modified Rankin Scale: (+exp2) • Barthel Index: (+exp2) • National Institute of Health Stroke Scale: (+exp2) E1 Vs E2 • Fugl-Meyer Assessment: (-) • Modified Rankin Scale: (-) • Barthel Index: (-) • National Institute of Health Stroke Scale: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about TBS

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **iTBS** to improve motor function when compared to **sham stimulation.**	9	Chen et al. 2019; Khan et al. 2019; Watanabe et al. 2018; Ackerley et al. 2016; Volz et al. 2016; Kim et al. 2015; Hsu et al. 2013; Sung et al. 2013; Talelli et al. 2012
1a	**cTBS** may not have a difference in efficacy when compared to **sham stimulation** for improving motor function.	3	Di Larazzo et al. 2016; Di Larazzo et al. 2014; Talelli et al. 2012

1b	**iTBS combined with low frequency rTMS** may produce greater improvements in motor function than **sham stimulation with or without iTBS**.	1	Sung et al. 2013
1a	There is conflicting evidence about the effect of **iTBS combined with low frequency rTMS** to improve motor function when compared to **sham stimulation with low frequency rTMS**.	2	Meng et al. 2020; Sung et al. 2013
1a	**iTBS** may not have a difference in efficacy when compared to **cTBS** for improving motor function.	2	Ackerley et al. 2014; Ackerley et al. 2010
1a	**cTBS with robotic therapy** may not have a difference in efficacy when compared to robotic therapy alone for improving motor function.	1	Di Larazzo et al. 2016;
1b	**iTBS** may not have a difference in efficacy when compared to **FES** for improving motor function.	1	Khan et al. 2019

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	**iTBS** may produce greater improvements in muscle strength than **sham stimulation**.	6	Watanabe et al. 2018; Volz et al. 2016; Kim et al. 2015; Ackerley et al. 2014; Sung et al. 2013 Ackerley et al. 2010
1a	**cTBS** may not have a difference in efficacy when compared to **sham stimulation** for improving muscle strength.	3	Ackerley et al. 2014; Di Larazzo et al. 2014; Ackerley et al. 2010
1b	**iTBS combined with low frequency rTMS** may produce greater improvements in muscle strength than **sham stimulation with or without iTBS**.	1	Sung et al. 2013
1a	**iTBS** may not have a difference in efficacy when compared to **cTBS** for improving muscle strength.	2	Ackerley et al. 2014; Ackerley et al. 2010

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **iTBS** to improve dexterity when compared to **sham stimulation.**	2	Chen et al. 2019; Talelli et al. 2012
1a	**cTBS** may not have a difference in efficacy when compared to **sham stimulation** for dexterity.	2	Di Lazzero et al. 2014; Talelli et al. 2012

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References
1b	**iTBS** may produce greater improvements in outcomes of stroke severity than **sham stimulation**.	1	Khan et al. 2019
1b	**iTBS** may not have a difference in efficacy when compared to **FES** for improving outcomes of stroke severity	1	Khan et al. 2019

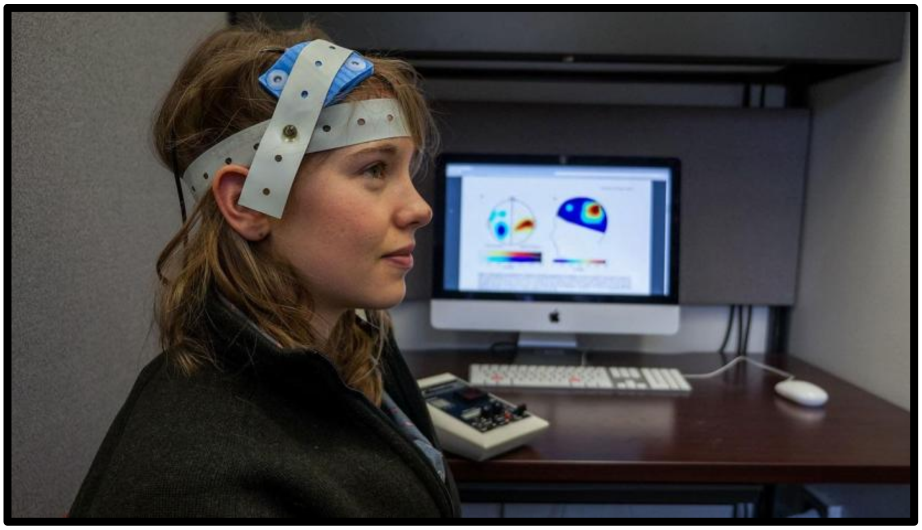
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**iTBS** may not have a difference in efficacy when compared to **sham stimulation** for improving performance of activities of daily living.	3	Chen et al. 2019; Khan et al. 2019; Sung et al. 2013
1b	There is conflicting evidence about the effect of **iTBS combined with low frequency rTMS** to improve performance of activities of daily living when compared to **sham stimulation with low frequency rTMS**.	2	Meng et al. 2020; Sung et al. 2013
1b	**iTBS** may not have a difference in efficacy when compared to **FES** for improving performance of activities of daily living.	1	Khan et al. 2019

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**iTBS** may produce greater improvements in spasticity than **sham stimulation**.	3	Chen et al. 2019; atanabe et al. 2018; Kim et al. 2015

Key points

Theta burst stimulation alone may be beneficial for spasticty and strength, but the literature is mixed for overall motor function and activities of daily living

Transcranial Direct Current Stimulation (tDCS)



Adopted from: https://tryniakaufman.com/2018/01/11/transcranial-direct-current-stimulation-the-drug-of-the-future/

Another form of non-invasive brain stimulation is transcranial direct-current stimulation (tDCS). This procedure involves the application of mild electrical currents (1-2 mA) conducted through two saline-soaked, surface electrodes applied to the scalp, overlaying the area of interest and the contralateral forehead above the orbit. Anodal stimulation is performed over the affected hemisphere and increases cortical excitability, while cathodal stimulation is performed over the unaffected hemisphere and decreases cortical excitability (Alonso-Alonso et al., 2007). Additionally, tDCS can be applied on both hemispheres concurrently, this is known as dual tDCS. 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).

54 RCTs were found that evaluated tDCS interventions for upper extremity motor rehabilitation.

19 RCTs compared anodal tDCS to sham stimulation (Bornheim et al. 2020; Achacheluee et al. 2018; Andrade et al. 2017; Marquez et al. 2017; Pavlova et al. 2017; Allman et al. 2016; Ilic et al. 2016; Mortensen et al. 2016; Sik et al. 2015; Au Yeung et al. 2014; Fusco et al. 2013; Khedr et al. 2013; Stagg et al. 2012; Hesse et al. 2011; Tanaka et al. 2011; Kim et al. 2010; Kim et al. 2009; Boggio et al. 2007; Fregni et al. 2005).

16 RCTs compared cathodal tDCS to sham stimulation or conventional therapy (Alisar et al. 2020; Marquez et al. 2017; Rabadi et al. 2017; Lee et al. 2015; Au Yeung et al. 2014; Fusco et al. 2014; Fusco et al. 2013; Khedr et al. 2013; Wu et al. 2013; Stagg et al. 2012; Zimmerman et al. 2012; Hesse et al. 2011; Nair et al. 2011; Kim et al. 2010; Boggio et al. 2007; Fregni et al. 2005).

Eight RCTs compared dual tDCS to sham stimulation or conventional therapy (Beaulieu et al. 2019; Doost et al. 2019; Koh et al. 2017; Goodwill et al. 2016; Sik et al. 2015; Cha et al. 2014; Lefebvre et al. 2014; Fusco et al. 2013; Lefebvre et al. 2013; Lindenberg et al. 2010).

Five RCTs compared anodal tDCS versus cathodal tDCS (Khedr et al. 2013; Stagg et al. 2012; Hesse et al. 2011; Boggio et al. 2007; Fregni et al. 2005). One RCT compared cathodal tDCS to dual tDCS (Del Felice et al. 2017). One RCT combined anodal tDCS with strength training

(Hendy et al. 2014). Three RCTs compared anodal or cathodal tDCS with CIMT to sham stimulation with CIMT (Figlewski et al. 2016; Rocha et al. 2016; Cunningham et al. 2015). One RCT combined dual tDCS with cyclic NMES and CIMT (Takebayshi et al. 2017).

Four RCTs compared dual or anodal tDCS with robotics compared to sham stimulation with robotics or robotics alone (Dehem et al. 2018; Mazzoleni et al. 2017; Straudi et al. 2016; Triccas et al. 2015). One RCT compared anodal tDCS with robotics to cathodal tDCS with robotics (Ochi et al. 2013). Two RCTs compared anodal or dual tDCS with brain computer interfaces to sham stimulation with brain computer interfaces (Hong et al. 2017; Ang et al. 2015). Two RCTs compared dual tDCS with functional electrical stimulation to sham tDCS with functional electrical stimulation (Salazar et al. 2020; Shaheiwola et al. 2018). Two RCTs compared anodal tDCS with or without peripheral nerve stimulation to peripheral nerve stimulation (Powell et al. 2016; Sattler et al. 2015). Two RCTs compared dual tDCS with low frequency rTMS and mirror therapy to sham tDCS and mirror therapy (Jin et al. 2019; D'Agata et al. 2016).

Two RCTs compared anodal or cathodal tDCS with virtual reality to virtual reality interventions with or without sham stimulation (Lee et al. 2014; Viana et al. 2014). One RCT compared TBS to tDCS (Nicolo et al. 2018)

The methodological details and results of all 54 RCTs are presented in Table 30.

Table 30. RCTs Evaluating tDCS Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Anodal tDCS versus sham stimulation		
Bornheim et al. (2020) RCT (8) N_{start}= 50 N_{end}= 46 TPS= Acute	E: Anodal tDCs C: Sham Duration: conventional rehab (2hr/5x/4wk) and tDCS (20min/5x/4wk)	• Wolf Motor Function Test: (+exp) • Handgrip strength: (+exp) • Fugl-Meyer Assessment Upper Extremity: (-) • Fugl-Meyers Assessment – Sensory: (+exp) • Semmes Weinstein Monofilament Test: (+exp) • Barthel Index: (-) • Stroke Impact Scale: (-)
Achacheluee et al. (2018) RCT crossover (6) N_{start}= 25 N_{end}= 15 TPS= Chronic	E1: Anodal tDCS at M1 and DLPFC E2: Anodal tDCS at M1 only C: Sham Duration: 20 min single session of tDCS	E1 vs C • Reaction time: (+exp$_1$) • Nine-Pin Pegboard test: (+exp$_1$) • Fugl–Meyer Assessment Upper Extremity: (-) E2 vs C • Reaction time: (-) • Nine-Pin Pegboard test: (-) • Fugl–Meyer Assessment Upper Extremity: (-) E1 vs E2 • Reaction time: (-) • Nine-Pin Pegboard test: (+exp1) • Fugl–Meyer Assessment Upper Extremity: (-)
Andrade et al. (2017) RCT (9) N_{Start} =60 N_{End} =60 TPS=Subacute	E1: Anodal Transcranial Direct Current Stimulation in Ipsilesional M1 and Constraint Induced Movement Therapy E2: Anodal Transcranial Direct Current Stimulation in Ipsilesional PMC and Constraint Induced Movement Therapy	E2 vs E1/C • Fugl-Meyer Assessment (+exp$_2$) • Modified Ashworth Scale (+exp$_2$) • Box and Block Test (+exp$_2$) • Medical Research Council (+exp$_2$) • Barthel Index (+exp$_2$) • Wilcoxon signed-rank test: (+exp)

	C: Sham Stimulation and Constraint Induced Movement Therapy Duration: 30min/d, 5d/wk for 6wk	
Pavlova et al. (2017) RCT (7) N_{Start} =11 N_{End} =11 TPS=Chronic	E: Anodal tDCS C: Sham tDCS Duration: 20min (2x/d), 5d/wk for 4wk	• Fugl-Meyer Assessment (-) • Wolf Motor Function Test (-) • Box and Block Test (-)
Allman et al. (2016) RCT (7) N_{Start}=26 N_{End}=24 TPS=Chronic	E: Anodal tDCS C: Sham tDCS Duration: 1hr/d, for 9d	• Action Research Arm Test (+exp) • Wolf Motor Function Test (+exp) • Fugl-Meyer Assessment (-)
Ilic et al. (2016) RCT (8) N_{Start}=26 N_{End}=25 TPS=Chronic	E: Anodal tDCS + occupational therapy C: Sham tDCS + occupational therapy Duration: 45min/d, 5d/wk for 2wk	• Jebsen-Taylor Hand Function Test (+exp) • Fugl-Meyer Assessment (-) • Grip Strength (-)
Mortensen et al. (2016) RCT (7) N_{Start}=16 N_{End}=15 TPS=Chronic	E: Anodal tDCS + occupational therapy C: Sham tDCS + occupational therapy Duration: 30min/d for 5d	• Grip Strength (+exp) • Stroke Impact Scale (-) • Jebsen-Taylor Hand Function Test (-)
Tanaka et al. (2011) RCT (6) N_{start}=8 N_{end}=8 TPS=Subacute	E: Anodal tDCS C: Sham Duration: 30min/d, 4d/wk for 5wk	• Grip strength (-)
Kim et al. (2009) RCT (7) N_{start}=10 N_{end}=10 TPS=Subacute	E: Anodal tDCS C: Sham Duration: 20min/d, 5d/wk for 6wk	• Box & Block Test (+exp) • Finger acceleration (+exp)
Cathodal tDCS versus sham stimulation or conventional therapy		
Alisar et al. (2020) RCT (6) N_{start}= 38 N_{end}=32 TPS= Chronic	E: Cathodal tDCS C: Sham Duration: 30min 5X/wk for 4wks	• Fugl-Meyers Assessment Upper Extremity: (-) • Brunnstrom Stages of Stroke Recovery: (-) • Functional Independence Measure: (-)
Rabadi et al. (2017) RCT (7) N_{Start} =16 N_{End} =12 TPS=Acute	E: Cathodal tDCS C: Sham tDCS Duration: 30min/d, 5d/wk for 2wk	• Action Research Arm Test (-)
Lee et al. (2015) RCT (6) N_{Start}=24 N_{End}=24 TPS=Chronic	E: Cathodal tDCS + physical therapy C: Physical therapy Duration: 30min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp)
Fusco et al. (2014) RCT (6) N_{Start}=14 N_{End}=11 TPS=Subacute	E: Cathodal tDCS + active electrode C: Sham tDCS Duration: 45min/d, 5d/wk for 2wk	• Canadian Neurologic Scale (-) • Nine Hole Peg Test (-) • Barthel Index (-) • Fugl-Meyer Assessment (-)
Wu et al.(2013) RCT (9) N_{Start}=90 N_{End}=90	E: Cathodal tDCS C: Sham tDCS Duration: 20min/d, 5d/wk for 4wk	• Modified Ashworth Scale (+exp)

TPS=Chronic		
Zimerman et al. (2012) RCT (6) N_{start}=12 N_{end}=12 TPS=Chronic	E: Cathodal tDCS C: Sham tDCS Duration: *Not Specified*	• Grip strength (-)
Nair et al. (2011) RCT (9) N_{start}= 14 N_{end}= 14 TPS= Chronic	E: Cathodal tDCS C: Sham Duration: 30min, 5d +60min therapy	• Fugl-Meyers Assessment Upper Extremity: (+exp) • Three Joint Range of Motion: (+exp)
Hummel et al. (2005) RCT (6) N_{start}=6 N_{end}=6 TPS=Chronic	E: Cathodal tDCS C: Sham tDCS Duration: 20min/d, 3d/wk for 4wk	• Jebsen-Taylor Hand Function test (+exp)
Dual tDCS versus sham stimulation or conventional therapy		

Beaulieu et al. (2019)
RCT (7)
N_{start}= 14
N_{end}= 14
TPS= Chronic
	E: Dual tDCS + strength training
	C: Sham + strength training
	Duration: 20min of tDCS stimulation for experimental with: strength training (60min/3x/4wk)
		• Fugl-Meyers Upper Extremity: (-)
		• Wolf Motor Function Test
		  • Time: (-)
		  • Weight to Box: (-)
		• Box and Block Test
		  • Affected Hand: (-)
		  • Unaffected Hand: (-)
		• Grip Strength
		  • Affected Hand: (-)
		  • Unaffected Hand: (-)
		• Motor Activity Log
		  • Amount of Use: (-)
		  • Quality of Movement: (-)
		• Modified Ashworth Scale
		  • Shoulder Extensors: (-)
		  • Elbow Flexors: (-)
		  • Wrist: (-)
		  • Fingers: (-)

Doost et al. (2019) RCT (8) N_{start}= 21 N_{end}= 21 TPS= Chronic Crossover	E: Dual tDCS (anodal ipsilesional) C: Sham Duration: 30min, 1x, 2-week washout	• Bimanual Skill Acquisition (CIRCUIT): (-) • Box and Block Test: (-) • Bimanual Reaching Task: (-)
Koh et al. (2017) RCT (8) N_{Start} =25 N_{End} =18 TPS=Chronic	E: Dual tDCS with Sensory Modulation C: Sham tDCS with Sensory Modulation Duration: 30min/d, 5d/wk for 8wk	• Fugl-Meyer Assessment (-) • Modified Ashworth Scale (-) • Action Research Arm Test (-) • Barthel Index (-)
Goodwill et al. (2016) RCT (7) N_{Start} =16 N_{End} =15 TPS=Chronic	E: Dual tDCS + upper limb training C: Sham tDCS + upper limb training Duration: 30min/d, 5d/wk for 3wk	• Tardieu Scale (-) • Grip Strength (-)
Lefebvre et al. (2015) RCT Crossover (5) N_{Start} =19 N_{End} =19 TPS=Chronic	E: Dual tDCS C: Sham tDCS Duration: 30min/d, 5d/wk for 3wk	• Purdue Pegboard Test (+exp)
Cha et al. (2014) RCT (6) N_{Start}=20 N_{End}=20	E: Dual tDCS C: Conventional training Duration: 30min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Box and Block Test (+exp)

TPS=Chronic		
Lefebvre et al. (2014) RCT (8) N_{Start}=19 N_{End}=19 TPS=Chronic	E: Dual tDCS C: Sham Duration: 20min/d, 5d/wk for 2wk	• Purdue Pegboard Test (+exp) • Precision grip (+exp)
Lefebvre et al. (2013) RCT (8) N_{Start}=18 N_{End}=18 TPS=Chronic	E: Dual tDCS C: Sham Duration: 30min/d, 4d/wk for 3wk	• Purdue Pegboard Test (+exp) • Maximal hand grip force (+exp)
Lindenberg et al. (2010) RCT (4) N_{start}=20 N_{end}=20 TPS=Chronic	E: Dual tDCS C: Sham Duration: 30min/d, 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test (+exp)
Anodal or cathodal tDCS versus sham stimulation		
Marquez et al. (2017) RCT Crossover (8) N_{Start} =25 N_{End} =25 TPS=Chronic	E1: Anodal tDCS E2: Cathodal tDCS C: Sham tDCS Duration: 20min/d for 6d	E1/E2 vs C • Jebsen-Taylor Hand Function test (-) • Grip Strength (-)
Au-Yeung et al. (2014) RCT Crossover (8) N_{Start}=10 N_{End}=10 TPS=Chronic	E1: Anodal tDCS E2: Cathodal tDCS C: Sham Duration: *Not Specified*	E1/E2 vs C • Purdue Pegboard Test (-) • Pinch strength (-)
Khedr et al.(2013) RCT (9) N_{Start}=40 N_{End}=40 TPS= Chronic	E1: Anodal tDCS E2: Cathodal tDCS C: Sham Duration: 25min/d for 6d	E1/E2 vs C • Orgogozo MCA scale (+exp, +exp2) • National Institute of Health Stroke Scale (-) • Barthel Index (+exp, +exp2) • Medical Research Council Scale (-) E1 vs E2 • Orgogozo MCA scale (-) • National Institute of Health Stroke Scale (-) • Barthel Index (-) • Medical Research Council Scale (-)
Stagg et al. (2012) RCT (6) N_{start}=13 N_{end}=13 TPS=Chronic	E1: Anodal tDCS E2: Cathodal tDCS C: Sham Duration: 80min/d, 3d/wk for 4wk	E1/E2 vs C • Grip strength (+exp, +exp2) E1 vs E2 • Grip strength (-)
Hesse et al. (2011) RCT (10) N_{start}=96 N_{end}=85 TPS=Chronic	E1: Anodal tDCS E2: Cathodal tDCS C: Sham Duration: 20min/d, 5d/wk for 6wk	E1/E2 vs C • Fugl-Meyer Assessment (-) E1 vs E2 • Fugl-Meyer Assessment (-)
Kim et al. (2010) RCT (7) N_{start}=18 N_{end}=16 TPS=Subacute	E1: Anodal tDCS E2: Cathodal tDCS C: Sham Duration: Not Specified	E2 vs C • Fugl-Meyer Assessment (+exp2) • Barthel Index (-) E1 vs C • Fugl-Meyer Assessment (-) • Barthel Index (-)
Boggio et al. (2007) RCT (6) N_{start}=4 N_{end}=4 TPS=Chronic	E1: Anodal tDCS E2: Cathodal tDCS C: Sham Duration: 20min, 1x/wk for 4wk	E1/E2 vs C • Jebsen-Taylor Hand Function test (+exp, +exp2) E1 vs E2 • Jebsen-Taylor Hand Function test (-)

Fregni et al. (2005) RCT (7) N_{start}=6 N_{end}=6 TPS= Chronic	E1: Anodal tDCS E2: Cathodal tDCS C: Sham Duration: *Not Specified*	E1/E2 vs C • Jebsen Taylor Hand Function test: (+exp, +exp2) E1 vs E2 • Jebsen Taylor Hand Function test: (-)
Anodal, cathodal or dual tDCS versus sham stimulation		
Sik et al. (2015) RCT (6) N_{start}=36 N_{end}=31 TPS=Subacute	E1: Anodal tDCS + PT + OT E2: Dual tDCS + PT + OT C: Sham tDCS + PT + OT Duration: *Not Specified*	E1/E2 vs C • Wolf Motor Function Test (+exp, +exp2) • Jebsen Taylor Hand Function Test (+exp, +exp2) • Kocaeli Functional Evaluation Test (+exp2) E1 vs E2 • Wolf Motor Function Test (-), • Jebsen Taylor Hand Function Test (-) • Kocaeli Functional Evaluation Test (-)
Fusco et al. (2013) RCT (7) N_{start}=9 N_{end}=9 TPS=Subacute	E1: Dual tDCS E2: Anodal tDCS E3: Cathodal tDCS C: Sham Duration: 15min/d for 2d	E1/E2/E3 vs C • Nine hole peg test (+exp, +exp2, +exp3) • Grasp force (-)
Cathodal versus dual tDCS stimulation		
Del Felice et al. (2017) RCT crossover (8) N_{Start} =10 N_{End} =10 TPS=Chronic	E: Cathodal Trans Direct Current Stimulation C: Dual tDCS Duration: 20min/d, 5d/wk for 3wk	• Modified Ashworth Scale (+exp) • Bhakta Finger Flexion Scale (-) • European Stroke Scale (-) • Action Research Arm Test (-) • Medical Research Council Scale (-) • Barthel Index (-)
Anodal tDCS with strength training compared to sham tDCS with strength training		
Hendy et al. (2014) RCT (7) N_{Start}=10 N_{End}=10 TPS=Chronic	E1: Strength training + anodal tDCS E2: Strength training + sham C: Anodal tDCS Duration: 20min/d, 2d/wk for 5wk	• Maximum voluntary dynamic strength for wrist extensors (-)
Anodal or cathodal tDCS with CIMT		
Figlewski et al. (2016) RCT (7) N_{Start}=44 N_{End}=44 TPS=Chronic	E: CIMT + Anodal tDCS C: CIMT + Sham tDCS Duration: 6hr/d for 9d	• Wolf Motor Function Test (+exp) • Grip Strength (-) • Arm Strength (-)
Rocha et al. (2016) RCT (8) N_{Start}=21 N_{End}=21 TPS=Chronic	E1: Anodal tDCS with CIMT E2: Cathodal tDCS with CIMT C: Sham tDCS with CIMT Duration: 1hr/d, 6d/wk for 2wk	E1 vs C • Fugl-Meyer Assessment (+exp) • Motor Acivity Log (-) • Grip Strength (-) E2 vs C • Fugl-Meyer Assessment (-) • Motor Acivity Log (-) • Grip Strength (-)
Cunningham et al. (2015) RCT (6) N_{Start}=12 N_{End}=12 TPS=Chronic	E: anodal tDCS + CIMT C: Sham tDCS + CIMT Duration: 30min/d, 3d/wk for 10wk	• 9 Hole Peg Test (-) • Motor Activity Log (-) • Fugl-Meyer Assessment (-)
Dual tDCS with cyclic NMES and CIMT		
Takebayshi et al. (2017) RCT (7) N_{Start} =20 N_{End} =19 TPS=Chronic	E: Dual tDCS combined with cyclic NMES with CIMT C: CIMT Duration: 2hr (2x/d), 5d/wk for 3wk	• Fugl-Meyer Assessment (+exp) • Motor Activity Log (+exp)

Dual or anodal tDCS with robotics compared to sham tDCS with robotics or robotics alone		
Dehem et al. (2018) RCT-crossover (6) N_{Start} =21 N_{End} =20 TPS=Chronic	E: Dual tDCS with Upper Limb Robotic Assisted Therapy C: Sham tDCS with Upper Limb Robotic Assisted Therapy Duration: 45min/d, 5d/wk for 6wk	• Box and Block Test (+exp) • Purdue Pegboard Test (-)
Straudi et al. (2016) RCT (6) N_{Start} =23 N_{End} =23 TPS=Subacute and chronic	E: Robot-assisted therapy + dual tDCS C: Robot-assisted therapy + sham tDCS Duration: 45min/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (-) • Box and Block Test (-) • Motor Acivity Log (-)
Mazzoleni et al. (2017) RCT (7) N_{Start} =24 N_{End} =24 TPS=Acute	E: Anodal tDCS with Wrist Robot-Assisted Training C: Wrist Robot-Assisted Training Duration: *Not Specified*	• Fugl-Meyer Assessment (-) • Modified Ashworth Scale (-) • Motricity Index (-) • Box and Block Test (-)
Triccas et al. (2015) RCT (8) N_{start}=23 N_{end}=22 TPS=Subacute	E: Anodal tDCS + robotic ArmeoSpring C: Sham tDCS + robotic ArmeoSpring Duration: 45min/d, 3d/wk for 4wk	• Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Motor Activity Log (-) • Stroke Impact Scale (-)
Anodal versus cathodal tDCS stimulation with robotics		
Ochi et al. (2013) RCT (7) N_{start}=18 N_{end}=16 TPS=Chronic	E: Anodal tDCS on affected hemisphere + robot assisted arm training C: Cathodal tDCS on unaffected hemisphere + robot assisted arm training Duration: 45min/d, for 5d	• Modified Ashworth Scale (+exp) • Fugl-Meyer Assessment (-) • Motor Activity Log (-)
Anodal or dual tDCS with brain computer interface-assisted motor imagery		
Hong et al. (2017) RCT (5) N_{Start} =19 N_{End} =19 TPS=Chronic	E: Brain computer interface -Assisted Motor Imagery with Dual tDCS C: Brain computer interface -Assisted Motor Imagery with Sham tDCS Duration: 20min/d, 5d/wk for 2wk	• Fugl-Meyer Assessment (-)
Ang et al. (2015) RCT (6) N_{Start} =19 N_{End} =19 TPS=Chronic	E: Anodal tDCS + motor imagery brain computer interface with robotic feedback C: Sham tDCS + motor imagery brain computer interface with robotic feedback Duration: 80min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (-)
Dual tDCS with FES		
Salazar et al. (2020) RCT (8) N_{start}= 30 N_{end}= 30 TPS= Chronic	E: Dual tDCS + FES C: Sham tDCS + FES Duration: 30min, 5x/wk, 2wks	Kinematics • Task Movement Time (Reaching) (+exp) • Mean Reaching Velocity (+exp) • Mean Return Velocity (-) • Peak Velocity (-) • Smoothness (-) • Elbow Range of Motion (-) • Grip Strength (+exp) • Fugl-Meyers Upper Limb (-)
Shaheiwola et al. (2018) RCT (6) N_{Start} =30 N_{End} =30 TPS=Chronic	E: Dual tDCS with FES C: Sham tDCS with FES Duration: 45min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (+exp) • Wolf Motor Function Test Score (+exp) • Modified Ashworth Scale (-)
Anodal tDCS with peripheral nerve stimulation		

Menezes et al. (2018) RCT (8) N_{start}= 22 N_{end}= 20 TPS= Chronic	E: Active repetitive peripheral nerve sensory stimulation (RPPS) + sham tDCS E2: Sham RRPS + active tDCS E3: Active RRPS + active tDCS C: Sham RRPS + sham tDCS Duration: 1 (2hrs RPPS, 20min tDCS) /session, 10-15d washout	E1 Vs C • Wrist Range of Motion (Flexion, Extension): (-) • Grip, Pinch Strength: (-) E2 Vs C • Wrist Range of Motion (Flexion, Extension): (-) • Grip, Pinch Strength: (-) E3 Vs C • Wrist Range of Motion (Flexion, Extension): (-) • Grip, Pinch Strength: (-) E1 Vs E2 Vs E3 • Wrist Range of Motion (Flexion, Extension): (-) • Grip, Pinch Strength: (-)
Powell et al. (2016) RCT (8) N_{Start} =11 N_{End} =10 TPS=Chronic	E1: Anodal tDCS followed by peripheral nerve stimulation E2: Peripheral nerve stimulation followed by tDCS Duration: *Not Specified*	• Fugl-Meyer Assessment (-) • Stroke Impact Scale (-)
Sattler et al. (2015) RCT (7) N_{Start}=20 N_{End}=20 TPS=Acute	E: Repetitive peripheral nerve stimulation + anodal tDCS C: Repetitive peripheral nerve stimulation Duration: 20min/d, 5d/wk for 4wk	• Jebsen Hand Function Test (+exp) • Grip Strength (-) • 9 Hole Peg Test (-) • Hand Tapping Test (-) • Fugl-Meyer Assessment (-)
Dual tDCS with low frequency rTMS and/or mirror therapy		
Jin et al. (2019) RCT (8) N_{start}= 30 N_{end}= 28 TPS= Chonic	E1: Dual tDCSs + mirror therapy (before) E2: Dual tDCSs + mirror therapy (during) C: Sham + mirror therapy Duration: 30 min (stimulation and mirror each) 5x/wk, 2wks	E1 Vs C • Fugle-Meyers Upper Extremity: (-) • Action Research Arm Test: (-) • Box and Block Test: (-) E2 Vs C • Fugle-Meyers Upper Extremity: (-) • Action Research Arm Test: (+exp2) • Box and Block Test: (-) E1 Vs E2 • Fugle-Meyers Upper Extremity: (-) • Action Research Arm Test: (+exp2) • Box and Block Test: (-)
D'Agata et al. (2016) RCT (6) N_{Start} =34 N_{End} =34 TPS=Chronic	E: Dual tDCS + low frequency (1Hz) rTMS + Mirror Therapy C: Sham tDCS + Mirror Therapy Duration: 1hr/wk, 5d/wk for 2wk	• Action Research Arm Test (+exp)
Anodal or cathodal tDCS with virtual reality		
Lee et al. (2014) RCT (7) N_{Start}=64 N_{End}=59 TPS=Chronic	E1: cathodal tDCS E2: Virtual reality E3: Cathodal tDCS + virtual reality Duration: 90min/d, 3d/wk for 4wk	E1 vs E2 • Manual Function Test (+exp) • Fugl-Meyer Assessment (+exp) • Modified Barthel Index (-) • Manual Muscle Test (-) • Modified Ashworth Scale (-) • Box and Block Test (-) E3 vs E2/E1 • Manual Function Test (+exp_3) • Fugl-Meyer Assessment (+exp_3) • Modified Barthel Index (-) • Manual Muscle Test (-) • Modified Ashworth Scale (-) • Box and Block Test (-)
Viana et al. (2014) RCT (9)	E: Virtual reality + anodal tDCS C: Virtual reality + sham	• Fugl-Meyer Assessment (-) • Wolf Motor Function Test (-)

N_{Start}=20 N_{End}=20 TPS=Chronic	Duration: 1hr/d, 3d/wk for 5wk	• Modified Ashworth Scale (-) • Grip strength (-)
	TBS versus tDCS	
Nicolo et al. (2018) RCT (9) N_{start}= 41 N_{end}= 41 TPS= Subacute	E1: Neuronavigated Continuous Theta Burst Stimulation (TBS) E2: Cathodal -tDCS C: Sham Duration: 30min, 3x/wk, 3wks	E1 Vs C • Fugl-Meyers Assessment Upper Extremity: (-) • Box and Block Test: (-) • Nine Hole Peg Test: (-) • Motor Activity Log-14 Quantitative Score: (-) • Jamar Dynamometer: (-) E2 Vs C • Fugl-Meyers Assessment Upper Extremity: (-) • Box and Block Test: (-) • Nine Hole Peg Test: (-) • Motor Activity Log-14 Quantitative Score: (-) • Jamar Dynamometer: (-) E1 Vs E2 • Fugl-Meyers Assessment Upper Extremity: (-) • Box and Block Test: (-) • Nine Hole Peg Test: (-) • Motor Activity Log-14 Quantitative Score: (-) • Jamar Dynamometer: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about tDCS

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **anodal tDCS** to improve motor function when compared to **sham stimulation**.	13	Bornheim et al. 2020; Achacheluee et al. 2018; Andrade et al. 2017; Marquez et al. 2017; Pavlova et al. 2017; Allman et al. 2016; Ilic et al. 2016; Mortensen et al. 2016; Sik et al. 2015; Hesse et al. 2011; Kim et al. 2010; Boggio et al. 2007; Fregni et al. 2005
1a	There is conflicting evidence about the effect of **cathodal tDCS** to improve motor function when compared to **sham stimulation or conventional therapy**.	12	Alisar et al. 2020; Nicolo et al. 2018; Maquez et al. 2017; Rabadi et al. 2017; Lee et al. 2015; Fusco et al. 2014; Hesse et al. 2011; Nair et al. 2011; Kim et al. 2010; Boggio et al. 2007; Fregni et al. 2005
1a	There is conflicting evidence about the effect of **dual tDCS** to improve motor function when compared to **sham stimulation or conventional therapy**.	6	Beaulieu et al. 2019; Doot et al. 2019; Koh et al. 2017; Sik et al. 2015; Cha et al. 2014; Lindenberg et al. 2010
1a	**Anodal tDCS** may not have a difference in efficacy when compared to **cathodal tDCS** for improving motor function.	3	Hesse et al. 2011; Boggio et al. 2007; Fregni et al. 2005

1b	**Cathodal tDCS** may not have a difference in efficacy when compared to **dual tDCS** for improving motor function.	1	Del Felice et al. 2017
1a	There is conflicting evidence about the effect of **anodal tDCS with CIMT** to improve motor function when compared to **sham tDCS with CIMT.**	3	Figlewski et al. 2016; Rocha et al. 2016; Cunningham et al. 2015
1b	**Cathodal tDCS with CIMT** may not have a difference in efficacy when compared to **sham tDCS with CIMT** for improving motor function.	1	Rocha et al. 2016
1b	**Dual tDCS with cyclic NMES and CIMT** may produce greater improvements in motor function than **CIMT**.	1	Takebayshi et al. 2017
1b	**Dual tDCS with upper limb robotics** may not have a difference in efficacy when compared to **sham tDCS with upper limb robotics** for improving motor function.	1	Straudi et al. 2016
1a	**Anodal tDCS with upper limb robotics** may not have a difference in efficacy when compared to **sham tDCS with upper limb robotics or upper limb robotics alone** for improving motor function.	2	Mazzoleni et al. 2017; Triccas et al. 2015
1b	**Anodal tDCS with upper limb robotics** may not have a difference in efficacy when compared to **cathodal tDCS with upper limb robotics** for improving motor function.	1	Ochi et al. 2013
1b	**Anodal or dual tDCS with brain computer interface-assisted motor imagery interventions** may not have a difference in efficacy when compared to **sham tDCS with brain computer interface-assisted motor imagery interventions** for improving motor function.	2	Hong et al. 2017; Ang et al. 2015
1a	There is conflicting evidence about the effect of **dual tDCS with FES** to improve motor function when compared to **sham tDCS with FES.**	2	Salazar et al. 2020; Shaheiwola et al. 2018
1a	**Anodal tDCS with peripheral nerve stimulation** may not have a difference in efficacy when compared to **peripheral nerve stimulation** for improving motor function.	2	Powell et al. 2016; Sattler et al. 2015
1a	There is conflicting evidence about the effect of **dual tDCS with rTMS and/or mirror therapy** to improve motor function when compared to **mirror therapy alone.**	2	Jin et al. 2019; D'Agata et al. 2016
1a	There is conflicting evidence about the effect of **anodal or cathodal tDCS with virtual reality training** to improve motor function when compared to **virtual reality training with or without sham tDCS.**	2	Lee et al. 2014; Viana et al. 2014
1b	**Cathodal tDCS** may produce greater improvements in motor function than **virtual reality training**.	1	Lee et al. 2014

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References

1b	There is conflicting evidence about the effect of **anodal tDCS** to produce greater improvements on measures of stroke severity when compared to **sham stimulation**.	1	Khedr et al. 2013
1a	**Cathodal tDCS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improvements on measures of stroke severity.	2	Fusco et al. 2014; Khedr et al. 2013
1b	**Anodal tDCS** may not have a difference in efficacy when compared to **cathodal tDCS** for improvements on measures of stroke severity.	1	Khedr et al. 2013
1b	**Cathodal tDCS** may not have a difference in efficacy when compared to **dual tDCS** for improvements on measures of stroke severity.	1	Del Felice et al. 2017

PROPRIOCEPTION

LoE	Conclusion Statement	RCTs	References
1b	**Anodal tDCS** may produce greater improvements in proprioception than **sham stimulation**.	1	Bornheim et al. 2020

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **anodal tDCS** to improve dexterity when compared to **sham stimulation**.	6	Achacheluee et al. 2018; Andrade et al. 2017; Pavlova et al. 2017; Kim et al. 2009; Au Yeung et al. 2014; Fusco et al. 2013
1a	**Cathodal tDCS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving dexterity.	5	Alisar et al. 2020; Nicolo et al. 2018; Au Yeung et al. 2014; Fusco et al. 2014; Fusco et al. 2013
1a	**Dual tDCS** may produce greater improvements in dexterity than **sham stimulation or conventional therapy**.	7	Beaulieu et al. 2019; Doost et al. 2019; Lefebvre et al. 2015; Cha et al. 2014; Lefebvre et al. 2014; Lefebvre et al. 2013; Fusco et al. 2013
1b	**Anodal tDCS with CIMT** may not have a difference in efficacy when compared to **sham tDCS with CIMT** for improving dexterity.	1	Cunningham et al. 2015
1a	**Dual tDCS with upper limb robotics** may not have a difference in efficacy when compared to **sham tDCS with upper limb robotics** for improving dexterity.	2	Dehem et al. 2018; Straudi et al. 2016

1b	**Anodal tDCS with upper limb robotics** may not have a difference in efficacy when compared to **sham tDCS with upper limb robotics or upper limb robotics alone** for improving dexterity.	1	Mazzoleni et al. 2017
1b	**Anodal tDCS with peripheral nerve stimulation** may not have a difference in efficacy when compared to **peripheral nerve stimulation** for improving dexterity.	1	Sattler et al. 2015
1b	**Dual tDCS and mirror therapy** may not have a difference in efficacy when compared to **mirror therapy alone** for improving dexterity.	1	Jin et al. 2019
1b	**Anodal or cathodal tDCS with virtual reality training** may not have a difference in efficacy when compared to **virtual reality training with or without sham tDCS** for improving dexterity.	1	Lee et al. 2014
1b	**Cathodal tDCS** may not have a difference in efficacy when compared to **virtual reality training** for improving dexterity.	1	Lee et al. 2014

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1b	**Anodal tDCS** may produce greater improvements in spasticity than **sham stimulation**.	1	Andrade et al. 2017
1b	**Cathodal tDCS** may produce greater improvements in spasticity than **sham stimulation or conventional therapy**.	1	Wu et al. 2013
1a	**Dual tDCS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving spasticity.	3	Beaulieu et al. 2019; Koh et al. 2017; Goodwill et al. 2016
1b	There is conflicting evidence about the effect of **cathodal tDCS** to improve spasticity when compared to **dual tDCS**.	1	Del Felice et al. 2017
1b	**Anodal tDCS with upper limb robotics** may not have a difference in efficacy when compared to **sham tDCS with upper limb robotics or upper limb robotics alone** for spasticity.	1	Mazzoleni et al. 2017
1b	**Anodal tDCS with upper limb robotics** may produce greater improvements in spasticity than **cathodal tDCS with upper limb robotics**.	1	Ochi et al. 2013
1b	**Dual tDCS with FES** may not have a difference in efficacy when compared to **sham tDCS with FES** for spasticity.	1	Shaheiwola et al. 2018
1a	**Anodal or cathodal tDCS with virtual reality training** may not have a difference in efficacy when compared to **virtual reality training with or without sham tDCS** for improving spasticity.	2	Lee et al. 2014; Viana et al. 2014

1b	**Cathodal tDCS** may not have a difference in efficacy when compared to **virtual reality training** for improving spasticity.	1	Lee et al. 2014

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Anodal tDCS** may not have a difference in efficacy when compared to **sham stimulation** for improving performance of activities of daily living.	5	Bornheim et al. 2020; Andrade et al. 2017; Mortensen et al. 2016; Khedr et al. 2013; Kim et al. 2010
1a	**Cathodal tDCS** may not have a difference in efficacy when compared to **sham stimulation** for improving performance of activities of daily living.	5	Alisar et al. 2020; Nicolo et al. 2018; Fusco et al. 2014; Khedr et al. 2013; Kim et al. 2010
1a	**Dual tDCS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving performance of activities of daily living.	2	Beaulieu et al. 2019; Koh et al. 2017
1b	**Anodal tDCS** may not have a difference in efficacy when compared to **cathodal tDCS** for improving performance of activities of daily living.	1	Khedr et al. 2013
1b	**Cathodal tDCS** may not have a difference in efficacy when compared to **dual tDCS** for improving performance of activities of daily living.	1	Del Felice et al. 2017
1a	**Anodal tDCS with CIMT** may not have a difference in efficacy when compared to **sham tDCS with CIMT** for improving performance of activities of daily living.	2	Rocha et al. 2016; Cunningham et al. 2015
1b	**Cathodal tDCS with CIMT** may not have a difference in efficacy when compared to **sham tDCS with CIMT** for improving performance of activities of daily living.	1	Rocha et al. 2016
1b	**Dual tDCS with upper limb robotics** may not have a difference in efficacy when compared to **sham tDCS with upper limb robotics** for improving performance of activities of daily living.	1	Straudi et al. 2016
1b	**Anodal tDCS with upper limb robotics** may not have a difference in efficacy when compared to **sham tDCS with upper limb robotics or upper limb robotics alone** for improving performance of activities of daily living.	1	Triccas et al. 2015
1b	**Anodal tDCS with upper limb robotics** may produce greater improvements in performance of activities of daily living than **cathodal tDCS with upper limb robotics**.	1	Ochi et al. 2013
1b	**Anodal tDCS with peripheral nerve stimulation** may not have a difference in efficacy when compared to **peripheral nerve stimulation** for improving performance of activities of daily living.	1	Powell et al. 2016

1b	**Anodal or cathodal tDCS with virtual reality training** may not have a difference in efficacy when compared to **virtual reality training with or without sham tDCS** for improving performance of activities of daily living.	1	Lee et al. 2014
1b	**Cathodal tDCS** may not have a difference in efficacy when compared to **virtual reality training** for improving performance of activities of daily living.	1	Lee et al. 2014

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	**Anodal tDCS** may not have a difference in efficacy when compared to **sham stimulation** for improving muscle strength.	10	Bornheim et al. 2020; Andrade et al. 2017; Marquez et al. 2017; Ilic et al. 2016; Mortensen et al. 2016; Au Yeung et al. 2014; Fusco et al. 2013; Khedr et al. 2013; Stagg et al. 2012; Tanaka et al. 2011
1a	**Cathodal tDCS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving muscle strength.	7	Nicolo et al. 2018; Marquez et al. 2017; Au Yeung et al. 2014; Khedr et al. 2013; Fusco et al. 2013; Stagg et al. 2012; Zimmerman et al. 2012
1a	**Dual tDCS** may not have a difference in efficacy when compared to **sham stimulation or conventional therapy** for improving muscle strength.	5	Beaulieu et al. 2019; Goodwill et al. 2016; Lefebvre et al. 2014; Fusco et al. 2013; Lefebvre et al. 2013
1a	**Anodal tDCS** may not have a difference in efficacy when compared to **cathodal tDCS** for improving muscle strength.	2	Khedr et al. 2013; Stagg et al. 2012
1b	**Cathodal tDCS** may not have a difference in efficacy when compared to **dual tDCS** for improving muscle strength.	1	Del Felice et al. 2017
1b	**Anodal tDCS with strength training** may not have a difference in efficacy when compared to **sham tDCS with strength training** for improving muscle strength.	1	Hendy et al. 2014
1a	**Anodal tDCS with CIMT** may not have a difference in efficacy when compared to **sham tDCS with CIMT** for improving muscle strength.	2	Figlewski et al. 2016; Rocha et al. 2016
1b	**Cathodal tDCS with CIMT** may not have a difference in efficacy when compared to **sham tDCS with CIMT** for improving muscle strength.	1	Rocha et al. 2016
1b	**Dual tDCS with FES** may produce greater muscle strength than **sham tDCS with FES**.	1	Salazar et al. 2020
1b	**Anodal tDCS with upper limb robotics** may not have a difference in efficacy when compared to **sham tDCS with upper limb robotics or upper limb robotics alone** for improving muscle strength.	1	Mazzoleni et al. 2017
1a	**Anodal tDCS with peripheral nerve stimulation** may not have a difference in efficacy when compared to **peripheral nerve stimulation** for improving muscle strength.	2	Menezes et al. 2018; Sattler et al. 2015

1a	**Anodal or cathodal tDCS with virtual reality training** may not have a difference in efficacy when compared to **virtual reality training with or without sham tDCS** for improving muscle strength.	2	Lee et al. 2014; Viana et al. 2014
1b	**Cathodal tDCS** may not have a difference in efficacy when compared to **virtual reality training** for improving muscle strength.	1	Lee et al. 2014

Key points

The literature is mixed regarding anodal, cathodal, or dual transcranial direct current stimulation, alone or in combination with other therapy approaches, for upper limb rehabilitation following stroke.

Pharmaceuticals

Botulinum Toxin

Adopted from: http://www.theinvestor.co.kr/view.php?ud=20180104000712

Botulinum toxin exerts a therapeutic effect by reducing overactivity in 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 et al. 2002; Simpson et al. 1996; Smith et al. 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 chemodenervation and neurolytic procedures like 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).

48 RCTs using botulinum toxin were included: 28 RCTs looked at botulinum toxin A compared to placebo (Wallace et al. 2020; Rekand et al. 2019; Prazeres et al. 2018; Rosales et al. 2018; Elovic et al. 2016; Wissel et al. 2016; Gracies et al. 2015; Hesse et al. 2012; Lam et al. 2012; Marciniak et al. 2012; Rosales et al. 2012; Wolf et al. 2012; Shaw et al. 2011; Kaji et al. 2010; Shaw et al. 2010; Kanovsky et al. 2009; McCrory et al. 2009; Meythaler et al. 2009; Simpson et al. 2009; Jahangir et al. 2007; Suputtitada and Suwanwela, 2005; Childers et al. 2004; Brashear et al. 2002; Bakheit et al. 2001; Bhakta et al. 2000; Smith et al. 2000; Simpson et al. 1996). Two RCTs looked at botulinum toxin B compared to placebo (Gracies et al. 2014; Brashear et al. 2004). One RCT looked at botulinum toxin A with upper limb rehabilitation compared to botulinum toxin A alone (Devier et al. 2017). Four RCTs looked at OnabotulinumtoxinA compared to letibotulinumtoxinA, NABOTA, Neurnox or tizanidine (Do et al. 2017; Nam et al. 2015; Seo et al. 2015; Simpson et al. 2009). Two RCTs looked at high versus low dosage botulinum toxin A (Masakdo et al. 2020; Francisco et al. 2002). A single RCT looked at botulinum toxin A combined with adhesive taping versus botulinum toxin A combined with manual muscle stretching, passive articular mobilization, and palmar splinting (Santamato et al. 2015). Three RCTs looked at ultrasound guided botulinum toxin A injections versus other approaches (Zeuner et al. 2017; Picelli et al. 2014; Santamato et al. 2014). Two RCTs looked at botulinum toxin A combined with NMES (Marvulli et al. 2016; Hesse et al. 1998). Two RCTs

looked at botulinum toxin A combined with mCIMT compared to botulinum toxin A (Nasb et al. 2019; Sun et al. 2010). A single RCT looked at botulinum toxin A combined with task-specific training compared to task-specific training alone (Umar et al. 2018). A single RCT comapared botox in combination with lycra orthosis (Giray et al. 2019), and a single RCT compared botox in combination with robotic therapy (Masakdo et al. 2020)

The methodological details and results of all 48 RCTs evaluating rTMS for the upper extremity motor rehabilitation are presented in Table 31.

Table 31. RCTs Evaluating Botulinum Toxin Injections for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Botulinum toxin A versus placebo, no injection or conventional rehabilitation		

Wallace et al. (2020)
RCT (8)
N_{start}=28
N_{end}=27
TPS=Chronic
	E: Botox
	C: Placebo
	Duration: rehab 45min-1.5hrs, 10x/4wks
		• Functional grasp and release task- time: (-)
		• Wrist stiffness: (-)
		• Finger stiffness: (-)
		• Modified Ashworth Scale:
		  • Wrist flexion: (-)
		  • Finger flexion: (-)
		• Wrist extension strength: (-)
		• Finger extension strength: (-)
		• Grip strength: (-)
		• Range of Motion-wrist extension: (-)
		• Range of Motion- wrist flexion: (-)
		• Range of Motion- finger flexion: (-)
		• Nine Hole Peg Test: (-)
		• Action Research Arm Test: (-)

Rekand et al. (2019) RCT (8) N_{start}=88 N_{end}=56 TPS=Chronic	E: Botox neuromuscular junction targeting C: Standard botox Duration: 4 wks	• Modified Ashworth Scale: (-) • Goal attainment scale: (-)

Prazares et al. (2018)
RCT (10)
N_{start}=40
N_{end}=36
TPS=Chronic
	E: Botox
	C: Placebo
	Duration: 30min, 2x/wk rehab
		• Fugl-Meyer Upper Extremity-Global: (-)
		  • Wrist stability: (-)
		  • Coordination and speed: (+con)
		  • Hand function: (-)
		• Modified Ashworth Scale:
		  • Elbow: (+exp)
		  • Wrist: (+exp)

Rosales et al. (2018) RCT (7) N_{Start} =42 N_{End} =40 TPS=Subacute	E: Abobotulinumtoxin A 500U C: Placebo	• Modified Ashworth Scale (+exp) • Upper extremity active motor function (-)
Elovic et al. (2016) RCT (6) N_{Start}=317 N_{End}=299 TPS=Chronic	E: 400U incobotulinumtoxinA C: Placebo	• Ashworth Scale (+exp) • Disability Assessment Scale (+exp)
Wissel et al. (2016) RCT (7) N_{start}=273 N_{end}=224	E: IncobotulinumtoxinA (340 - 365MU) C: Placebo Duration: 24 - 32wks	• Patient rating on Goal Attainment Scale: (-) • Interference with work (SF-12): (+exp)

TPS=Chronic		
Gracies et al. (2015) RCT (8) N_{Start}=243 N_{End}=229 TPS=Chronic	E1: Single 500U AbobotulinumtoxinA E2: Single 1000U AbobotulinumtoxinA C: Placebo	E1/E2 vs. C • Modified Ashworth Scale (+exp, +exp$_2$) • Disability Assessment Scale (-)
Ward et al. (2014) RCT (8) N_{start}=274 N_{end}=253 TPS=Chronic	E: Botox (max 800U) C: Placebo Duration: 24wks or 10wks after second injection (32)	• Principal active function goal: (-) • Secondary active and passive goals: (-)
Hesse et al. (2012) RCT (7) N_{start}=18 N_{end}=18 TPS=Acute	E: 150U Xeomin C: No injection	• Modified Ashworth Scale score (+exp) • Resistance to Passive Movement Scale (+exp) • Fugl-Meyer Assessment (-)

Lam et al. (2012)
RCT (8)
N_{start}= 55
N_{end}= 51
TPS= Chronic
	E: Botox (type A)
	C: Placebo
	Duration: max 1000U (+ therapy 2x/wk, splitting 3hrs, 5x/wk) 24wks total
		• Goal Attainment Scaling: (+exp)
		• Tardieu
		  • Shoulder: (+exp)
		  • Elbow: (-)
		• Modified Ashworth Scale
		  • Shoulder: (-)
		  • Elbow: (+exp)
		  • Finger: (+exp)
		• Passive Range of Motion
		  • Shoulder: (-)
		  • Elbow: (-)
		  • Finger: (-)

Marciniak et al. (2012) RCT (5) N_{Start}=21 N_{End}=19 TPS=Chronic	E: 100-150U of botulinum toxin type A (BTX-A) into the pectoralis major and teres major muscles in the shoulder extensors. C: Placebo	• Modified Ashworth Scale (-) • Passive range of motion (+exp) • Fugl-Meyer Assessment (+exp) • Functional Independence Measure (-) • Disability Assessment Scale (+exp)

Rosales et al. (2012)
RCT (9)
N_{start}= 163
N_{end}= 151
TPS= Subacute
	E: Botox 500U
	C: Placebo
	Duration: 24 wks
		• Modified Ashworth Scale: (+exp)
		• Barthel Index (-)
		• Modified Rankin score (-)
		• functional motor assessment (-)
		• Range of Motion, passive
		  • Elbow: (+exp)
		  • Wrist: (+exp)
		  • Finger: (-)
		• Range of Motion, active
		  • Elbow (-)
		  • Wrist (-)
		  • Finger (-)

Wolf et al. (2012) RCT (9) N_{start}=25 N_{end}=22 TPS=Chronic	E: 300U Botox (BTX-A) C: Placebo	• Wolf Motor Function test (-)
Shaw et al. (2011) RCT (8) N_{start}=333 N_{end}=329	E: 100-200 U Dysport + 4 weeks therapy C: Therapy only	• Action Research Arm Test (-) • Modified Ashworth Scale (+exp) • 9-Hole Peg Test (-) • Barthel Index (-)
Kaji et al. (2010) RCT (9) N_{start}=109 N_{end}=109	E1: 120 U Botox (BoNTA) C1: Placebo E2: 200 U Botox (BoNTA) C2: Placebo	E2 vs C2 • Modified Ashworth Scale (+exp$_2$) • Disability Assessment Scale (+exp$_2$) E1 vs C1

TPS=Chronic		• Modified Ashworth Scale (-) • Disability Assessment Scale (+exp_1)
Shaw et al. (2010) RCT (6) N_{Start}=333 N_{End}=199 TPS=Subacute	E: Botulinum toxin type A (BTX-A, Dysport) injections + upper limb therapy C: Upper limb therapy	• Action Research Arm Test (-) • Modified Ashworth Scale (+exp) • Motricity Index (+exp) • Grip Strength (-) • 9-Hole Peg Test (-) • Barthel Index (-)
Kanovský et al. (2009) RCT (8) N_{start}= 148 N_{end}= 145 TPS= Chronic	E: Botulinum neurotoxin NT 201 C: Placebo Duration: 12wks (max 400U btx)	• Modified Ashworth Scale: • Wrist: (+exp) • Finger: (-) • Thumb: (+exp) • Elbow: (-) • Forearm: (-) • Disability Assessment Scale: (+exp)
McCory et al. (2009) RCT (10) N_{start}= 96 N_{end}= 90 TPS= Chronic Multi-site	E: Botox (750-1000U) C: Placebo dose matched Duration: 2 injections, 12 weeks apart, 24 weeks total time before assessment	• Goal Attainment Scale: (+exp) • Modified Ashworth Scale: (+exp) • Modified Motor Assessment Scale: (-) • Patient Disability Scale: (-)
Meythaler et al. (2009) RCT (6) N_{start}=21 N_{end}=18 TPS=Chronic	E: 100 U Botox (BTX-A) + therapy C: Saline + therapy	• Motor Activity Log (-) • Ashworth Scale (-) • Barthel Index (-)
Simpson et al. (2009) RCT (8) N_{start}=60 N_{end}=41 TPS=Subacute	E1: Up to 500 U of BoNT-Type A E2: Tizanidine C: Placebo	E1 vs C • Modified Ashworth Scale (+exp) • Disability Assessment Scale (+exp) E2 vs C • Modified Ashworth Scale (-) • Disability Assessment Scale (-) E1 vs E2 • Modified Ashworth Scale (+exp) • Disability Assessment Scale (+exp_1)
Jahangir et al. (2007) RCT (6) N_{start}=27 N_{end}=27 TPS=Chronic	E: 50 U Botox (BTX-A) C: Placebo	• Modified Ashworth Scale (+exp) • Barthel Index (-)
Suputtitada & Suwanwela (2005) RCT (6) N_{start}=45 N_{end}=40 TPS=Chronic	E1: 350U BTX (Dysport) E2: 500U BTX (Dysport) E3: 1000U BTX (Dysport) C: Placebo	E1/E2/E3 vs C • Modified Ashworth Scale (+exp, +exp_2, +exp_3) E2/E3 vs C • Action Research Arm Test (+exp_2, +exp_3) E1/E2 vs C • Barthel Index (+exp, +exp_2)
Childers et al. (2004) RCT (7) N_{start}=91 N_{end}=91 TPS=Chronic	E1: 90U BTX (type A) E2: 180U BTX (type A) E3: 360U BTX (type A) C: Placebo	E1/E2/E3 vs C • Modified Ashworth Scale (+exp, +exp_2, +exp_3) • Functional Independence Measure (-)
Brashear et al. (2002) RCT (7) N_{start}=126 N_{end}=122 TPS=Chronic	E: Botulinum toxin A (50 U) C: Placebo	• Disability Assessment Scale (+exp) • Ashworth Scale (+exp)
Bakheit et al. (2001) RCT (8)	E: Total of 1000 IU of BtxA (Dysport) into 5 muscles of the affected arm	• Modified Ashworth Scale score (+exp) • Active/passive range of motion (-)

N_{start}=59 N_{end}=58 TPS=Chronic	C: Placebo injections	• Barthel Index (-)
Bhakta et al. (2000) RCT (7) N_{start}=40 N_{end}=38 TPS=Chronic	E: Total of 1000 IU Dysport (n=20) C: Placebo (n=20) divided between elbow, wrist, and finger flexors	• Modified Ashworth Scale (+exp) • Active range of motion (-)
Smith et al. (2000) RCT (7) N_{start}=25 N_{end}=25 TPS=Chronic	E1: 500 U of botulinum toxin E2: 1000 U of botulinum toxin E3: 1500 U of botulinum toxin C: Placebo	E1/E2/E3 vs C • Modified Ashworth Scale at fingers (+exp) • Active range of movement (-) • Frenchay Arm Test (-)
Simpson et al. (1996) RCT (8) N_{start}=37 N_{end}=37 TPS=Chronic	E1: Single treatment of 75 U BTX-A E2: 150 U BTX-A E3: 300 U BTXA C: Placebo	E1/E3 vs C • Modified Ashworth Scale (+exp_1, +exp_3) E1/E2/E3 vs C • Functional Independence Measure (-) • Fugl-Meyer Scale (-)
Botulinum toxin B versus placebo		
Gracies et al. (2014) RCT (9) N_{Start}=24 N_{End}=24 TPS=Chronic	E1: 10000 U Botox (type B) E2: 15000 U Botox (type B) C: Placebo	E1/E2 vs C • Modified Ashworth Scale (-) • Modified Frenchay Scale (-)
Brashear et al. (2004) RCT (7) N_{start}=15 N_{end}=15 TPS=Chronic	E: 10000 U of BTX-B C: Placebo	• Modified Ashworth scale (-)
Botulinum toxin A combined with upper limb rehabilitation versus botulinum toxin A		
Devier et al. (2017) RCT (5) N_{Start} =31 N_{End} =29 TPS=Chronic	E: OnabotulinumtoxinA with upper limb rehabilitation C: OnabotulinumtoxinA	• Fugl-Meyer Assessment (+exp) • Modified Ashworth Scale (-) • Disability Assessment Scale (-)
OnabotulinumtoxinA versus letibotulinumtoxinA, NABOTA, Neuronox, tizanidine		
Do et al. (2017) RCT (8) N_{Start} =187 N_{End} =169 TPS=Chronic	E: LetibotulinumtoxinA (Botulax) C: OnabotulinumtoxinA	• Modified Ashworth Scale (-) • Global Assessment in Spasticity (-) • Disability Assessment Scale (-)
Nam et al. (2015) RCT (7) N_{Start}=197 N_{End}=177 TPS=Subacute	E: Botulinum toxin type A (NABOTA) up to 360 U depending on degree of spasticity and muscle group C: Onabotulinum toxin A (Botox) up to 360 U depending on degree of spasticity and muscle group	• Modified Ashworth Scale (-) • Disability Assessment Scale (-)
Seo et al. (2015) RCT (10) N_{Start}=196 N_{End}=170 TPS=Chronic	E1: 360 U Neu-BoNT-A (Neuronox) E2: 360 U Botox	• Modified Ashworth Scale (-) • Disability Assessment Scale (-) •
Simpson et al. (2009) RCT (8) N_{start}=60 N_{end}=41	E1: Up to 500 U of BoNT-Type A E2: Tizanidine C: Placebo	E1 vs C • Modified Ashworth Scale (+exp) • Disability Assessment Scale (+exp) E2 vs C

TPS=Subacute		• Modified Ashworth Scale (-) • Disability Assessment Scale (-) E1 vs E2 • Modified Ashworth Scale (+exp) • Disability Assessment Scale (+exp)
High versus low dosage botulinum toxin A		
Masakado et al. (2020) RCT (7) N_{start}= 100 N_{end}= 90 TPS= Not reported Muli-site	E1: High dose botox A (400) E2: Low dose botox A (250) C1: High dose placebo C2: low dose placebo Duration: 12wks	E1 Vs C1 • Modified Ashworth Scale – Wrist: (+exp1) • Disability Assessment Scale: (-) E1 Vs E2 • Modified Ashworth Scale – Wrist: (-) • Disability Assessment Scale: (+exp1) E2 Vs C2 • Modified Ashworth Scale – Wrist: (+exp2) • Disability Assessment Scale: (-)
Francisco et al. (2002) RCT (7) N_{start}=13 N_{end}=9 TPS=Acute	E1: High volume BTX-A (50 units/1 mL saline: 1.2 mL delivered per muscle) E2: Low volume BTX-A (100 units/1 mL saline: 0.6 mL delivered per muscle)	• Modified Ashworth Scale: (-)
Botulinum toxin A combined with adhesive taping versus botulinum toxin A combined with manual muscle stretching, passive articular mobilization, and palmar splinting		
Santamato et. al (2015) RCT (7) N_{Start}=70 N_{End}=70 TPS=Chronic	E: 50-200 U Botox (type A) + adhesive taping for 10d C: 50-200 U Botox (type A) + manual muscle stretching, passive articular mobilization, and palmar splint	• Modified Ashworth Scale (+exp) • Disability Assessment Scale (+exp)
Ultrasound guided botulinum toxin A injections		
Zeuner et al. (2017) RCT-Crossover (5) N_{Start} =30 N_{End} =23 TPS=Chronic	E: Ultrasound guided Botulinum Toxin A Injections followed by electromyographic (EMG) Guided Botulinum Toxin A Injections (100-400mu) C: EMG Guided Botulinum Toxin A Injections followed by Ultrasound Guided Botulinum Toxin A Injections (100-400mu)	• Modified Ashworth Scale (-) • Barthel Index (-) • Disability Assessment Scale (-)
Picelli et al. (2014) RCT (8) N_{Start}=60 N_{End}=60 TPS=Chronic	E1: Botox A Injections (500u) under sonographic guidance E2: Botox A Injection (500u) using electrical stimulation guidance C: Botox A Injection (500u) using manual needle placement	E1 vs C • Modified Ashworth Scale (+exp) • Tardieu Spasticity angle (+exp) • Passive range of motion (+exp) E2 vs C • Modified Ashworth Scale (wrist): (+exp_2) • Tardieu Spasticity angle (+exp_2) • Passive range of motion (+exp_2) E1 vs E2 • Modified Ashworth Scale (-) • Tardieu Spasticity angle (-) • Passive range of motion (-)

Santamato et al. (2014) RCT (4) N_{Start}=30 N_{End}=30 TPS=Chronic	E: BoNT-A injection using ultrasound guidance (dosages determined by investigator) C: BoNT-A using manual needle placement via palpitation and anatomical landmarks (dosages determined by investigator)	• Modified Ashworth Scale (+exp)
Botulinum toxin A combined with NMES		
Marvulli et al. (2016) RCT (6) N_{Start}=36 N_{End}=36 TPS=Chronic	E: Botulinum toxin A therapy (118±34 U) + occupational therapy (OT) + functional electrical stimulation C: Botulinum toxin A therapy (116±36 U) + OT Duration: *Not Specified*	• Modified Ashworth Scale (+exp) • Passive range of Motion (+exp) • Action Research Arm Test (+exp)
Hesse et al. (1998) RCT (7) N_{start}=24 N_{end}=24 TPS=Chronic	E1: 1000 U Btx A + cyclic NMES E2: 1000 U of Btx A E3: Placebo + cyclic NMES C: Placebo Duration: Daily injections for 3 mo For electrical stimulation: 30 min/d, 2d/ wk for 4 wk	E1 vs E2 vs E3 vs C • Modified Ashworth Scale (-) E1 vs E2/C • Reduction in difficulties with cleaning palm (+exp)
Botulinum toxin A combined with mCIMT		

Nasb et al. (2019)
RCT (6)
N_{start}= 64
N_{end}= 53
TPS= Subacute
	E: Botox + mCIMT
	C: Botox + Conventional therapy
	Duration: 1hr, 6x/wk, 4wks rehab (glove 3hr total for mCIMT)
		• Modified Ashworth Scale:
		  • Elbow: (-)
		  • Wrist: (-)
		  • Finger: (-)
		• Barthel Index: (+exp)
		• Fugl-Meyers Upper Extremity: (+exp)

Sun et al. (2010) RCT (6) N_{start}=32 N_{end}=32 TPS=Chronic	E: 1,000 U Dysport + mCIMT C: 1,000 U Dysport + conventional rehabilitation Duration : 2hr/d, 3d/wk for 3 mo	• Modified Ashworth Scale (+exp) • Motor Activity Log (+exp) • Action Research Arm Test (+exp)
Botulinum toxin A combined with task-specific training versus task-specific training		
Umar et al. (2018) RCT (5) N_{Start} =46 N_{End} =41 TPS=NR	E: Botulinum Toxin A with Task-Specific Training C: Task-Specific Training	• Fugl-Meyer Assessment (-) • Motor Assessment Scale (-)
Botulinum Toxin A combined with Orthotics		
Giray et al. (2019) RCT (7) N_{start}= 20 N_{end}= 20 TPS= Not reported (over 3mo)	E: Botox + lycra orthosis C: Botox only Duration: (Ortho 8hrs/d, 5d/wk, 3wks (rehab 2hrs/d,5d/wk, 3wks	• Fugle-Meyers Assessment Upper Extremity: (-) • Modified Ashworth Scale: • Elbow: (-) • Wrist: (-) • Finger Thumb: (-) • Pronation: (-) • Motricity Index Upper Extremity: (-) • Box and Block Test: (-) • Stroke Impact Scale: (-)
Botulinum Toxin A combined with Robotics		

Gandolfi et al. (2019)
RCT (8)
N_{start}= 32
N_{end}= 32
TPS= Chronic
	E: Robot assisted therapy + Botox (end efficacy)
	C: Conventional therapy with Botox
	Duration: 45min, 2x/wk, 5wks
		• Modified Ashworth Scale: (-)
		• Fugle-Meyers Assessment Upper Extremity: (-)
		• Medical Research Council Scale (Upper Limb): (+exp)
		  • Shoulder Flexion: (-)
		  • Shoulder Abduction: (+exp)

		• Shoulder Rotation: (+exp) • Elbow Flexion: (+exp) • Elbow Extension: (-) • Forearm Supination: (-) • Wrist Flexion: (-) • Wrist Extension: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Botulinum Toxin

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Botulinum toxin A** may not have a difference in efficacy when compared to **placebo, no injection or conventional therapy** for improving motor function.	12	Wallace et al. 2020; Prazeres et al. 2018; Rosales et al. 2018; Hesse et al. 2012; Marciniak et al. 2012; Rosales et al. 2012; Wolf et al. 2012; Shaw et al. 2011; Shaw et al. 2010; McCrory et al. 2009; Suputtitada and Suwanwela, 2005; Simpson et al. 1996
2	**Botulinum toxin A combined with upper limb rehabilitation** may produce greater improvements in motor function than **botulinum toxin A alone**.	1	Devier et al. 2017
1b	**Botulinum toxin A combined with functional electrical stimulation** may produce greater improvements in motor function than **botulinum toxin A**.	1	Marvulli et al. 2016
1a	**Botulinum toxin A combined with mCIMT** may produce greater improvements in motor function than **botulinum toxin A**.	2	Nasb et al. 2019; Sun et al. 2010
2	**Botulinum toxin A combined with task-specific training** may not have a difference in efficacy when compared to **task-specific training alone** for improving motor function.	1	Umar et al. 2018
1b	**Botulinum toxin A combined with orthotics** may not have a difference in efficacy when compared to **botulinium toxin alone** for improving motor function.	1	Giray et al. 2019
1b	**Botulinum toxin A combined with robotics** may not have a difference in efficacy when compared to **botulinium toxin alone** for improving motor function.	1	Gandolfi et al. 2019

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Botulinum toxin A** may not have a difference in efficacy when compared to **placebo, no injection or**	16	Rekand et al. 2019; Ward et al. 2016; Wissel et al. 2016; Lam et al. 2012; Marcinak et al. 2012; Rosales et al. 2012; Shaw et al. 2011; Shaw et al. 2010; McCrory

	conventional therapy for improving performance of activities of daily living.		et al. 2009; Meythaler et al. 2009; Jahangir et al. 2007; Suputtiada & Suwanwela, 2005; Childers et al. 2004; Bakheit et al. 2001; Smith et al. 2000; Simpson et al. 1996
1b	**Botulinum toxin B** may not have a difference in efficacy when compared to **placebo** for improving performance of activities of daily living.	1	Gracies et al. 2014
2	**Ultrasound guided botulinum toxin A injections** may not have a difference in efficacy when compared to **electromyography guided botulinum toxin A injections** for improving performance of activities of daily living.	1	Zeuner et al. 2017
1a	**Botulinum toxin A combined with mCIMT** may produce greater improvements in performance of activities of daily living than **botulinum toxin A**.	2	Nasb et al. 2019; Sun et al. 2010
2	**Botulinum toxin A combined with task-specific training** may not have a difference in efficacy when compared to **task-specific training alone** for improving performance of activities of daily living.	1	Umar et al. 2018
1b	**Botulinum toxin A combined with orthotics** may not have a difference in efficacy when compared to **botulinium toxin alone** for improving performance on activities of daily living.	1	Giray et al. 2019

DEXTERITY

LoE	Conclusion Statement	RCTs	References
1a	**Botulinum toxin A** may not have a difference in efficacy when compared to **placebo, no injection or conventional therapy** for improving dexterity.	3	Wallace et al. 2020; Shaw et al. 2011; Shaw et al. 2010
1b	**Botulinum toxin A combined with orthotics** may not have a difference in efficacy when compared to **botulinium toxin alone** for improving dexterity.	1	Giray et al. 2019

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References
1a	**Botulinum toxin A** may not have a difference in efficacy when compared to **placebo, no injection or conventional therapy** for improving range of motion.	7	Wallace et al. 2020; Lam et al. 2012; Marciniak et al. 2012; Rosales et al. 2012; Bakheit et al. 2001; Bhakta et al. 2000; Smith et al. 2000
1b	**Ultrasound guided botulinum toxin A injections** may produce greater improvements in range of motion than **manual needle placement injections**.	1	Picelli et al. 2014
1b	**Electrical stimulation guided botulinum toxin A injections** may produce greater improvements in	1	Picelli et al. 2014

	range of motion than **manual needle placement injections**.		
1b	**Ultrasound guided botulinum toxin A injections** may not have a difference in efficacy when compared to **electrical stimulation guided botulinum toxin A injections** for improving range of motion.	1	Picelli et al. 2014
1b	**Botulinum toxin A combined with functional electrical stimulation** may produce greater improvements in range of motion than **botulinum toxin A**.	1	Marvulli et al. 2016

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References
1b	**Botulinum toxin A** may not have a difference in efficacy when compared to **placebo, no injection or conventional therapy** for improving measures of stroke severity.	1	Rosales et al. 2012

MUSCLE STRENGTH

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **Botulinium Toxin A** to improve muscle strength when compared to **placebo, no injection or conventional therapy**.	2	Wallace et al. 2020; Shaw et al. 2010
1b	**Botulinum toxin A combined with orthotics** may not have a difference in efficacy when compared to **botulinium toxin alone** for improving muscle strength.	1	Giray et al. 2019
1b	**Botulinum toxin A combined with robotics** may not have a difference in efficacy when compared to **botulinium toxin alone** for improving muscle strength.	1	Gandolfi et al. 2019

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1a	**Botulinum toxin A** may produce greater improvements in spasticity than **placebo, no injection or conventional therapy**.	26	Masakdo et al. 2020; Wallace et al. 2020; Rekand et al. 2019; Prazeres et al. 2018; Rosales et al. 2018; Elovic et al. 2016; Gracies et al. 2015; Hesse et al. 2012; Lam et al. 2012; Marciniak et al. 2012; Rosales et al. 2012; Shaw et al. 2011; Kaji et al. 2010; Shaw et al. 2010; Kanovsky et al. 2009; McCrory et al. 2009; Meythaler et al. 2009; Simpson et al. 2009; Jahangir et al. 2007; Suputtitada and Suwanwela, 2005; Childers et al. 2004; Brashear et al. 2002; Bakheit et al. 2001; Bhakta et al. 2000; Smith et al. 2000; Simpson et al. 1996

1a	**Botulinum toxin B** may not have a difference in efficacy when compared to **placebo** for improving spasticity.	2	Gracies et al. 2014; Brashear et al. 2004
2	**Botulinum toxin A combined with upper limb rehabilitation** may not have a difference in efficacy when compared to **botulinum toxin A alone** for improving spasticity.	1	Devier et al. 2017
1b	**LetibotulinumtoxinA, NABOTA and neuronox** may not have a difference in efficacy when compared to **onabotulinumtoxinA** for improving spasticity.	3	Do et al. 2017; Nam et al. 2015; Seo et al. 2015
1b	**Botulinum toxin A** may produce greater improvements in spasticity than **tizanidine**.	1	Simpson et al. 2009
1b	**High volume botulinum toxin A** may not have a difference in efficacy when compared to **low volume botulinum toxin A** for improving spasticity.	1	Francisco et al. 2002
1b	**Botulinum toxin A combined with adhesive taping** may produce greater improvements in spasticity than **botulinum toxin A combined with manual muscle stretching, passive articular mobilization, and palmar splinting**.	1	Santamato et al. 2015
2	**Ultrasound guided botulinum toxin A injections** may not have a difference in efficacy when compared to **electromyography guided botulinum toxin A injections** for improving spasticity.	1	Zeuner et al. 2017
1b	**Ultrasound guided botulinum toxin A injections** may produce greater improvements in spasticity than **manual needle placement injections**.	2	Santamato et al. 2014; Picelli et al. 2014
1b	**Electrical stimulation guided botulinum toxin A injections** may produce greater improvements in spasticity than **manual needle placement injections**.	1	Picelli et al. 2014
1b	**Ultrasound guided botulinum toxin A injections** may not have a difference in efficacy when compared to **electrical stimulation guided botulinum toxin A injections** for improving spasticity.	1	Picelli et al. 2014
1b	**Botulinum toxin A combined with functional electrical stimulation** may produce greater improvements in spasticity than **botulinum toxin A**.	1	Marvulli et al. 2016
1b	**Botulinum toxin A combined with cyclic NMES** may not have a difference in efficacy when compared to **botulinum toxin A, cyclic NMES, or placebo** for improving spasticity.	1	Hesse et al. 1998
1a	There is conflicting evidence about the effect of **Botulinum toxin A combined with mCIMT** to improve spasticity when compared to **botulinum toxin alone.**	2	Nasb et al. 2019; Sun et al. 2010
1b	**Botulinum toxin A combined with orthotics** may not have a difference in efficacy when compared to **botulinium toxin alone** for improving spasticity.	1	Giray et al. 2019

1b	**Botulinum toxin A combined with robotics** may not have a difference in efficacy when compared to **botulinium toxin alone** for improving spasticity.	1	Gandolfi et al. 2019

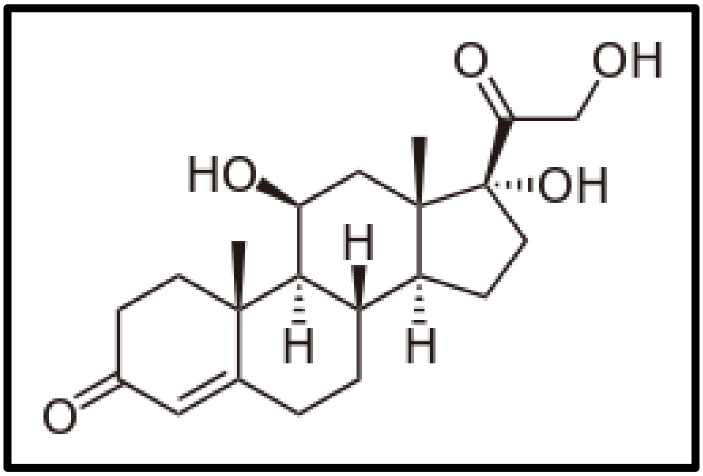
Key points

Botulinum A likely improves spasticity in the upper limb following stroke, but not range of motion or activities of daily living. The effect on general upper limb motor function is conflicting and less clear.

Botulinum toxin A in combination with other types of therapeutic approaches may be beneficial for certain aspects of upper limb function.

Botulinum toxin B has been less well studied to date in comparison to botulinum toxin A.

Steroids



Adopted from: https://en.wikipedia.org/wiki/Corticosteroid

Corticosteroids have been used to treat pain and functional limitations in hemiplegic patients (Dogan et al. 2013). Patients suffering from stroke experience high rates of inflammation and corticosteroids are prescribed to lessen the inflammation (Yasar et al. 2011).

The methodological details and results of a single RCT (Yasar et al. 2011) evaluating intra-articular steroid use for upper extremity motor rehabilitation are presented in Table 32.

Table 32. RCT Intra-articular Steroid Use for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Yasar et al. (2011) RCT (9) N_{Start}=26 N_{End}=26 TPS=Subacute	E1: Intra-Articular Steroid Injection E2: Suprascapular Nerve Block Injection Duration: *Not Specified*	• Range of Motion (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Steroids

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Intra-articular steroid injections** may not have a difference in efficacy when compared to **suprascapular nerve block injections** for improving range of motion.	1	Yasar et al. 2011

Key points

There is little reported literature on steroid use for upper limb rehabilitation following stroke. Steroid injections may not be beneficial for upper limb rehabilitation following stroke.

Cerebrolysin

Adopted from: http://www.gerovitalshop.eu/it/home/18-cerebrolysin-5ml.html

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

Two RCTs were identified comparing cerebrolysin to a placebo (Chang et al. 2016; Muresanu et al. 2016).

The methodological details and results of two RCTs evaluating cerebrolysin for upper extremity motor rehabilitation are presented in Table 33.

Table 33. RCTs Evaluating Cerebrolysin for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Chang et al. (2016) RCT (6) N_{start}=70 N_{end}=66 TPS=Acute	E: Cerebrolysin (30mL diluted with 70mL saline) + conventional therapy C: Placebo + conventional therapy Duration: 1x/d for 6wk	• Action Research Arm Test (+exp) • National Institute of Health Stroke Scale (+exp) • Barthel Index (+exp) • Modified Rankin Scale (+exp)
Muresanu et al. (2016) RCT (9) N_{start}=208 N_{end}=196 TPS=Acute	E: Cerebrolysin (30mL diluted with 70mL saline) + physical/occupational therapy C: Placebo + physical/occupational therapy Duration: 1x/d for 3wk	• Fugl-Meyer Assessment (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Cerebrolysin

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Cerebrolysin** may produce greater improvements in motor function than **placebo**.	2	Chang et al. 2016; Muresanu et al. 2016

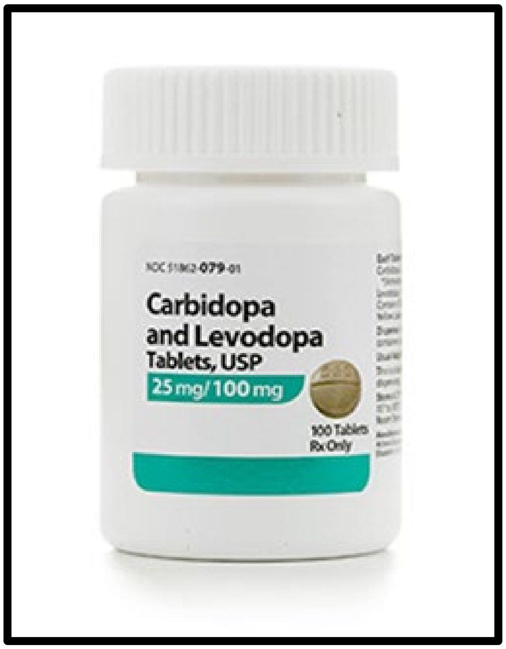
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Cerebrolysin** may produce greater improvements in activities of daily living than **placebo**.	1	Chang et al. 2016

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Cerebrolysin** may produce greater improvements in measures of stroke severity than **placebo**.	1	Chang et al. 2016

Key points

Cerebrolysin may be beneficial for aspects of upper limb function following stroke.

Levodopa



Adopted from: https://www.maynepharma.com/products/us-products/generic-products/generic-products-catalog/carbidopalevodopa-tablets/

Levodopa has been the hallmark pharmaceutical for the treatment of Parkinson's disease. However, its ability to affect motor movements in Parkison's disease is limited by its narrow therapeutic window, short half-life, and poor bioavailability (Tambassco et al. 2018).

Two RCTs were indentified comparing levodopa to a placebo (Rosser et al. 2008; Restemeyer et al. 2007).

The methodological details and results of two RCTs evaluating levodopa treatment for upper extremity motor rehabilitation in stroke survivors are presented in Table 34.

Table 34. RCTs Evaluating Levodopa Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) **Study Design (PEDro Score)** **Sample Size$_{start}$** **Sample Size$_{end}$** **Time post stroke category**	**Interventions** **Duration: Session length, frequency per week for total number of weeks**	**Outcome Measures** **Result (direction of effect)**
Rosser et al. (2008) RCT (5) N_{start}=18 N_{end}=18 TPS=Chronic	E: Levodopa (100mg) + Cabidopa (25mg) C: Placebo (125mg) Duration: 1hr physio (3x) + Levodopa (3x)	• Performance in a simple motor task (+exp)
Restemeyer et al. (2007) RCT (9) N_{start}=10 N_{end}=10 TPS=Chronic	E: Levodopa (100mg) C: Placebo (100mg) Duration: 1hr physio (2x) + Levodopa (2x)	• Nine Hole Peg Test (-) • Grip strength (-) • Action Research Arm Test (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group

+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Levodopa

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **Levodopa** to improve motor function when compared to **placebo**.	2	Rosser et al. 2008; Restemeyer et al. 2007

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Levodopa** may not have a difference in efficacy when compared to **placebo** for improving muscle strength.	1	Restemeyer et al. 2007

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Levodopa** may not have a difference in efficacy when compared to **placebo** for improving dexterity.	1	Restemeyer et al. 2007

Key points

The evidence is mixed regarding Levodopa for upper limb rehabilitation following stroke.

Statins and Antihypertensives

Adopted from: https://www.aarp.org/health/drugs-supplements/info-2016/new-guidelines-on-who-should-take-statins-cs.html

HMG-CoA reductase inhibitors (statins) are widely used worldwide due to their anti-atherosclerotic, anti-inflammatory, and immunomodulatory properties (Lin et al. 2015). This suggests that statins may have a beneficial role in infection, in fact, statins are found to have beneficial effects on the prevention and treatment of infections in diseases including cerebrovascular accidents (Lin et al. 2015). Statins are also believed to have a neuroprotective effect and are conducive to promoting autophagy in neurological disorders (Lin et al. 2015). Some antihypertenives have also been examined for stroke recovery.

Three RCTs were identified that examined statins and antihypertensives.

Two RCTs compared atorvastatin with a placebo (Zhang et al. 2017; Wang et al. 2017). One RCT compared antihypertensives (Jose et al. 2017)

The methodological details and results of the three RCTs evaluating atorvastatin and anthypertensives for upper extremity motor rehabilitation are presented in Table 35.

Table 35. RCT Evaluating Atorvastatin and Antihypertenantisives Use for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Wang et al. (2017) RCT (5) N_{start}=96 N_{end}=96 TPS=NR	E: (atorvastatin (20 mg) and clopidogrel (75 mg) daily) C: Conventional care Duration: 3months	• Fugl Meyer Assessment (+exp) • Barthel Index (+exp)
Zhang et al. (2017) RCT (6) N_{Start}=78 N_{End}=75 TPS=Acute	E: Atorvastatin (20mg) C: Placebo (20mg) Duration: Atorvastatin daily for 6wk	• Modified Rankin Scale (+exp) • Barthel Index (+exp) • NIHSS (-)
Antihypertensives		
Jose et al. (2017) RCT (5) N_{start}= 110 N_{end}= 98 TPS= Not reported	E1: Telmisartan E2: Amlodipine C: Mannitol Duration: Not reported	E1 Vs C • National Institute of Health Stroke Scale (+exp1) E2 Vs C • National Institute of Health Stroke Scale (+exp1) E1 Vs E2 • National Institute of Health Stroke Scale (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Atorvastatin

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Atorvastatin** may produce greater improvements in motor function **placebo**	1	Wang et al. 2017

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Atorvastatin** may produce greater improvements in activities of daily living than **placebo**.	2	Wang et al. 2017; Zhang et al. 2017

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **atorvastatin** to improve measures of stroke severity when compared to **placebo**.	1	Zhang et al. 2017
2	**Telmisartan** may produce greater improvements in measures of stroke severity than **mannitol or amlodipine**.	1	Joese et al., 2017

Key points

The evidence is mixed regarding atorvastatin for upper limb rehabilitation following stroke.

Antidepressants

Adopted from: https://www.newportacademy.com/resources/treatment/teens-antidepressants-side-effects-risks-holistic-treatment/

Antidepressants of various kinds are available for medical use, including tricyclics (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs, such as venlafaxine, duloxetine and milnacipran), and other agents (mirtazapine, reboxetine, bupropion). SSRIs and SNRIs are two commonly prescribed agents that work by acting to inhibit the reuptake of serotonin and norepinephrine, respectively, from the synaptic cleft (Cipriani et al. 2012). 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 serotoninergic 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 et al. 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).

Nine RCTs were identified that examined antidepressants.

Six RCTs compared antidepressants to placebo (Ward et al. 2017; Mohammadianinejad et al. 2014; Chollet et al. 2011; Berends et al. 2009; Zittel et al. 2008; Zittel et al. 2007). One RCT compared fluoxetine and rTMS combined (Bonin Pinto et al. 2019). Two RCTs compared nortriptyline to fluoxetine (Mikami et al. 2011; Robinson et al. 2000).

The methodological details and results of the nine RCTs evaluating antidepressants for upper extremity motor rehabilitation are presented in Table 36.

Table 36. RCTs Evaluating Antidepressants Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Ward et al. (2017) RCT (7) N_{Start} =12 N_{End} =9 TPS=Chronic	E: Atomoxetine 40 mg with Task-Oriented Upper Extremity Training C: Placebo with Task-Oriented Upper Extremity Training	• Fugl-Meyer Assessment (+exp) • Action Research Arm Test (-) • Wolf Motor Function Test (-)
Mohammadianinejad et al. (2014) RCT (6) N_{Start}=80 N_{End}=66 TPS=Acute	E: Lithium carbonate (300mg) C: Placebo Duration: Lithium Carbonate 300mg (2x/d) for 30d	• National Institutes of Health Stroke Scale (+exp) • Fugl-Meyer Assessment (+exp)
Chollet et al. (2011) RCT (9) N_{start}=118 N_{end}=113 TPS=Chronic	E: Fluoxetine (20mg) C: Placebo Duration: Ingested daily (orally) for 3mo	• Fugl Meyer Assessment (+exp) • National Institutes of Health Stroke Scale (-) • Modified Rankin Scale (+exp)
Berends et al. (2009) RCT Crossover (8) N_{start}= 10 N_{end}= 10 TPS= Chronic	E: Fluoextine C: Placebo Duration: Single dose	• Grip Strength: (-) • Motricity Index: (-)
Zittel et al. (2008) RCT (8) N_{start}=8 N_{end}=8 TPS=Chronic	E: Citalopram (40mg) C: Placebo (40mg) Duration: Citalopram (2x)	• Nine Hole Peg Test (+exp) • Hand grip strength (-)
Zittel et al. (2007) RCT (6) N_{start}=10 N_{end}=10 TPS=Chronic	E: Reboxetine (6mg) C: Placebo (6mg) Duration: Reboxetine (2x)	• Tapping speed (+exp) • Grip strength (+exp)
Fluoxetine and rTMS		
Bonin Pinto et al. (2019) RCT (8) N_{start}= 27 N_{end}= 26 TPS= Chronic	E: Low frequency rTMS + Fluoxetine C1: Fluoxetine (20mg, 90d) C2: Placebo Duration: 18x, 5d/wk for 2 wks, 1x/wk for 8wks 20min)	E vs C1 • Jebson Hand Function Test: (+exp) • Fugl Meyer Assessment: (+exp) E vs C2 • Jebson Hand Function Test: (+exp) • Fugl Meyer Assessment: (+exp) C1 vs C2 • Jebson Hand Function Test: (+con2) • Fugl Meyer Assessment: (+con2)
Notriptyline + Fluoxetine versus Placebo		
Mikami et al. (2011) RCT (8) 1 yr follow-up analysis of Robinson et al. 2000 N_{start}=104 N_{end}=97 TPS=Chronic	E1: Nortriptyline (100mg) E2: Fluoxetine (40mg) C: Placebo Duration: Fluoxetine or Nortriptyline daily for 12wk	E1/E2 vs C • Modified Rankin Scale (+exp_1, +exp_2)
Robinson et al. (2000) RCT (8) N_{start}=104	E1: Nortriptyline (100mg) E2: Fluoxetine (40mg) C: Placebo	E1 vs E2/C • Functional Independence Measure (+exp_1)

N_{end}=97 TPS=Chronic	Duration: Fluoxetine or Nortriptyline daily for 12wk	

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Antidepressants

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **antidepressants** to improve motor function when compared to **placebo treatment**.	4	Bonino Pinto et al. 2019; Ward et al. 2017; Mohammadianinejad et al. 2014; Chollet et al. 2011
1b	**Fluoxetine with rTMS** may produce greater improvements in motor function than **fluoxdetine alone or placebo treatment.**	1	Bonino Pinto et al. 2019

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Antipressants** may not have a difference in efficacy when compared to **placebo treatment** for improving muscle strength.	3	Bereneds et al. 2009; Zittel et al. 2008; Zittel et al. 2007

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Antidepressants** may produce greater improvements in performance of activities of daily living than **placebo treatment**.	1	Robinson et al. 2000

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Antidepressants** may produce greater improvements in dexterity than **placebo treatment**.	3	Bonino Pinto et al. 2019; Zittel et al. 2008; Zittel et al. 2007;
1b	**Fluoxetine with rTMS** may produce greater improvements in dexterity than **fluoxetine alone or placebo treatment.**	1	Bonino Pinto et al. 2019

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Antidepressants** may produce greater improvements in measures of stroke severity than **placebo treatment**.	3	Mohammadianinejad et al. 2014; Chollet et al. 2011; Mikami et al. 2011

Key points

Antidepressants may be beneficial for aspects of upper limb function following stroke.

Central Nervous System Stimulants

Adopted from: https://www.narconon.org/drug-information/amphetamine-health-risks.html

Central nervous system stimulants are drugs that increase cortical excitability, often provided to manage arousal states by enhancing neural transmission. Central nervous system stimulants increase the synaptic concentration and transmission of dopamine, serotonin, and noradrenaline throughout the brain, and neurobehavioral gains ascribed to central nervous system stimulants include enhanced arousal, mental processing speed, and/or motor processing speed (Herrold et al. 2014). Common stimulants used in rehabilitation include amphetamines and methylphenidates. Methylphenidate has been shown to enhance motor recovery after partial cortex ablation in rodents, and to modulate poststroke cerebral reorganization, improving motor function in stroke patients (Wang et al. 2014). Stimulants such as amphetamines have been reported to enhance plasticity through axonal sprouting (Papadopoulos et al. 2009). Some pharmacetuicals, like theophylline, can act by modulating GABA neurotransmission and decrease inhibition to indirectly increase neuronal excitability (Schambra et al. 2016).

Six RCTs were identified that examined central nervous stimulants.

Four RCTs compared a central nervous stimulant to placebo (Schuster et al. 2011; Gladstone et al. 2006; Tardy et al. 2006; Platz et al. 2005a). One RCT examined methylphenidate in combination with dual tDCS (Wang et al. 2014). One RCT compared theophylline to placebo (Schambra et al. 2016).

The methodological details and results of the six RCTs evaluating antidepressants for upper extremity motor rehabilitation are presented in Table 37.

Table 37. RCTs Evaluating Central Nervous Stimulants for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Schuster et al. (2011) RCT (9) N_{start}=16 N_{end}=15 TPS=Chronic	E: Dexamphetamine (10mg) C: Placebo Duration: 20min/d, 2d/wk for 5wk	• Chedoke-McMaster Stroke Assessment (+exp)
Gladstone et al. (2006) RCT (7) N_{start}= 71 N_{end}= 67 TPS=Acute Multi-Site	E: Dextroamphetamine (10mg, 90min before physiotherapy) C: Placebo Duration: 2x/wk, 5wks	• Fugle-Meyers Assessment Upper Extremity (-) • Functional Independence Measure: (-) • Chedoke-Mcmaster Disability Inventory: (-)
Tardy et al. (2006) RCT (9) N_{start}=8 N_{end}=8 TPS=Chronic	E: Methylphenidate (20mg) C: Placebo Duration: 2d/wk for 4wk	• Finger tapping scores (+exp) • Hand grip strength (-)
Platz et al. (2005a) RCT (9) N_{start}=31 N_{end}=29 TPS=Chronic	E: d-amphetamine (10mg) C: Placebo Duration: 45min/d, 3d/wk for 4wk	• TEMPA (+exp)
Methylphenidate + tDCS		
Wang et al. (2014) RCT (7) N_{start}=9 N_{end}=9 TPS=Subacute	E1: Dual tDCS + methylphenidate (20mg) E2: Dual tDCS + placebo drug E3: Sham tDCS + methylphenidate C: Sham tDCS + placebo drug Duration: 20min/d, 3d/wk for 4wk	E1 vs E2/E3 • Purdue Pegboard Test: (+exp)
Theophylline vs Placebo		
Schambra et al. (2016) RCT (6) N_{start}= 20 N_{end}= 18 TPS= Chronic	E: Theophylline C: Placebo Duration: 1 dose, 300mg, 1wk minimum washout period for conditions	• Pinch strength: (-) • Nine Hole Peg Test: (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Central Nervous Stimulants

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Dexamphetamine and methylphenidate** may produce greater improvements in motor function than **placebo treatment**.	3	Schuster et al. 2011; Gladstone et al. 2006; Platz 2005a

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Dexamphetamine and methylphenidate** may not have a difference in efficacy when compared to **placebo treatment** for improving muscle strength.	1	Tardy et al. 2006
1b	**theophylline** may not have a difference in efficacy when compared to **placebo treatment** for improving muscle strength.	1	Schambra et al. 2016

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Dexamphetamine and methylphenidate** may produce greater improvements in dexterity than **placebo treatment**.	1	Tardy et al. 2006
1b	**Methylphenidate combined with dual tDCS** may produce greater improvements in dexterity than **dual tDCS or methylphenidate**.	1	Wang et al. 2014
1b	**theophylline** may not have a difference in efficacy when compared to **placebo treatment** for improving dexterity.	1	Schambra et al. 2016

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Dexamphetamine and methylphenidate** may produce greater improvements in performance of activities of daily living than **placebo treatment**.	1	Gladstone et al. 2006

Key points

Dexamphetamine or methylphenidate may be beneficial for aspects of upper limb function following stroke.

Methylphenidate combined with dual transcranial direct current stimulation may be beneficial for upper limb rehabilitation following stroke.

Neuroprotectants

Adopted from: https://mstrust.org.uk/a-z/neuroprotection

During ischemic stroke there is rapid reduction in cerebral blood flow, leading to reduced perfusion of oxygen and nutrients to brain area impacted by the occlusion. Depletion of ATP production in neurons initiates a cascade of pathophysiological processes that include rising intracellular calcium and production of inflammatory cytokines (Jeyaseelan et al. 2008). Compensatory mechanisms contribute to membrane destabilization, mitochondrial dysfunction and apoptosis causing cellular damage (Jeyaseelan et al. 2008). Neuroprotectants are a class of compounds that aim to protect the postischemic neuronal tissue from the aforementioned pathological process' and include calcium and glutamate antagonists, AMPA antagonists' free radical scavengers and anti-inflammatory agents (Lyden and Wahlgren 2000). Many of these compounds have shown promise in pre-clinical models but few have made successful transition to human application (Lyden and Wahlgren 2000).

The methodological details and results of the two RCTs are presented Table 38.

Table 38. RCTs Evaluating Neuroprotectant Pharmaceuticals for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Traditional Medicines		
Kong et al. (2009) RCT (7) N_{start}=40 N_{end}=32 TPS=acute	E: NeuroAid (MLC 601) C: Placebo Duration: 4 capsules 3 times a day for 4 weeks	• Fugl-Meyers Assessment (-) • National Institute of Stroke Scale (-) • Functional independence measure (-)
Phosphodiesterase inhibitors		
Di Cesare et al. 2016 RCT (10) N_{start}=139 N_{end}=137 TPS=acute	E: Phosphodiesterase inhibitor 6mg C: Placebo Duration: 1 6mg capsule/day for 90 days	• Modified Rankin Scale (-) • National Institute of Stroke Scale (-) • Barthel Index (-) • Box and Block Test (-) • Grip Strength (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Neuroprotectants

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Neuroaid** may not have a difference in efficacy when compared to **placebo treatment** for improving motor function.	1	Kong et al. 2009

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Phosphodiesterase inhibitors** may not have a difference in efficacy when compared to **placebo treatment** for improving muscle strength.	1	Di Cesare et al. 2016

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Phosphodiesterase inhibitors** may not have a difference in efficacy when compared to **placebo treatment** for improving dexterity.	1	Di Cesare et al. 2016

ACTIVITIES OF DAILY LIVING			
LoE	Conclusion Statement	RCTs	References
1b	**Neuroaid** may not have a difference in efficacy when compared to **placebo treatment** for improving performance on activities of daily living	1	Kong et al. 2009
1b	**Phosphodiesterase inhibitors** may not have a difference in efficacy when compared to **placebo treatment** for improving performance on activities of daily living.	1	Di Cesare et al. 2016

STROKE SEVERITY			
LoE	Conclusion Statement	RCTs	References
1b	**Neuroaid** may not have a difference in efficacy when compared to **placebo treatment** for improving measures of stroke severity.	1	Kong et al. 2009
1b	**Phosphodiesterase inhibitors** may not have a difference in efficacy when compared to **placebo treatment** for improving measures of stroke severity.	1	Di Cesare et al. 2016

Key points

Neuroprotectants may not be beneficial for upper limb rehabilitation

Acupuncture

Adopted from: https://www.mccaffreyhealth.com/acupuncture-for-chronic-pain/

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 method 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". There is a range of possible acupuncture mechanisms that may contribute to the health benefits experienced by stroke patients (Park et al. 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. With respect to stroke rehabilitation, the benefit of acupuncture has been evaluated most frequently for pain relief and recovery from hemiparesis.

24 RCTs for acupuncture were identified.

13 RCTs compared acupuncture to conventional care or sham (Wang et al. 2020; Chen et al. 2016; Hou et al. 2014; Bai et al. 2013; Gao et al. 2013; Zhuangl et al. 2012; Wayne et al. 2005; Alexander et al. 2004; Sze et al. 2002; Kjendhal et al. 1997; Hu et al. 2993; Naeser et al. 1992). Seven RCTs compared one acupuncture technique to another (Wei et al. 2019; Cui et al. 2014; Ni et al. 2013; Zhang et al. 2013; Fragoso & Ferreira, 2012; Zhao et al. 2009; Gosman-Hedstom et al. 1998). One RCT compared acupuncture in combination with CIMT to acupuncture alone (Song et al. 2016). One RCT compared acupuncture with TENS to acupuncture alone

(Hopwood et al. 2008). Two RCTs examined acupuncture combined with rTMS (Kim et al. 2020; Zhao et al. 2018).

The methodological details and results of all 19 RCTs evaluating acupuncture for upper extremity motor rehabilitation are presented in Table 39.

Table 39. Summary of RCTS with Examining Acupuncture for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Acupuncture compared to conventional therapy or sham		

Wang et al. (2020)
RCT (8)
N_{start}=139
N_{end}=130
TPS=Subacute
	E: Acupuncture
	C: Conventional rehabilitation
	Duration: 6x/wk, 4wks
	(both rehab (45min)
	and acupuncture)
		• Fugl-Meyer Upper Extremity: (+exp)
		  • Upper limb: (-)
		  • Lower Limb: (+exp)
		• Barthel Index: (-)

Chen et al. (2016) RCT (8) N_{Start}=250 N_{End}=250 TPS=Chronic	E: Acupuncture C: Conventional therapy Duration: 45min/d, 6d/wk for 3wk	• National Institute of Health Stroke Scale (+exp) • Fugl-Meyer Assessment (+exp)
Liu et al. (2016) RCT (6) N_{Start}=38 N_{End}=31 TPS=Chronic	E: Manual acupuncture + standard care C: Standard care Duration: *Not Specified*	• National Institute of Health Stroke Scale (-) • Fugl-Meyer Assessment (-) • Functional Independence Measure (-) • Barthel Index (-) • Modified Rankin Scale (-)
Hou et al. (2014) RCT (4) N_{start}= 552 N_{end}= 488 TPS= Acute Multi-Site	E: Acupuncture C: Conventional therapy (with piracetam) Duration: 1x/d, 3wks \~40min	• Modified Ashworth Scale: (+exp) • Shoulder Abduction: (+exp) • Pronation of Forearm: (+exp) • Elbow Flexion: (+exp) • Wrist Flexion: (+exp) • Finger Flexion: (+exp) • Neurological Deficit Grades (1-5): (+exp)
Bai et al. (2013) RCT (9) N_{Start}=120 N_{End}=120 TPS=NR	E1: Acupuncture E2: Physical therapy E3: Acupuncture + physical therapy Duration: *Not Specified*	E1 vs E2 • Fugl-Meyer Assessment (-) • Modified Barthel Index (-) E1 vs E3 • Fugl-Meyer Assessment (-) • Modified Barthel Index (-) E2 vs E3 • Fugl-Meyer Assessment (-) • Modified Barthel Index (-)
Gao et al. (2013) RCT (6) N_{start}= 106 N_{end}= 106 TPS=Acute	E1: Contralateral acupuncture E2: Ipsilateral acupuncture C: Conventional therapy (no acupuncture) Duration: 45min/d, 30d	E1 Vs C • Neurological Deficit Score: (+exp1) • Modified Barthel Index: (+exp1) • Fugle-Meyers Assessment Upper Extremity: (+exp1) E2 Vs C • Neurological Deficit Score: (+exp2) • Modified Barthel Index: (+exp2) • Fugle-Meyers Assessment Upper Extremity: (+exp2) E1 Vs E2 • Neurological Deficit Score: (+exp1) • Modified Barthel Index: (+exp1) • Fugle-Meyers Assessment Upper Extremity: (+exp1)

Zhuangl et al. (2012) RCT (7) N_{start}=295 N_{end}=274 TPS=Chronic	E1: Acupuncture E2: Physiotherapy E3: Acupuncture + physiotherapy Duration: 1hr/d, 6d/wk for 4wk	• Fugl-Meyer Assessment (-) • Barthel Index (-) • Neurologic Defect Scale (-)
Wayne et al. (2005) RCT (9) N_{start}=33 N_{end}=33 TPS=Chronic	E: Acupuncture C: Sham Duration: 45min/d, 2d/wk for 10wk	• Fugl-Meyer Assessment (-) • Modified Ashworth scores (-) • Arm range of motion (-) • Barthel Index (-)
Alexander et al. (2004) RCT (6) N_{start}=32 N_{end}=28 TPS=Acute	E: Acupuncture + Standard Rehabilitation C: Standard Rehabilitation Duration: 30min/d, 2d/wk for 10 wk	• Fugl-Meyer Assessment (-) • Functional Independence Measure (-)
Sze et al. (2002) RCT (7) N_{start}=106 N_{end}=106 TPS=Acute	E: Acupuncture + Standard Therapy C: Standard Therapy Duration: 45min/d, 2d/wk for 10wk	• Fugl-Meyer Assessment (-) • Barthel Index (-) • Functional Independence Measure (-) • National Institutes of Health Stroke Scale (-)
Kjendhal et al. (1997) RCT (6) N_{start}=45 N_{end}=41 TPS=Subacute	E: Acupuncture C: Standard Therapy Duration: 30min/d, 3-4d/wk for 6wk	• Motor Assessment Scale (+exp) • Sunnaas Index (+exp)
Hu et al. (1993) RCT (4) N_{start}=30 N_{end}=NR TPS=Acute	E: Acupuncture C: Supportive Therapy + Conventional Rehabilitation Duration: *Not Specified*	• Scaninavian stroke study Neurological score (+exp) • Barthel Index (-)
Naeser et al. (1992) RCT (6) N_{start}=16 N_{end}=16 TPS=Subacute	E: Acupuncture C: Sham Acupuncture Duration: 1hr/d, 5d/wk for 4wk	• Boston Motor Inventory range of motion (+exp)
Acupuncture vs acupuncture		
Wei et al. (2019) RCT (4) N_{start}=40 N_{end}=40 TPS=Subacute	E: Acupuncture + neuromuscular joint facilitation C: Acupuncture Duration: 30min, 1x/d, 6x/wk	• Passive Range of Motion: (+exp) • Fugl Meyer Upper Extremity: (+exp) • Barthel Index: (-)
Cui et al. (2014) RCT (6) N_{Start}=60 N_{End}=60 TPS=NR	E: Yin Yang manipulation C: Conventional needling manipulation Duration: *Not Specified*	• Elbow spasm (+exp) • Clinical Spasticity Index (+exp)
Ni et al. (2013) RCT (7) N_{Start}=165 N_{End}=165 TPS= NR	E: Standard Acupuncture with Shixuan & Xiaohai acupoints C: Standard Acupuncture only Duration: *Not Specified*	• Finger grip strength (+exp) • Fugl-Meyer Assessment (+exp)
Zhang et al. (2013) RCT (6) N_{start}=36 N_{end}=36 TPS=Subacute	E: Chinese acupuncture C: Western acupuncture Duration: 6d/wk for 6wks	• Modified Ashworth Scale: (+exp) • Clinical Spasticity Index: (+exp)

Fragoso & Ferreira (2012) RCT (6) N_{start}=32 N_{end}=32 TPS=Chronic	E1: Acupuncture at Tianquan (PC2) E2: Acupuncture at Quchi (LI11) Duration: 20min/d, 5d/wk for 4wk	• Maximal Isometric Voluntary Contraction during elbow flexion (-)
Zhao et al. (2009) RCT (6) N_{start}=131 N_{end}=120 TPS=Chronic	E: Experimental acupuncture C: Traditional acupuncture Duration: 20min/d 5d/wk for 4wks	• Modified Ashworth Scale: (+exp) • Fugl Meyer Assessment Upper Extremity: (+exp) • Barthel Index: (+exp)
Gosman-Hedstom et al. (1998) RCT (7) N_{start}=104 N_{end}=98 TPS=Acute	E1: Superficial acupuncture E2: Deep acupuncture C: No acupuncture Duration: 1hr/d, 2d/wk for 10 wk	E1 vs E2 vs C • Scaninavian stroke study Neurological score (-) • Barthel Index (-) • Sunnaas Index (-)
Acupuncture combined with CIMT		
Song et al. (2016) RCT (5) N_{Start}=30 N_{End}=30 TPS=Acute	E: Scalp cluster acupuncture + constraint-induced movement therapy C: Body acupuncture + traditional rehabilitation Duration: 6hr/d, (needles twisted 2-3x), 6d/wk for 2wk	• Fugl-Meyer Assessment (-)
Acupuncture combined with TENS		
Hopwood et al. (2008) RCT (7) N_{start}=105 N_{end}=105 TPS=Acute	E: Acupuncture with TENS C: Acupuncture with sham TENS Duration: 1hr/d, 3d/wk for 4wk	• Barthel Index (-) • Motricity Index (-)
Acupuncture versus rTMS		

Kim et al. (2020)
RCT (6)
N_{start}= 60
N_{end}= 42
TPS= Acute
	E1: Scalp acupuncture (SA)
	E2: Repetitive transcranial magnetic stimulation (rTMS)
	E3: SA and electromagnetic convergence stimulation (SAEM-CS)
	C: Conventional therapy
	Duration:5x plus 5x of experimental conditions for 3wks
		E1 Vs C
		• Fugle-Meyers Assessment: (-)
		• National Institute Health Stroke Scale: (-)
		• Modified Barthel Index: (-)
		• Functional Independence Measure: (-)
		• Nine Hole Peg Test: (-)
		• Modified Rankin Scale: (-)
		• Modified Ashworth Scale:
		  ◦ Elbow: (-)
		  ◦ Ankle: (-)
		• Grip Test
		  ◦ Dominant hand: (-)
		  ◦ Non-dominant hand: (-)
		E2 Vs C
		• Fugle-Meyers Assessment: (-)
		• National Institute Health Stroke Scale: (-)
		• Modified Barthel Index: (+exp2)
		• Functional Independence Measure: (-)
		• Nine Hole Peg Test: (-)
		• Modified Rankin Scale: (-)
		• Modified Ashworth Scale:
		  ◦ Elbow: (-)
		  ◦ Ankle: (-)
		• Grip Test
		  ◦ Dominant hand: (-)
		  ◦ Non-dominant hand: (-)
		E3 Vs C
		• Fugle-Meyers Assessment: (-)
		  ◦ Upper extremity: (-)

		• Lower extremity: (-)
		• National Institute Health Stroke Scale: (-)
		• Modified Barthel Index: (-)
		• Functional Independence Measure: (-)
		• Nine Hole Peg Test: (-)
		• Modified Rankin Scale: (-)
		• Modified Ashworth Scale:
		  • Elbow: (-)
		  • Ankle: (-)
		• Grip Test
		  • Dominant hand: (-)
		  • Non-dominant hand: (-)
		<u>E1 Vs E2 Vs E3</u>
		• Fugle-Meyers Assessment: (+exp2)
		• National Institute Health Stroke Scale: (-)
		• Modified Barthel Index: (-)
		• Functional Independence Measure: (-)
		• Nine Hole Peg Test: (-)
		• Modified Rankin Scale: (-)
		• Modified Ashworth Scale:
		  • Elbow: (-)
		  • Ankle: (-)
		• Grip Test
		  • Dominant hand: (-)
		  • Non-dominant hand: (-)

<u>Zhao et al.</u> (2018) RCT (7) N_{start}=28 N_{end}=17 TPS=Subacute	E: Low frequency rTMS + acupuncture C: Acupuncture Duration: 1x/d for 2 wks	• Fugl Meyer Upper Extremity: (+exp) • Modified Barthel Index: (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Acupuncture

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Acupuncture** may not have a difference in efficacy when compared to **conventional therapy or sham** for improving motor function.	11	Kim et al. 2020; Wang et al. 2020; Chen et al. 2016; Liu et al. 2016; Han et al. 2015; Gao et al. 2013; Bai et al. 2013; Zhuangl et al. 2012; Wayne et al. 2005; Alexander et al. 2004; Sze et al. 2002
1b	**Standard acupuncture with Shixuan & Xiaohai acupoints and experimental acupuncture** may produce greater improvements in motor function than **standard or traditional acupuncture**.	1	Ni et al. 2013
2	**Experimental acupuncture** may produce greater improvements in motor function than **standard or traditional acupuncture**.	1	Zhao et al. 2009
2	**Acupuncture with neuromuscular joint facilitation** may produce greater improvements in motor function than **acupuncture**.	1	Wei et al. 2019

2	**Scalp cluster acupuncture combined with CIMT** may not have a difference in efficacy when compared to **body acupuncture with traditional rehabilitation** for improving motor function.	1	Song et al. 2016
1a	There is conflicting evidence about the effect of **Acupuncture combined with rTMS** to improve motor function when compared to **acupuncture alone.**	2	Kim et al. 2020; Zhao et al. 2018

DEXTERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Acupuncture** may not have a difference in efficacy when compared to **conventional therapy or sham** for improvements on dexterity.	1	Kim et al. 2020
1b	**Acupuncture combined with rTMS** may not have a difference in efficacy when compared to **acupuncture alone** for improving performance of dexterity.	1	Kim et al. 2020

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Acupuncture** may not have a difference in efficacy when compared to **conventional therapy or sham** for improvements in spasticity.	4	Kim et al. 2020; Cui et al. 2014Hou et al. 2013; Wayne et al. 2005
2	**Experimental acupuncture** may produce greater improvements in spasticity than **traditional acupuncture**.	1	Zhao et al. 2009
1b	**Acupuncture combined with rTMS** may not have a difference in efficacy when compared to **acupuncture alone or rTMS alone** for improving spasticity.	1	Kim et al. 2020
1b	**Chinese acupuncture** may produce greater improvements in spasticity than **Western acupuncture**.	1	Zhang et al. 2013

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Acupuncture with neuromuscular joint facilitation** may produce greater improvements in range of motion than **acupuncture**.	1	Wei et al. 2019

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Acupuncture** may produce greater improvements in range of motion than **conventional therapy or sham**.	3	Hou et al. 2014; Wayne et al. 2009; Naeser et al. 1992

STROKE SEVERITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Acupuncture** may not have a difference in efficacy when compared to **conventional therapy or sham** for improvements on measures of stroke severity.	7	Kim et al. 2020; Liu et al. 2016; Hou et al. 2014; Gao et al. 2013; Zhuangl et al. 2012; Sze et al. 2002; Hu et al. 1993
1b	**Superficial acupuncture** may not have a difference in efficacy when compared to **deep acupuncture** for improvements on measures of stroke severity.	1	Gosman-Hedstrom et al. 1998
1b	**Acupuncture combined with rTMS** may not have a difference in efficacy when compared to **acupuncture alone or rTMS alone** for improving on measures of stroke severity.	1	Kim et al. 2020

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Acupuncture** may not have a difference in efficacy when compared to **conventional therapy or sham** for improving performance of activities of daily living.	11	Kim et al. 2020; Wang et al. 2020; Liu et al. 2016; Bai et al. 2013; Gao et al. 2013; Zhuangl et al. 2012; Wayne et al. 2005; Alexander et al. 2004; Sze et al. 2002; Kjendhal et al. 1997; Hu et al.1993
1b	**Acupuncture combined with TENS** may not have a difference in efficacy when compared to **acupuncture with sham stimulation** for improving performance of activities of daily living.	1	Hopwood et al. 2008
1b	**Superficial acupuncture** may not have a difference in efficacy when compared to **deep acupuncture** for improving performance of activities of daily living.	1	Gosman-Hedstom et al. 1998
2	**Experimental acupuncture** may produce greater improvements in performance of activities of daily living than **traditional acupuncture**.	1	Zhao et al. 2009
2	**Acupuncture with neuromuscular joint facilitation** may not have a difference in efficacy when compared to **acupuncture** for improving performance of activities of daily living.	1	Wei et al. 2019
1a	There is conflicting evidence about the effect of **Acupuncture combined with rTMS** to improve performance of activities of daily living when compared to **acupuncture alone.**	2	Kim et al. 2020; Zhao et al. 2018

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Scalp acupuncture** may not have a difference in efficacy when compared to **conventional therapy** for improving muscle strength.	1	Kim et al. 2020
1a	**Standard acupuncture with Shixuan & Xiaohai acupoints and acupuncture at Tianquan PC2** may	2	Ni et al. 2013; Fragoso and Ferreira, 2012

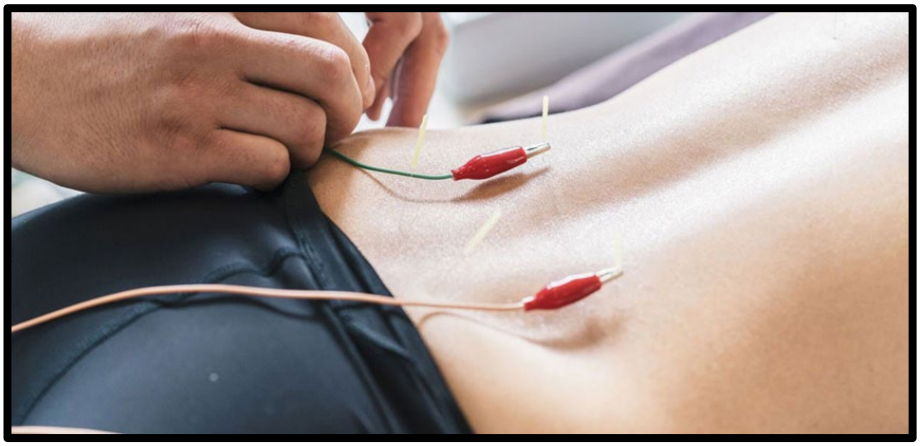
	produce greater improvements in muscle strength than **standard acupuncture only and acupuncture at Quchi LI11**.		
1b	**Acupuncture combined with TENS** may not have a difference in efficacy when compared to **acupuncture with sham stimulation** for improving muscle strength.	1	Hopwood et al. 2008
1b	**Acupuncture combined with rTMS** may not have a difference in efficacy when compared to **acupuncture alone or rTMS alone** for improving muscle strength	1	Kim et al. 2020

Key points

Acupuncture alone compared to conventional therapy may not be beneficial for upper limb rehabilitation following stroke.

Acupuncture combined with conventional or other therapy approaches may not be beneficial for upper limb function. Some forms of acupuncture may be more beneficial than others.

Electroacupuncture and Transcutaneous Electrical Acupoint Stimulation



Adopted from: https://www.promotionhealthcare.com/electroacupuncture-treatment-pain-injuries/

Electroacupuncture is a variant of acupuncture techniques practiced in traditional Chinese medicine, the difference being that a minute electrical current of similar intensity to that of a bioelectric current produced endogenously in the body is applied to the needles used (Wang et al. 2014). The needle is often placed on meridian points throughout the body (Wang et al. 2014). Similarly, transcutaneous electrical acupoint stimulation (TEAS) stimulates meridian points believed to be associated with a medical condition with electrical impulses given through needles (Zhao et al. 2015). The two techniques have very similar mechanisms of action and their influence on afferent stimulation to the body (Zhao et al. 2015).

13 RCTs were found that evaluated electroacupuncture.

Seven RCTs compared electroacupuncture to conventional care or sham stimulation (Zhao et al. 2015; Au-Yeung et al. 2014; Wang et al. 2014; Yao et al. 2014; Hsing et al. 2012; Hsieh et al. 2007; Schaechter et al. 2007). Two RCTs compared electroacupunture against, or in combination with, moxibuston (Wen et al. 2014; Moon et al. 2003). One RCT compared electroacupuncture with massage to conventional care (Li et al. 2012) and one RCT compared electroacupuncture with strength training to conventional care (Mukherjee et al. 2007b). One RCT looked at electroacupuncture combined with neuronavigation-assisted aspiration compared to neuronavigation-assisted aspiration, electroacupuncture or conventional therapy (Zhang et al. 2017).

The methodological details and results of all 13 RCTs evaluating electroacupuncture and transcutaneous electrical acupoint stimulation for the upper extremity motor rehabilitation are presented in Table 40.

Table 40. RCTs Evaluating Electroacupuncture and Transcutaneous Electrical Acupoint Stimulation Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Zhao et al.(2015) RCT (9) N_{Start}=60 N_{End}=60 TPS=Chronic	E1: Transcutaneous electrical acupoint stimulation (TEAS) (100Hz) E2: Transcutaneous electrical acupoint stimulation (TEAS) (2Hz) C: Sham stimulation Duration: 0, 2, or 100Hz/d, 5d/wk for 4wk	E1 vs C • Modified Ashworth Scale (+exp) • Disability Assessment Scale (-) • Global Assessment Scale (-) Barthel Index (-) E2 vs C • Modified Ashworth Scale (+exp$_2$) • Disability Assessment Scale (-) • Global Assessment Scale (-) • Barthel Index (-) E1 v E2 • Modified Ashworth Scale (+exp) • Disability Assessment Scale (-) • Global Assessment Scale (-) • Barthel Index (-)
Au-Yeung et al. (2014) RCT (6) N_{Start}=73 N_{End}=60 TPS=Acute	E1: Electroacupoint stimulation E2: Sham stimulation C: Conventional therapy (control) Duration: 20Hz/d, 1h/d, 5d/wk for 4wk	E1 vs. C • Hand grip strength (+exp) • Index grip pinch (+exp) E2 vs C & E1 vs E2 • Hand grip strength (-) • Index grip pinch (-) • Action Research Arm Test (-)
Wang et al. (2014) RCT (6) N_{Start}=20 N_{End}=15 TPS=Chronic	E: Electroacupuncture C: No stimulation with no needle manipulation Duration: 50Hz/d, 20min/d, 2d/wk for 6wk	• Elbow joint muscle tone (+exp) • Wrist joint muscle tone (-)
Yao et al. (2014) RCT (5) N_{Start}=68 N_{End}=65 TPS=Chronic	E: Relaxed needling + electroacupuncture C: Ordinary needling Duration: 5Hz, 30min/d, 3d/wk for 8wk	• Fugl-Meyer Assessment (+exp)
Hsing et al. (2012) RCT (7) N_{start}=62 N_{end}=62 TPS=Subacute	E: Scalp electro-acupuncture C: Sham acupuncture Duration: 2 to 100Hz, 30min/d, 2d/wk for 5wk	• Barthel Index (-) • Rankin Scale (-)
Hsieh et al. (2007) RCT (8) N_{start}=63 N_{end}=63 TPS=Subacute	E: Electroacupuncture C: No acupuncture Duration: 20min/d, 2d/wk for 4wk	• Functional Independence Measure (-) • Fugl-Meyer Assessment (+exp)
Schaechter et al. (2007) RCT (5) N_{start}= 8 N_{end}= 7 TPS= Chronic	E: Electroacupuncture C: Sham Duration: 2x/wk, 10wks	• Modified Ashworth Scale, wrist (-) • Range of Motion (-)
Electroacupuncture and moxibustion therapy		
Wen et al. (2014) RCT (7) N_{Start}=300 N_{End}=276 TPS=Acute	E: Electroacupuncture + moxibustion C: Basic therapy Duration: 2 to 15Hz, 5-7d/wk for 4wk	Fugl-Meyer Assessment (-)

Moon et al. (2003) RCT (5) N_{start}=35 N_{end}=31 TPS=Subacute	E1: Electroacupuncture E2: Moxibustion C: Routine acupuncture Duration: 50Hz, 30min/d, 3d/wk for 3wk	E1 vs E2/C • Modified Ashworth scale (+exp)
Electroacupuncture combined with massage		
Li et al. (2012) RCT (6) N_{start}=120 N_{end}=120 TPS=Acute	E: Electroacupuncture + massage C: Rehabilitation therapy Duration: 25min/d, 5d/wk, 6wk	• Fugl-Meyer Assessment (-) • Modified Rankin Scale (+exp)
Electroacupuncture combined with strength training		
Mukherjee et al. (2007b) RCT (4) N_{start}=7 N_{end}=7 TPS=Subacute	E: Electroacupuncture + strength training C: Strength training Duration: 2Hz, 40min/d, 2d/wk for 6wk	• Modified Ashworth Scale (+exp)
Electroacupuncture of acupoints versus non-acupoints		
Chau et al. (2009) RCT (4) N_{start}= 23 N_{end}= 19 TPS= Acute	E: Electro-acupuncture on motor acupuncture points C: Electro-acupuncture on non-motor acupuncture points Duration: 30min, 3x/wk, 8wks	• Barthel's Index: (-) • Fugl Meyes Upper Extremity: (-) • Motricity Index: (-) • Grip Power: (-)
Neuronavigation-assisted aspiration + electroacupuncture		
Zhang et al. (2017) RCT (7) N_{Start}=240 N_{End}=233 TPS=Acute	E1: Neuronavigation-assisted aspiration + electroacupuncture E2: Neuronavigation-assisted aspiration E3: Electroacupuncture C: Conventional therapy Duration: 30min (2x per day) for 8wk	E1 vs E2 • Fugl-Meyer Assessment (+exp) • Modified Ashworth Scale (+exp) • Barthel Index (+exp) E1 vs E3 • Fugl-Meyer Assessment (+exp) • Modified Ashworth Scale (+exp) • Barthel Index (+exp) E1 vs E4 • Fugl-Meyer Assessment (+exp) • Modified Ashworth Scale (+exp) E3 vs E4 • Fugl-Meyer Assessment (+exp_3) • Modified Ashworth Scale (+exp_3)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Electroacupuncture and Transcutaneous Electrical Acupoint Stimulation

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Electroacupuncture and transcutaneous electrical acupoint stimulation** may produce greater improvements in motor function than **conventional therapy or sham stimulation/ordinary needling.**	4	Zhang et al. 2017; Au-Yeung et al. 2014; Yao et al. 2014; Hsieh et al. 2007
1b	**Electroacupuncture combined with moxibuston** may not have a difference in efficacy when compared to **conventional therapy** for improving motor function.	1	Wen et al. 2014

1b	**Electroacupuncture combined with massage** may not have a difference in efficacy when compared to **conventional therapy** for improving motor function.	1	Li et al. 2012
2	**Electroacupuncture on motor acupoints** may not have a difference in efficacy when compared to **electroacupuncture on non-motor acupoints** for improving motor function.	1	Chau et al. 2009
1b	**Electroacupuncture combined with neuronavigation-assisted aspiration** may produce greater improvements in motor function than **neuronavigation-assisted aspiration, electroacupuncture and conventional therapy on their own**.	1	Zhang et al. 2017

SPASTICITY

LoE	Conclusion Statement	RCTs	References
1a	**Electroacupuncture and transcutaneous electrical acupoint stimulation** may produce greater improvements in spasticity than **conventional therapy or sham stimulation/ordinary needling.**	5	Zhang et al. 2017; Zhao et al. 2015; Wang et al. 2014; Schaechter et al., 2007; Moon et al. 2003
2	**Electroacupuncture** may produce greater improvements spasticity than **moxibuston.**	1	Moon et al. 2003
2	**Electroacupuncture combined with strength training** may produce greater improvements spasticity than **strength training alone.**	1	Mukherjee et al. 2007
1b	**Electroacupuncture combined with neuronavigation-assisted aspiration** may produce greater improvements in spasticity than **neuronavigation-assisted aspiration, electroacupuncture and conventional therapy on their own**.	1	Zhang et al. 2017

STROKE SEVERITY

LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **electroacupuncture and transcutaneous electrical acupoint stimulation** to improve scores on measures of stroke severity when compared to **conventional therapy or sham stimulation/ordinary needling.**	2	Hsing et al. 2012; Li et al. 2012

RANGE OF MOTION

LoE	Conclusion Statement	RCTs	References

2	**Electroacupuncture and transcutaneous electrical acupoint stimulation** may not have a difference in efficacy when compared to **conventional therapy or sham stimulation/ordinary needling** for improving range of motion.	1	Schaechter et al., 2007

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Electroacupuncture and transcutaneous electrical acupoint stimulation** may not have a difference in efficacy when compared to **conventional therapy or sham stimulation/ordinary needling** for improving performance of activities of daily living.	3	Zhao et al. 2015; Hsing et al. 2012; Li et al., 2012; Hsieh et al. 2007;
2	**Electroacupuncture on motor acupoints** may not have a difference in efficacy when compared to **electroacupuncture on non-motor acupoints** for improving perofmrance of activities of daily living.	1	Chau et al. 2009
1b	**Electroacupuncture combined with neuronavigation-assisted aspiration** may produce greater improvements in activities of daily living **neuronavigation-assisted aspiration and electroacupuncture on their own**.	1	Zhang et al. 2017

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Electroacupuncture and transcutaneous electrical acupoint stimulation** may produce greater improvements in muscle strength than **conventional therapy or sham stimulation/ordinary needling.**	1	Au-Yeung et al. 2014
2	**Electroacupuncture on motor acupoints** may not have a difference in efficacy when compared to **electroacupuncture on non-motor acupoints** for improving muscle strength.	1	Chau et al. 2009

Key points

Electroacupuncture may be beneficial for some aspects of rehabilitation in the upper limb following stroke.

Meridian Acupressure and Massage Therapy

Adopted from: http://physiotherapeutic.ca/servi-physio/111-massage-therapy

Meridian acupressure is a form of treatment whereby finger pressure is applied to meridian points on the body (Yang et al. 2017). There are two types of meridian points: yin and yang (Yang et al. 2017). Yin meridians run from the feet to the torso, and from the torso to the fingertips on the inside of the arms (Cui et al. 2014). On the other hand, yang meridians run from the fingers to the face and from the face to the feet (Cui et al. 2014). Acupressure increases blood (qi) flow to the areas it is applied in (Di et al. 2017).

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 (Holland & Pokorny, 2001). 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 (College of Massage Therapists of Ontario, 2018). The benefits of massage therapy are suggested to be increased blood flow, relief of muscle spasms and release of β-endorphins (Wei et al. 2017). One of the more common forms of massage therapy is the traditional Chinese massage therapy also known as Tui Na (Yang et al. 2017).

Seven RCTs were found evalutating meridian acupressure and massage against conventional care (Wang et al. 2019; Di et al. 2017; Yang et al. 2017a; Yang et al. 2017b; Thanakiatpinyo et al. 2014; Yue et al. 2013; Kang et al. 2009).

The methodological details and results of all seven RCTs evaluating meridian acupressure and massage therapy for upper extremity motor rehabilitation are presented in Table 41.

Table 41. RCTs Evaluating Meridian Acupressure and Massage Therapy Interventions for Upper Extremity Motor Rehabilitation

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Wang et al. (2019) RCT (7) N_{start}=444 N_{end}=397 TPS=Mixed	E: Tui Na massage C: Conventional rehabilitation Duration: rehab 5x/wk, 4wks 230hrs massage 40min 5x/wk 4wks	• Modified Ashworth Scale (1-3mo): • Elbow flexion: (-) • Wrist flexion: (+exp) • Finger flexion: (+exp) • Fugl Meyer Assessment (1-3mo): (+exp) • Modified Barthel Index (1-3mo): (-) • Modified Ashworth Scale (4-6mo): • Elbow flexion: (+exp) Wrist flexion: (-) • Finger flexion: (-) • Fugl Meyer Assessment (4-6mo): (-) • Modified Barthel Index (4-6mo): (-) • Modified Ashworth Scale (7-12mo): • Elbow flexion: (-) • Wrist flexion: (-) • Finger flexion: (-) • Fugl Meyer Assessment (7-12mo): (-) • Upper: (-) • Modified Barthel Index (7-12mo): (-)
Di et al. (2017) RCT (5) N_{Start} =150 N_{End} =150 TPS=Subacute	E: Tui Na Therapy C: Conventional therapy Duration: 30min/d, 5d/wk for 4wk	• Modified Ashworth Scale (+exp)
Yang et al. (2017a) RCT (8) N_{Start}=90 N_{End}=74 TPS=Subacute	E: Tui Na C: Placebo Tui Na Duration: 20-25min/d, 5d/wk for 4wk	• Modified Ashworth Scale (+exp) • Fugl-Meyer Assessment (-) • Modified Barthel Index (-)
Yang et al. (2017b) RCT (8) N_{Start}=90 N_{End}=79 TPS=Subacute	E: Tui Na C: Placebo Therapy Duration: 20-25min/d, 5d/wk for 4wk	• Fugl-Meyer Assessment (-) • Modified Barthel Index (-)
Thanakiatpinyo et al. (2014) RCT (7) N_{Start}=50 N_{End}=45 TPS=Chronic	E: Thai massage C: Physical therapy Duration: 30min/d, 2d/wk for 6wk	• Modified Ashworth Scale (-) • Barthel Index (-)
Yue et al. (2013) RCT (6) N_{start}=78 N_{end}=72 TPS=Chronic	E: Acupressure C: Routine care Duration: 45min/d, 5d/wk, 4wk	• Barthel Index (+exp) • Fugl-Meyer Assessment (+exp)
Kang et al. (2009) RCT (5) N_{start}=56 N_{end}=56 TPS=Chronic	E: Meridian acupressure C: Standard care Duration: 10min/d, 7d/wk for 2wk	• Grip power (+exp) • Passive range of motion (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Meridian Acupressure and Massage Therapy

MOTOR FUNCTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Meridian acupressure and massage therapy** may not have a difference in efficacy when compared to **conventional therapy or placebo massage therapy** for improving motor function.	4	Wang et al., 2019; Yang et al. 2017; Yang et al. 2017; Yue et al. 2013;

MUSCLE STRENGTH			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Meridian acupressure and massage therapy** may produce greater improvements in muscle strength than **conventional therapy**.	1	Kang et al. 2009

RANGE OF MOTION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Meridian acupressure and massage therapy** may produce greater improvements in range of motion than **conventional therapy**.	1	Kang et al. 2009

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Meridian acupressure and massage therapy** may not have a difference in efficacy when compared to **conventional therapy or placebo massage therapy** for improving performance of activities of daily living.	5	Wang et al. 2019; Yang et al. 2017; Yang et al. 2017; Thanakiatpinyo et al. 2014; Yue et al. 2013

SPASTICITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **meridian acupressure and massage therapy** to improve spasticity when compared to **conventional therapy or placebo massage**	4	Wang et al. 2019 ; Di et al. 2017; Yang et al. 2017; Thanakiatpinyo et al. 2014

Key points

Meridian acupressure and massage may not improve motor function or activities of daily living post-stroke. The literature is mixed regarding its effects on spasticity.

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