Motor recovery after stroke: a systematic review

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Loss of functional movement is a common consequence of stroke for which a wide range of interventions has been developed. In this Review, we aimed to provide an overview of the available evidence on interventions for motor recovery after stroke through the evaluation of systematic reviews, supplemented by recent randomised controlled trials. Most trials were small and had some design limitations. Improvements in recovery of arm function were seen for constraint-induced movement therapy, electromyographic biofeedback, mental practice with motor imagery, and robotics. Improvements in transfer ability or balance were seen with repetitive task training, biofeedback, and training with a moving platform. Physical fitness training, high-intensity therapy (usually physiotherapy), and repetitive task training improved walking speed. Although the existing evidence is limited by poor trial designs, some treatments do show promise for improving motor recovery, particularly those that have focused on high-intensity and repetitive task-specific practice.

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Introduction

Stroke is a common global health-care problem that is serious and disabling.[1] In high-income countries, stroke is the third most common cause of death and is the main cause of acquired adult disability.[1,2] However, as most patients with stroke survive the initial injury, the biggest effect on patients and families is usually through long-term impairment, limitation of activities (disability), and reduced participation (handicap).

The most common and widely recognised impairment caused by stroke is motor impairment, which can be regarded as a loss or limitation of function in muscle control or movement or a limitation in mobility.[3] Motor impairment after stroke typically affects the control of movement of the face, arm, and leg of one side of the body[1] and affects about 80% of patients. Therefore, much of the focus of stroke rehabilitation, and in particular the work of physiotherapists and occupational therapists, is on the recovery of impaired movement and the associated functions. There seems to be a direct relation between motor impairment and function; for example, independence in walking (function) has been correlated with lower-limb strength (impairment).[4] Therefore, the ultimate goal of therapy for lower-limb motor impairment is to improve the function of walking and recovery of movement. In this Review, motor impairment and its associated functional activities are regarded as part of a continuum.

Motor impairment can be caused by ischaemic or haemorrhagic injury to the motor cortex, premotor cortex, motor tracts, or associated pathways in the cerebrum or cerebellum.[1] Such impairments affect an individual's ability to complete everyday activities (disability) and affect participation in everyday life situations.[5] A lack of consistency is evident among researchers and clinicians in the use of terminology that describes changes in motor ability after stroke.[6] Changes in motor ability might occur via several mechanisms: restitution, substitution, or compensation.[7] Levin and co-workers,[6] however, distinguished motor recovery and motor compensation in accordance with the WHO International Classification of Functioning, Disability and Health framework and proposed that motor recovery relates to: restoration of function in neural tissue that was initially lost; restoration of ability to perform movement in the same way as before injury; and successful task completion as typically done by individuals who are not disabled. Types of motor compensation in these three areas include the acquisition by neural tissue of a function that it did not have before the injury; performance of a movement in a new way; and successful task completion by use of different techniques.[6]

In accordance with these definitions, in this Review we focused on outcomes associated with body functions or structure (impairment) and activity (functional). We favoured activity outcomes when these were used in addition to impairment outcomes as these were believed to be more clinically useful. However, we did not focus on motor recovery or motor compensation separately, as many of the outcomes (particularly those measuring activity) do not distinguish between improvements associated with increasing compensation and movement patterns. Although we recognise the potential limitations of this approach, this Review can only outline the outcomes used in the trials.

Motor recovery after stroke is complex and confusing. Many interventions have been developed to try to aid motor recovery (recovery of impairment and associated function), and many randomised controlled trials and systematic reviews have been done.[8] Most of these interventions do not explicitly target a specific pathophysiological process and have been tested using a variety of patient groups and outcome measures. We have, therefore, taken a pragmatic, empirical approach to describing and reviewing these interventions.

In this Review, we summarise the available evidence for the treatment of motor impairment and restoration of motor function after stroke. Our aims were to: (i) summarise the available evidence from systematic reviews of randomised controlled trials; (ii) identify areas for which interventions show promise of efficacy; and (iii) relate this information to the current guideline advice on clinical management.

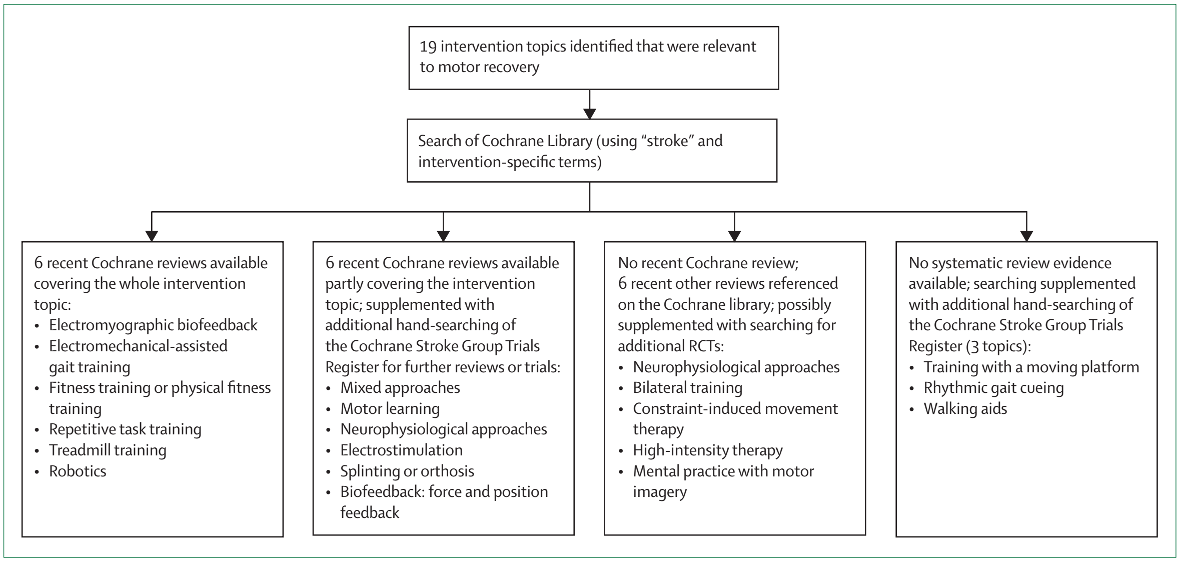

Figure 1: **Selection of systematic reviews of interventions for motor recovery after stroke**
Further details are provided in table 1. RCT=randomised controlled trial.

We used a range of approaches to identify relevant interventions, which included expert opinion,[9] the views of multidisciplinary focus groups, and systematic searching of relevant texts and guidelines.[10] A focus on recovery of impairment of specific muscles, muscle groups (such as muscle tone or muscle length), or related impairments (such as pain or contractures) was beyond the scope of this Review. Instead, we focus on the effect of interventions on recovery in four key areas of movement and function that were believed to best encapsulate the targets of the available interventions: (1) upper-limb (arm and hand) movement and function; (2) gait (walking ability; as this is a primary function of the lower limbs); (3) balance (as this is a primary function of the trunk); and (4) mobility (as this combines upper-limb function, lower-limb function, and balance to enable normal movements).

Methods

Search strategy and selection criteria

We hand-searched the Cochrane Library for all systematic reviews that included randomised trials of interventions to promote motor recovery (recovery of impairment or related function) after stroke and that had been registered with the Cochrane Stroke Group by March, 2009. We chose this approach because several systematic reviews have been done in (or overlap with) this area. We therefore sought to use the best available systematic reviews and to supplement these (when necessary) with additional information from recent randomised controlled trials. If a Cochrane systematic review was identified that fully covered the intervention of interest, further searching for systematic reviews or trials was undertaken only for reports published after the search date of the identified review. If a systematic review was identified that did not cover all four of the outcomes of interest (described earlier), further searching was carried out to identify systematic reviews or trials specific to that outcome. If a Cochrane review was not available, we searched the Cochrane Library for other systematic reviews relevant to the topic. Search terms included "stroke" and intervention-specific terms such as "approaches to therapy", "motor learning", "neurophysiological", "bilateral training", "biofeedback", "constraint-induced movement therapy", "electromyographic biofeedback", "electromechanical", "elecrostimulation", "fitness training", "physical fitness training", "intensity", "mental practice", "motor imagery", "moving platform", "repetitive task training", "gait cueing", "splinting", "orthosis", "robotics", "treadmill training", and "walking aids". The Cochrane Stroke Group Trials Register[8] was used for any further searching for randomised trials by use of keyword searches and hand-searching of recent outputs of the register. This trial register is probably the most complete resource of its kind. Finally, any statements about clinical practice were checked against the most recently updated clinical practice guidelines.[11]

Inclusion criteria were as follows: adults with a clinical diagnosis of stroke; any intervention aimed specifically at upper-limb function, balance, gait, or mobility during rising to stand, sitting down, stair climbing, transferring (eg, wheelchair to bed or bed to chair), or wheelchair use after stroke (pharmacological and surgical interventions were excluded); and comparisons of interventions against no treatment, placebo, or standard care. A wide range of outcomes associated with four areas of movement and function were included: (1) for upper-limb function, we prioritised arm-function tests (eg, action research arm test, motor assessment scale, Frenchay arm test) before impairment scales (eg, Fugl-Meyer scale, Motricity index), and when necessary, measures of arm and hand function were combined to give one estimate of arm and hand function; (2) for balance, we included measures such as the Berg balance scale, measures of weight distribution, and postural sway during sitting and standing; (3) for gait, we included measures such as functional ambulation, gait speed, stride length, and gait endurance; and (4) for mobility, we included measures of mobility in functions of daily living, such as assessments of ability to rise to stand (eg, the timed up-and-go test), stair climbing, transfers, and wheelchair mobility. The post-intervention outcome data were sought; when these were not available, we used the data collected at the end of scheduled follow-up.

Two of three authors (FC and AP or PL) reviewed each reference and allocated it to a particular intervention. The following information was extracted from systematic reviews: number of studies, number of participants, intervention characteristics and comparisons, and outcomes reported. If an appraisal of trials was required (ie, had not already been included in a systematic review), each included trial was critically appraised and data extracted by use of a standard appraisal form.

Data analysis

When possible, means and standard deviations for each outcome from each treatment group were extracted and combined within meta-analyses to derive a standardised mean difference and 95% CI. This expresses the difference between intervention and control group mean results on an outcome in terms of standard deviation units. In some cases, the standardised mean difference or other measure of effect was extracted directly from a systematic review.

If additional trials were identified that were not included in the systematic review, these were added into the analysis and new estimates of effect were obtained. Several of the identified reviews presented an analysis of outcomes in a different way from our outcomes of interest. In these cases we re-analysed the trials to cover our outcomes of interest. In some cases we also grouped together trials with slightly different comparators (eg, placebo, control, and usual care) to gain one estimate of intervention effect. For these reasons the summary estimate and conclusions of this analysis might vary slightly from those of the identified reviews. Trials that did not present means and standard deviations were either excluded from data analysis or, in a few cases, imputations were made for the missing data and calculations were made to derive means and standard deviations. When more than one subgroup was presented in a trial we split the subgroups and included both of the subgroups. We excluded randomised controlled trials from the analysis if first-phase data were not presented. Review Manager 5 software (RevMan. Copenhagen: the Nordic Cochrane Centre, The Cochrane Collaboration, 2008) was used for all analyses and results were analysed by use of the standardised mean difference with a fixed effects model, unless there was substantial heterogeneity, in which case a random effects model was used.

	Description	Target	Cochrane or other review (relevant RCTs included)	Additional RCTs identified	Total RCTs included	Allocation concealment (adequate; unclear; not adequate)	Masked assessor	Intention-to-treat analysis
Mixed approaches	Uses treatment components that originate in various theoretical approaches	Upper limb Lower limb	See neurophysiological approaches CR[14] (5 RCTs)[15–19]	.. 0	.. 5	.. 5; 0; 0	.. 4	.. 0
Motor learning	Assumes neurologically impaired people learn in the same way as healthy people; focus on context-specific cognitive learning by use of feedback and practice	Upper limb Lower limb	See neurophysiological approaches CR[14] (3 RCTs)[20–22]	.. 0	.. 3	.. 3; 0; 0	.. 3	.. 0
Neurophysiological approaches	Various therapeutic approaches based on neurophysiological knowledge and theories, most commonly the Bobath approach	Upper limb Lower limb	Other review[23] (2 RCTs)[24,25] CR[14] (2 RCTs)[17,27]	3[26–28] 0	5 2	2; 3; 0 2; 0; 0	3 2	1 0
Bilateral training	Involves use of both upper limbs to perform identical activities simultaneously but independently	Upper limb	Other review[29] (0 RCT)	2[30,31]	2	1; 1; 0	2	0
Biofeedback: force and position feedback	On a force platform, special force sensors measure the weight under each foot and the position or movement of the body's centre of pressure; information (feedback) about the distribution of weight between the legs and about movement of the centre of pressure can be given to the patient by use of visual or auditory feedback	Upper limb Lower limb: force and position	0 CR[32] (6 RCTs)[33–38] 0	0 1[39] 6[40–45]	0 7 6	.. 1; 6; 0 1; 4; 1	.. 2 2	.. 0 0
Constraint-induced movement therapy	Involves restraint of the intact limb, in combination with a large number of repetitions of task-specific training	Upper limb*	Other review[46] and health technology assessment report[47] (13 RCTs)[48–60]	9[61–69]	22	4; 17; 1	19	4

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	Description	Target	Cochrane or other review (relevant RCTs included)	Additional RCTs identified	Total RCTs included	Allocation concealment (adequate; unclear; not adequate)	Masked assessor	Intention-to-treat analysis
(Continued from previous page)								
Electromyographic biofeedback	Involves the use of instrumentation applied to muscles with external electrodes to capture motor unit electrical potentials; the instrumentation converts the potentials into audio or visual information	Upper limb	CR[70] (4 RCTs)[71–74]	0	4	1; 1; 2	2	0
		Lower limb	CR[70] (5 RCTs)[75–79]	0	5	4; 0; 1	3	0
Electromechanical-assisted gait training	Electromechanical devices can be used to give non-ambulatory patients intensive gait training, using either robot-driven orthoses or driven foot plates	Lower limb	CR[80] (8 RCTs)[81–88]	0	8	7; 1; 0	4	5
Electrostimulation	Electrostimulation can be delivered to the peripheral neuromuscular system by external or internal electrodes, at a range of frequencies, intensities, and patterns of delivery	Upper limb†	CR[89] (10 RCTs)[90–99]	5[100–104]	15	2; 11; 2	8	0
		Lower limb	CR[89] (5 RCTs)[78,105–108]	1[109]	6	2; 2; 2	2	2
Fitness training or physical fitness training	Physical fitness training is defined as a planned, structured regimen of regular physical exercise performed to improve one or more components of physical fitness; training interventions are typically targeted at the improvement or maintenance of either cardiorespiratory fitness or strength and muscular endurance	Lower limb	CR[110] (updated trial information gained through personal communication from Saunders DH, University of Edinburgh; 17 RCTs)[15–17,22,84,111–122]	0	17	0; 17; 0	13	9
High-intensity therapy	Increased amount of focused therapy or interventions compared with a reference group	Upper limb	Other[123] (4 RCTs)[124–127]	0	4	3; 1; 0	4	1
		Lower limb	Other[122] (6 RCTs)[17–19,124,128,129]	0	6	4; 2; 0	6	3
Mental practice with motor imagery	Cognitive rehearsal of a physical action; aims to improve goal-orientated movement or stabilisation of a given movement	Upper limb	Other[130] (3 RCTs)[131–133]	1[134]	4	0; 4; 0	3	0
		Lower limb	Other[130] (0 RCTs)	0	0	..	..	..
Training with a moving platform	Standing on a moving platform allows subjects to practise responding to external perturbations	Lower limb	0	2[135,136]	2	0; 2; 0	0	0
Repetitive task training	Active motor sequence performed repetitively within a single training session, aimed towards a clear functional goal	Upper limb	CR[137] (8 trials)[25,27,124,138–142]	0	8	5; 2; 1	6	1
		Lower limb	CR[137] (11 RCTs)[20–22,25,27,124,138,143–146]	0	11	7; 3; 1	11	1
Rhythmic gait cueing	Involves auditory cueing (metronome) or visual cueing (visual indicator) to provide a rhythmical prompt to optimise the timing of movements	Lower limb	0	4[43,44,147,148]	4	1; 3; 0	2	1
Robotics	Robotic devices enable high-intensity, repetitive, task-specific, and interactive treatment of the upper limb independent of a therapist	Upper limb‡	CR[149] (10 RCTs)[150–159]	0	10	3; 4; 3	7	2
Splinting or orthosis	Splints or othoses are external, removable devices that are used to meet several clinical aims: a decrease in spasticity and pain, improvement in functional movement, and prevention of contracture, over-stretching, and oedema	Upper limb	CR[160] (2 RCTs)[161,162]	1[163]	3	2; 1; 0	3	2
		Lower limb	CR[160] (11 randomised cross-over trials)[164–174]	0	11	0; 10; 1	0	0
Treadmill training plus bodyweight support	Involves walking on a treadmill, with some bodyweight supported via a harness; this increases the amount of task-specific practice that can be completed	Lower limb	CR[175] (8 RCTs)[88,114,115,176–180]	0	8	4; 3; 1	6	1
Walking aids	Walking aids can include canes, 3-point or 4-point sticks, crutches, and walking frames (zimmer frames), and aim to increase balance and stability during standing and walking	Lower limb	0	..	..	..	..	..

There is some overlap of trials that contribute to more than one intervention category. Some trials could not be included in the final analysis because data were not suitable for pooling. CR=Cochrane review. RCT=randomised controlled trial. *Two trials[51,63] could not be included in the final analysis. †Four trials[101–104] could not be included in the final analysis. ‡One trial[150] could not be included in the final analysis.

***Table 1:* Outline of interventions reviewed, sources of evidence (systematic reviews or randomised trials), and trial characteristics**

Clinically, a standardised mean difference of 0·2 suggests a small effect, 0·5 means a moderate effect, and 0·8 or more indicates a large effect.[12] We also used a semi-quantitative Clinical Evidence classification of effectiveness,[13] whereby two of three reviewers (FC and AP or PL) classified the effect of each intervention as beneficial, likely to be beneficial, a trade-off between benefits and harm, unlikely to be beneficial, likely to be ineffectual or harmful, or has unknown effectiveness. The decision was based on the results of the statistical analyses, combined with a considered judgment on the power of the studies and their heterogeneity and consistency of effect.

Results

Interventions identified

We identified 19 categories of intervention relevant to motor recovery after stroke that were included in a Cochrane review, other review, or individual randomised trial (figure 1; table 1). We identified one intervention (the use of walking aids) for which we were unable to identify any relevant evidence.

Evidence identified

Table 1 outlines the intervention categories (with an accompanying description and rationale for that intervention), intervention targets (upper limb or lower limb, balance, or gait), and the main sources of evidence identified. Sources include the relevant Cochrane review or similar high-quality systematic review, the relevant trials within the review, additional trials identified, and, hence, total number of trials included in the assessment of the effects of that intervention. In most cases, we identified a systematic review (ten Cochrane reviews and seven other reviews including one health technology assessment report) and, in nine cases, we supplemented this information with data from additional randomised controlled trials.

Table 1 also includes the key design features of the identified trials that are likely to affect the reliability of their conclusions: whether there was adequate concealment of treatment allocation; whether the outcome assessor was blinded to treatment allocation; and whether intention-to-treat analysis was used.

Most of the analyses of the effects of an intervention on a particular outcome are informed by a relatively small number of randomised trials (average of three trials per analysis) that each recruited a relatively small number of participants (average of 70 people per trial). Additionally, many of the trials identified were not done to the highest quality. In particular, adequate allocation concealment was reported in only 36% of trials (although only 8% had poor concealment), blinding of outcome assessment was reported in 67%, and an intention-to-treat analysis was done in only 19% of trials.

Arm function

The first analyses investigated the effect of interventions on measures of arm movement or related functions. Figure 2 summarises the results for upper-limb interventions targeting the recovery of arm or hand function. A range of measures of arm function were reported, of which the most common were the action research arm test, motor assessment scale, and Fugyl-Meyer scale. Several interventions have a potential effect on arm function, at least within the selected populations that have been studied. These interventions include constraint-induced movement therapy, electromyographic (EMG) biofeedback, mental practice with motor imagery, and robotics. Additionally, repetitive task training and electrostimulation showed a borderline effect.

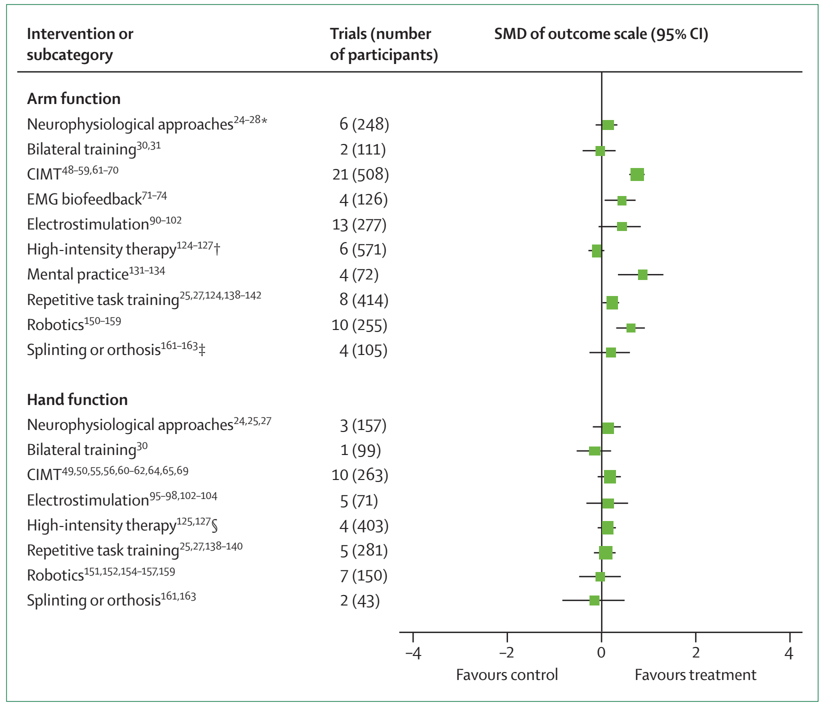

Figure 2: **Interventions to improve upper-limb motor recovery after stroke**

This figure summarises the results for upper-limb interventions targeting the recovery of arm or hand function, and shows the intervention category, number of trials (participants recruited) plus the SMD and 95% CI for the effect of the intervention on the outcome measure. The most common measures of arm outcome were the action research arm test, motor assessment scale, and the Fugyl-Meyer scale. The most common measures of hand function were various peg tests and the hand component of the action research arm test. CIMT=constraint-induced movement therapy. EMG=electromyographic biofeedback. SMD=standardised mean difference. *One trial had two subgroups and these were, therefore, analysed as different trials (thus, the number of trials reported is 6). †Two trials had two subgroups, which were analysed as different trials (number of trials reported is 6). ‡One trial had two subgroups, which were analysed as different trials (number of trials reported is 4). §Both trials had two subgroups, which were analysed as different trials (number of trials reported is 4).

On reviewing the validity of these observations, the results for constraint-induced movement therapy seem the most robust. In general, the effect size (standardised mean difference) was large, the quality of trials was high (table 1) and a relatively large number of trials and participants have been studied. Generally applicable conclusions are limited by the variety of constraint-induced movement therapy approaches studied and the fact that all trials have focused on very selected populations (eg, those with limited arm impairment or who are able to tolerate prolonged constraint). Trials of EMG biofeedback are limited by their small size, frequent failure to use a blinded outcome assessor, and inadequate allocation concealment (table 1). Trials of mental practice and of robotics have relatively large effect sizes but are limited by the small numbers of participants. Owing to these limitations, the results from these reviews of EMG biofeedback, mental practice, and robotics could easily be overturned by new trials.

Hand function

The most common measures of hand function were various peg tests or the hand component of the action research arm test. None of the interventions identified

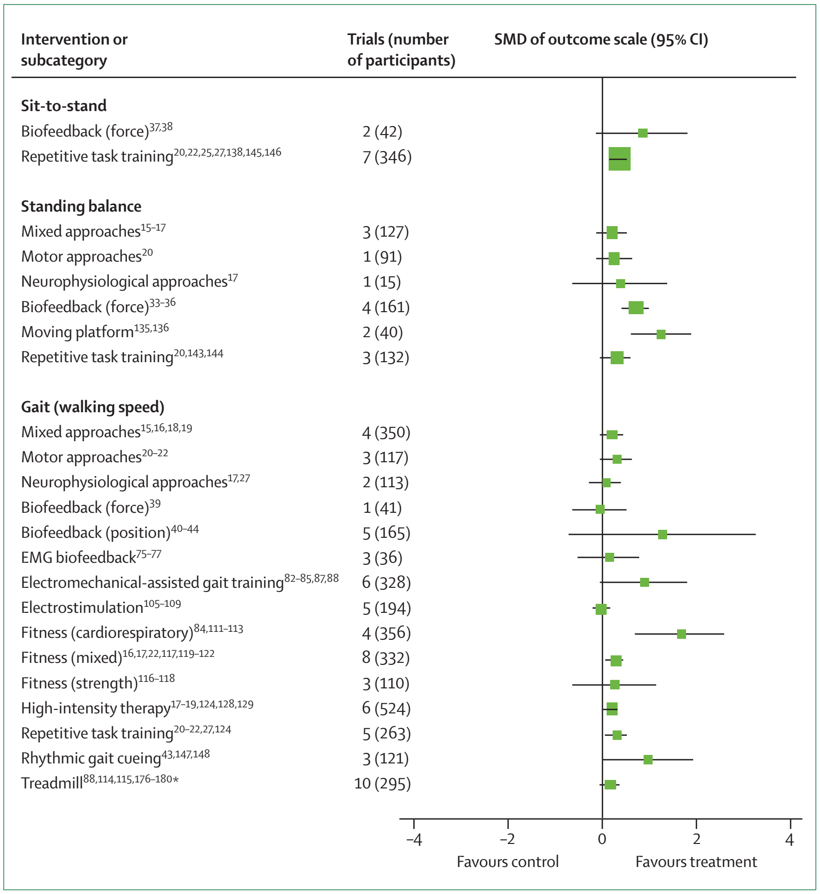

Figure 3: **Interventions to improve balance, gait, or mobility after stroke**
The figure summarises the results for lower-limb interventions targeting the recovery of sit-to-stand ability, standing balance, and gait, and shows the intervention category, number of trials (participants recruited) plus the SMD and 95% CI for the effect of the intervention on the outcome measure. Sit-to-stand ability was measured using assessments such as the timed up-and-go test. Standing balance was usually measured using the Berg balance scale, measures of weight distribution, or postural sway during sitting and standing. Gait was assessed using measures of walking speed. SMD=standardised mean difference. *One trial had two subgroups and these were, therefore, analysed as different trials (thus, the number of trials reported is 10).

showed a consistent pattern of improvement in hand function (figure 2).

Mobility: sit to stand

Figure 3 summarises the key outcomes for interventions targeted at balance, gait, or mobility. We could identify only two interventions that consistently used an outcome that reflected mobility during rising to stand by use of such as the timed up-and-go test. Biofeedback using a force plate was tested only in two small trials with no significant effect measured. Repetitive task training was tested in seven trials with 346 participants and showed a significant improvement in sit-to-stand ability that was of moderate size. In general, these trials were of high quality with good allocation concealment and blinding of outcome assessment, although, similar to all the trials reviewed, there was a frequent failure to use an intention-to-treat analysis. These results could be overturned by a relatively small number of new trials.

Standing balance

Figure 3 summarises the results for outcomes targeted at improving standing balance. Most trials used measures such as the Berg balance scale, measures of weight distribution, or postural sway during sitting and standing. Two interventions showed a pattern of improvement in measures of standing balance. Biofeedback using a force plate was tested in four trials (161 participants) by use of a measure of weight distribution. Most of these trials were limited by the fact that they did not report the use of a blinded outcome assessment. A second measure of balance (postural sway) was not significantly improved in three trials (71 participants) of biofeedback using a force plate. Training with a moving platform was the other positive intervention, but this finding was based on only two trials with 44 participants. Unfortunately, neither of these trials used explicit blinding of outcome assessment. Repetitive task training did not reach statistical significance (p=0·10). In summary, none of these review results seemed to be sufficiently robust to provide a reliable estimate of effect.

Walking ability (gait)

Figure 3 also summarises the results for interventions targeted at walking ability (gait). The outcome scores included predominantly measures of gait speed, although the same trials often included measures of stride length, gait endurance, and functional ambulation (table 2). Several interventions showed a pattern of apparent improvement in walking speed. These approaches included cardiorespiratory physical fitness training, fitness training incorporating a mixture of cardio-respiratory and strength training, high-intensity therapy (usually physiotherapy), and repetitive task training. Overall, these four groups of studies showed small-to-moderate effect sizes and reasonable trial quality with concealment of allocation and blinded outcome assessment. However, the trials tended to be small with little attention to describing an intention-to-treat analysis. Only the findings for cardiorespiratory physical fitness training provided robust evidence for a benefit on walking ability.

Evidence in context

In addition to the numerical meta-analyses reported in figures 2 and 3, we also carried out a semi-quantitative classification of effectiveness (table 2), whereby two of three reviewers (FC and AP or PL) classified the effect of each intervention on the basis of published criteria.[13] These conclusions were also compared with the findings of the most recently updated clinical practice guidelines from the Royal College of Physicians.[11] In general, the considered judgment categories match those of the meta-analyses and the clinical practice guidelines. The main areas of discrepancy are with EMG biofeedback, biofeedback using force feedback, and electro-mechanical-assisted gait training; the guidelines suggest that these interventions should not be used on a routine basis or should be used in selected patients only. The other discrepancy is that the guidelines recommend the selective use of treadmill training plus body-weight support, whereas the Cochrane Review[175] did not identify any clear and consistent benefit. These discrepancies could indicate differences in the way we have combined and analysed trial evidence. More probably, they might occur because of the process of considered judgment undertaken by clinical guideline review panels, which takes into account factors such as the perceived relevance, applicability, availability, and value of a particular intervention.

Conclusions

We have identified a broad range of interventions that have been developed to assist motor recovery (movement and related functions) after stroke. Many of these interventions have been subjected to evaluation in randomised controlled trials and their results synthesised in systematic reviews. Before discussing the implications of our Review, it is worth considering the strength and weaknesses of our approach.

Strengths and weaknesses

The main strengths of our overview approach are the explicit, systematic, and comprehensive methods to try to

	Evidence and considered judgment	SMD (95% CI)	RCP guideline	Comments
Mixed approaches[14]				
Lower limb	Balance while standing: unknown effectiveness; 3 trials[15–17] (n=127) Gait (walking speed): unknown effectiveness; 4 trials[15,16,18,19] (n=350)	0·20 (–0·15 to 0·55) 0·20 (–0·07 to 0·46)	Currently insufficient information to support the use of one specific approach to physiotherapy treatment	..
Motor learning approaches or task-specific training[14]				
Lower limb	Balance while standing: unknown effectiveness; 1 trial[20] (n=91) Gait (walking speed): unknown effectiveness; 3 trials[20–22] (n=117)	0·25 (–0·17 to 0·66) 0·31 (–0·06 to 0·67)	See above	..
Neurophysiological approaches (Bobath)[14,23]				
Upper limb	Arm function: unknown effectiveness; 6 trials[24–28] (292 recruited; n=248 analysed) Hand function: unknown effectiveness; 3 trials[24,25,27] (208 recruited; n=157 analysed)	0·11 (–0·14 to 0·36) 0·13 (–0·19 to 0·44)	See above	Upper limb: 5 RCTs identified; however, 1 trial had 2 subgroups and these were, therefore, analysed as different trials (thus, the number of trials reported is 6)
Lower limb	Balance while standing: unknown effectiveness; 1 trial[17] (n=15) Gait (walking speed): unknown effectiveness; 2 trials[17,27] (n=113)	0·37 (–0·68 to 1·41) 0·06 (–0·32 to 0·43)		
Bilateral training[29]				
Upper limb	Arm function: unknown effectiveness; 2 trials[30,31] (118 recruited; n=111 analysed) Hand function: unknown effectiveness; 1 trial[30] (106 recruited; n=99)	–0·05 (–0·42 to 0·33) –0·15 (–0·55 to 0·24)	Bilateral training involving functional tasks and repetitive arm movements should be used to improve dexterity and grip strength for patients with continuing limitation on arm function	..
Biofeedback: force and position feedback[32]				
Lower limb: force	Gait: unknown effectiveness; 1 trial[39] (n=41) Balance while standing (weight distribution): likely to be beneficial; 4 trials[33–36] (n=161) Balance while standing (postural sway): unknown effectiveness; 3 trials[34–37] (n=71) Mobility (sit-to-stand): unknown effectiveness; 2 trials[37,38] (n=42)	–0·05 (–0·66 to 0·56) –0·71 (–1·03 to –0·39) –0·10 (–0·57 to 0·36) 0·85 (–0·15 to 1·84)	Biofeedback should not be used on a routine basis	Cochrane review evidence covering force feedback from standing platform; reported meta-analyses include visual and auditory biofeedback combined, provided in different modes and frequencies
Lower limb: position	Gait (gait speed): unknown effectiveness; 5 trials[40–44] (189 recruited; n=165 analysed) Gait (stride length): unknown effectiveness; 2 trials[44,45] (n=37)	1·29 (–0·78 to 3·37) 2·63 (–2·64 to 7·91)		
Constraint-induced movement therapy[46,47]				
Upper limb	Arm function: likely to be beneficial; 21 trials[48–59,61–70] (774 recruited; n=508 analysed) Hand function: unknown effectiveness; 10 trials[49,50,55,56,60–62,64,65,69] (510 recruited; n=263 analysed)	0·73 (0·54 to 0·91) 0·17 (–0·07 to 0·42)	Constraint-induced movement therapy should be offered to specific patient groups	Restrictive inclusion criteria
Electromyographic biofeedback[70]				
Upper limb	Arm function: likely to be beneficial; 4 trials[71–74] (n=126)	0·41 (0·05 to 0·77)	Biofeedback should not be used on a routine basis	..
Lower limb	Gait (time to walk set distance): unknown effectiveness; 3 trials[75–77] (n=36) Gait (stride length): unknown effectiveness; 2 trials[78,79] (n=32)	0·13 (–0·55 to 0·80) 0·05 (–0·08 to 0·19)		
Electromechanical-assisted gait training[80]				
Lower limb	Gait (independent walking): likely to be beneficial; 8 trials[81–88] (n=414); odds ratio for walking 3·06 (1·85–5·06) Gait (walking speed): unknown effectiveness; 6 trials[82–85,87,88] (n=328) Gait (walking): likely to be beneficial; 3 trials[83–85] (n=216)	 0·89 (–0·11 to 1·89) 1·32 (0·32 to 1·33)	Guidelines do not mention electromechanical-assisted gait training	..

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	Evidence and considered judgment	SMD (95% CI)	RCP guideline	Comments
(Continued from previous page)				
Electrostimulation[89]				
Upper limb	Arm function: likely to be beneficial; 13 trials[90–102] (331 recruited; n=277 analysed)	0·47 (–0·03 to 0·97)	Functional electrical stimulation of the arm or leg should not be used on a routine basis	..
	Hand function: unknown effectiveness; 5 trials[95,98,102–104] (126 recruited; n=71 analysed)	0·12 (–0·34 to 0·59)		
Lower limb	Gait (walking speed): unknown effectiveness; 5 trials[105–109] (206 recruited; n=194 analysed)	–0·02 (–0·30 to 0·26)	..	
	Gait (stride length): unknown effectiveness; 2 trials[78,105] (n=34)	0·35 (–0·93 to 1·63)		
Fitness training: physical fitness training[110]				
Lower limb: cardiorespiratory training	Gait (chosen walking speed): likely to be beneficial; 4 trials[84,111–113] (n=356)	1·66 (0·66 to 2·66)	All patients should participate in aerobic training unless there are contraindications unrelated to stroke	Most mixed training interventions are confounded by training time; without this there is no clear evidence of any benefits Little can be concluded about mixed training interventions Functional ambulation was also likely to be beneficial for cardiorespiratory training, as were timed up-and-go outcomes for cardiorespiratory plus strength training Unknown effectiveness for measures of balance while standing, stair climbing, and community ambulation Conclusions are unchanged if maximum (rather than chosen) walking speed is selected
	Gait (endurance) likely to be beneficial; 4 trials[84,113–115] (n=309)	1·86 (0·87 to 2·87)		
Lower limb: strength training	Gait (chosen walking speed): unknown effectiveness; 3 trials[116–118] (n=110)	0·26 (–0·74 to 1·26)		
	Gait (endurance): unknown effectiveness; 2 trials[117,118] (n=90)	0·83 (–0·17 to 1·83)		
Lower limb: cardiorespiratory plus strength training	Gait (chosen walking speed): likely to be beneficial; 8 trials[16,17,22,117,119–122] (n=332)	0·27 (0·05 to 0·49)		
	Gait (endurance): likely to be beneficial; 4 trials[15,16,21,117] (n=177)	0·39 (0·09 to 0·69)		
High-intensity therapy[123]				
Upper limb	Arm function: unknown effectiveness; 6 trials[124–127] (612 recruited; n=571 analysed)	–0·11 (–0·38 to 0·17)	Patients should undergo as much therapy as is appropriate to their needs as they are willing and able to tolerate; in the early stages, every day they should receive a minimum of 45 min of each therapy that is required	Upper limb: 4 RCTs identified; however, 2 trials had 2 subgroups and these were, therefore, analysed as different trials (thus, the number of trials reported is 6 for arm function and 4 for hand function)
	Hand function: unknown effectiveness; 4 trials[125,127] (419 recruited; n=403 analysed)	0·09 (–0·11 to 0·30)		
Lower limb	Gait (walking speed): likely to be beneficial; 6 trials[17–19,124,128,129] (n=524); summary effect size in standard deviation units 0·19 (0·01–0·36)			
Mental practice with motor imagery[130]				
Upper limb	Arm function: likely to be beneficial; 4 trials[131–134] (74 recruited; n=72 analysed)	0·84 (0·34 to 1·33)	Patients should be encouraged to use mental practice of an activity as an adjunct to conventional therapy, to improve arm function	..
Moving platform				
Lower limb	Balance while standing (postural sway): likely to be beneficial; 2 trials[135,136] (n=44 recruited; n=40 analysed)	1·25 (0·58 to 1·93)	Guidelines do not mention moving platform training	..
Repetitive task training[137]				
Upper limb	Arm function: unknown effectiveness; 8 trials[25,27124,138–142] (467 recruited; n=414 analysed)	0·19 (–0·01 to 0·38)	Task-specific training should be used to improve activities of daily living and mobility: standing up and sitting down; gait speed and gait endurance Patients should be given as much opportunity as possible to practise repeatedly and in different settings any tasks or activities that are affected	Similar results for walking distance
	Hand function: unknown effectiveness; 5 trials[25,27,138–140] (324 recruited; n=281 analysed)	0·05 (–0·18 to 0·29)		
Lower limb	Balance while standing: unknown effectiveness; 3 trials[20,143,144] (137 recruited; n=132 analysed)	0·29 (–0·06 to 0·63)		
	Mobility (sit-to-stand): likely to be beneficial; 7 trials[20,22,25,27,138,145,146] (397 recruited; n=346 analysed)	0·35 (0·13 to 0·56)		
	Gait (walking speed): likely to be beneficial; 5 trials[20–22,27,124] (311 recruited; n=263 analysed)	0·29 (0·04 to 0·53)		
	Gait (functional ambulation): likely to be beneficial; 5 trials[25,27,124,143,144] (295 recruited; n=238 analysed)	0·25 (–0·00 to 0·51)		
Rhythmic gait cueing				
Lower limb	Gait (gait speed): unknown effectiveness; 3 trials[43,147,148] (n=121)	0·97 (–0·10 to 2·04)	Guidelines do not mention rhythmic gait cueing	..
	Gait (stride length): likely to be beneficial; 4 trials[43,45,147,148] (n=135)	1·26 (0·20 to 2·33)		
Robotics[149]				
Upper limb	Arm function: likely to be beneficial; 10 trials[150–159] (295 recruited; n=255 analysed)	0·81 (0·40 to 1·22)	Robot-assisted therapy should be used as an adjunct to conventional therapy when the goal is to reduce arm impairment	Differences between groups could be attributed to increased duration of intervention
	Hand function: unknown effectiveness; 7 trials[151,152,154–157,159] (215 recruited; n=150 analysed)	0·12 (–0·87 to 1·12)		

(Continues on next page)

	Evidence and considered judgment	SMD (95% CI)	RCP guideline	Comments
(Continued from previous page)				
Splinting or orthosis[160]				
Upper limb	Arm function: unknown effectiveness; 4 trials[161–163] (109 recruited; n=105 analysed) Hand function: unknown effectiveness; 2 trials[161,163] (46 recruited; n=43 analysed)	0·10 (–0·27 to 0·48) –0·18 (–0·87 to 0·51)	Inflatable arm splints enveloping the hand, forearm, and elbow, and resting wrist and hand splints should not be used routinely	3 RCTs identified; 1 trial had 2 subgroups
Lower limb	Data available only from randomised cross-over trials with no first phase data; these trials are not included in our analysis		Guidelines state that ankle–foot orthosis should only be used to improve walking and/or balance, and should be tried in patients with foot drop	
Treadmill training plus body weight support[175]				
Lower limb	Gait (walking speed): unknown effectiveness; 10 trials[88,114,115,176–180] (n=295) Gait (dependence on personal assistance to walk): unknown effectiveness; 5 trials[88,114,176–178] (n=178); relative risk of dependence 1·10 (0·90–1·34)	0·16 (–0·08 to 0·39)	These approaches should be used in selective cases only	8 RCTs identified but 2 trials had 2 subgroups and these were, therefore, analysed as different trials (thus, the number of trials reported is 10)
Walking aids				
Lower limb	No RCT data available	..	Patients with limited mobility should be assessed for, provided with, and taught how to use any mobility aids	Searching did not identify any RCTs A Cochrane review is ongoing

Evidence of effect in the identified randomised trials is presented as a considered judgment (see Methods of the Review and Clinical Evidence[13]). Results of any meta-analysis of relevant outcomes are summarised as the SMD (difference between treatment and control group mean expressed in standard deviation units) and 95% CI. The final column comments on the information and associates this with the more recently updated clinical practice guideline (RCP Stroke guideline[11]). RCP=Royal College of Physicians. RCT=randomised controlled trial. SMD=standardised mean difference.

Table 2: **Summary of evidence for interventions aimed at promoting motor recovery after stroke**

identify all relevant high-quality evidence. We focused on randomised controlled trials, which are least likely to provide biased estimates of effect, and used comprehensive searching to identify relevant systematic reviews and trials. Where possible, we used an explicit and unbiased approach to data analysis, and any conclusions were considered with reference to the key design features of the available evidence. Finally, bearing in mind that a meta-analysis can sometimes produce misleading results, we tried to put this evidence in context by including a semi-quantitative assessment (considered judgment) with further cross-referencing to the most recent clinical practice guidelines.[11] We are not aware of any previous review of the topic that has taken such a robust and comprehensive approach.

The main weaknesses relate to the heterogeneity of the available data, such that our Review could not provide clear guidance on which intervention should be given to a particular patient in a particular situation. First, there is substantial heterogeneity among the identified trials in terms of the participants, settings, the amount and duration of the intervention and control comparators, method of intervention delivery, and the timing of outcome measures. The methodological rigour of the studies also varied and many studies had several methodological limitations. Second, the standardised effect measures we used expressed the effect of the intervention on some form of motor function (or, failing that, motor impairment) outcome score. Because a range of different outcomes have been included, direct comparisons between interventions might be difficult. Finally, even trials that have good methodological features (ie, have good internal validity) have generally been small in size, have recruited a selected participant population, and have used outcome measures at the level of impairment or limb function. There are few multicentre randomised trials that have tested interventions in routine clinical settings on relatively large numbers of patients and that have used outcome measures that indicate activity and participation, as well as motor recovery.

Evidence for interventions

Despite the limitations, we believe that this overview does provide a relatively concise and informative summary from which to discuss the available evidence for interventions aimed at promoting motor recovery after stroke. We believe there is evidence that several interventions might be beneficial or at least show promise for further research.

The most promising interventions for upper-limb (arm) function seem to be constraint-induced movement therapy, for which there has been a substantial number of trials, including one multicentre study.[63] The main challenge in applying the evidence of benefit from constraint-induced movement therapy is that the intervention is time-consuming and tiring, presenting major challenges to compliance. Hence, all the trials of this intervention have recruited highly selected participant populations with resulting diminished external validity of the evidence. Modified constraint-induced movement therapy is now being investigated with the aim of developing a more widely applicable intervention. Promising effects on motor recovery of the arm were seen in trials of mental practice,[131–134] EMG biofeedback,[71–74] and robotics.[150–159] However, none of these interventions has had sufficient evaluation to come to a conclusion about their effectiveness in a routine clinical setting, and all could have their conclusions changed by a relatively small number of new trials. Very limited evidence seems to be available for interventions to improve hand function.

Interventions that seem promising (but again inconclusive) for balance while standing include biofeedback (force feedback)[33–40] and training with a moving platform.[135,136] Repetitive task training seems to be beneficial for mobility during rising to stand,[20,22,25,27,138,145,146] and the clinical challenge seems to be in developing an explicit, practical, reproducible, and auditable intervention that includes these beneficial effects. Interventions that seem promising for improving gait include fitness training (both cardiorespiratory training[84,111,112] and a mixture of cardiorespiratory and strength training[16,17,22,117–121]), high-intensity therapy (usually physiotherapy),[17–19,124,128,130] and repetitive task training.[20–22,27,124,137] The current limited evidence suggests that mixed physiotherapy treatment approaches, electromechanical-assisted gait training, rhythmic gait cueing, and walking aids also merit further robust investigation.

General themes

Of the interventions that we have identified to show promise, most could be argued to involve elements of intensive, repetitive task-specific practice (constraint-induced movement therapy, robotics, mental practice, repetitive task training, increased intensity therapy, physical fitness training, electromechanical-assisted gait training, mixed physiotherapy treatment approaches, rhythmic gait cueing, and training with a moving platform). This observation lends support to the belief that high-intensity repetitive task-specific practice might be the most effective principle when trying to promote motor recovery after stroke.

Despite the undoubted progress in the evaluation of interventions to improve motor recovery after stroke, much more work is still needed to be able to provide prescriptive advice for specific problems in specific patients. The general advice from recent clinical guidelines broadly reflects that of the clinical trials. The main areas of discrepancy between the results of meta-analyses and clinical practice guidelines seem to reflect the appropriate conclusion that the clinical trial evidence is based on very selected populations (eg, individuals who have minimum levels of recovery, no cognitive impairment, who are able to walk independently, and who are considered at least 2 weeks after stroke); furthermore, at present, it is not possible to translate this into broad, practical recommendations for the wider patient population.

Recommendations for treatment

There are still many gaps and shortcomings in the evidence base for interventions to promote motor recovery after stroke. To a large extent, individual clinical decisions will continue to rely on the knowledge and judgment of the individual therapists. At present, the evidence base for clinical practice can provide only broad indicative guidance. The main general recommendations seem to be that the alleviation of motor impairment and restoration of motor function should (as much as possible) focus on high-intensity, repetitive task-specific practice with feedback on performance.

Recommendations for research

A large amount of research is required to define much more clearly the interventions that carry benefit, and to quantify that benefit in a routine clinical setting. No individual treatment for motor recovery is likely to be applicable to every patient with stroke so trials will have to clearly define their target populations. More research is also needed to meet the challenge of implementing complex interventions in a routine clinical setting. Current trials that are addressing some of these concerns include those of early mobilisation, repetitive task training, and treadmill training. A wide range of outcome measures have been reported in the clinical trials, as reviewed here. There is a real need to focus on a smaller number of robust, standardised, and relevant outcome measures and to ensure that all trials include these measures in a common dataset to enable future comparison.

Contributors

All authors contributed equally to the search of papers and the writing and revision of the Review.

Conflicts of interest

We have no conflicts of interest.

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