Brain Neurorehabil. 2022 Jul;15(2):e12
https://doi.org/10.12786/bn.2022.15.e12
pISSN 1976-8753·eISSN 2383-9910

Brain & NeuroRehabilitation

Special Review
Updates in Neurorehabilitation

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Update on Stroke Rehabilitation in Motor Impairment

OPEN ACCESS

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Received: May 31, 2022
Revised: Jun 17, 2022
Accepted: Jun 23, 2022
Published online: Jul 20, 2022

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HIGHLIGHTS

- Motor impairment in stroke patients diminishes activities of daily living.
- Rehabilitation therapy that promotes the recovery of motor function is crucial.
- With technological advances, rehabilitation methods continue to be developed.

Brain Neurorehabil. 2022 Jul;15(2):e12
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Funding
None.

Conflict of Interest
The author has no potential conflicts of interest to disclose.

ABSTRACT

Motor impairment due to stroke limits patients' mobility, activities of daily living, and negatively affects their return to the workplace. It also reduces patients' quality of life and increases the socioeconomic burden of stroke. Therefore, optimizing the recovery of motor impairment after stroke is a very important goal for both individuals and society as a whole. The emergence and improvement of various technologies in the Fourth Industrial Revolution have exerted a major influence on the development of new rehabilitation methods and efficiency enhancements for existing methods. This review categorizes rehabilitation methods that promote the recovery of motor function into upper limb function and lower limb function and summarizes recent advances in stroke rehabilitation. Although debate continues regarding the effects of some rehabilitation therapies, it is hoped that the evidence will be improved through ongoing research so that clinicians can treat patients with a higher level of evidence.

Keywords: Motor Impairment; Stroke; Rehabilitation

INTRODUCTION

Stroke is one of the most common causes of death and disability worldwide. Although the mortality rate due to stroke has decreased, the incidence of stroke has increased, resulting in an increased socioeconomic burden [1]. In order to reduce this burden, intensive rehabilitation should be performed to maximize stroke patients' ability to perform activities of daily living during the recovery period, along with secondary prevention measures to reduce the risk of stroke recurrence. The need for rehabilitation services for stroke patients will continue to grow.

Motor impairment is a major cause of diminished performance of activities of daily living in stroke patients. It was previously believed that the central nervous system, had no ability to regenerate or change; thus, clinicians focused on teaching patients compensatory strategies. However, with the increasing awareness that brain plasticity, neural regeneration, and rehabilitation therapy can promote recovery, the focus has shifted toward treatments that maximize neurological recovery in the early stages [2]. Therefore, rehabilitation therapy using a restorative approach is implemented for the first 3 to 6 months post-stroke, when recovery is most active.

Many efforts have been made to maximize the neurological recovery of motor impairment during recovery after stroke, and numerous studies have investigated rehabilitation methods. The core technologies of the Fourth Industrial Revolution, including mobile technologies, robots, artificial intelligence, and virtual and augmented reality, are bringing about many changes in medical technology [3]. Stroke rehabilitation methods using these technologies are also being developed.

The purpose of this review was to summarize recent advances in stroke rehabilitation therapy for motor impairment. Rehabilitation for motor impairment in stroke patients can be broadly categorized into upper and lower extremities. Herein, I discuss the following rehabilitation therapies: treadmill training, functional electric stimulation (FES) for gait, biofeedback, repetitive transcranial magnetic stimulation (rTMS), robot-assisted therapy, and virtual reality training for the lower extremities; constraint-induced movement therapy (CIMT), mirror therapy, motor imagery training (MIT), and FES for upper extremity function; FES for shoulder subluxation; and rTMS, robot-assisted therapy, and virtual reality training for the upper extremities.

MOTOR REHABILITATION FOR LOWER LIMB FUNCTION

Treadmill training

According to the Clinical Practice Guideline for Stroke Rehabilitation in Korea released in 2016, treadmill training is strongly recommended to improve gait speed, endurance, and distance for stroke patients who can or cannot walk independently [4]. A 2017 Cochrane review stated that treadmill training for stroke patients could help improve their gait speed and endurance in a short period of time and that it was beneficial for patients who could walk to some extent at the time of treatment initiation; however, there was insufficient evidence regarding the long-term effects of treadmill training on the improvement of gait speed and endurance [5].

In 2020, Munari et al. [6] reported a pilot study on the effect of backward treadmill training on stroke patients. Eighteen chronic stroke patients underwent the training, which was conducted in three 40-minute sessions per week for 4 weeks, and the patients were divided into forward and backward treadmill training groups. The backward treadmill training group showed greater improvements in the 10-minute walking test and balance evaluation [6]. The researchers suggested that the central pattern generator mechanism could explain the effect of backward treadmill training. It is known that facilitating hip extension and knee flexion with the foot positioned behind the trunk is helpful for restoring motor function in patients with a synergistic pattern in the lower extremities.

In another randomized controlled trial, virtual reality training was implemented along with treadmill training to improve patient participation and their walking ability. Compared with the control group, the experimental group did not show significant differences in patient participation and gait parameters, but the potential of this modality as a treatment tool was confirmed [7]. Recent trends in research have shifted from classical treadmill training toward the use of rehabilitation robots based on treadmill training, as described below.

FES for gait

The Clinical Practice Guideline for Stroke Rehabilitation in Korea suggests that FES is effective in improving the strength of hip and ankle weakened by stroke and strongly recommends this modality for improving gait function in stroke patients with foot drop [4]. A recent meta-analysis reported that FES significantly improved the gait speed of stroke patients compared to the control group [8]. In a systematic literature review, combining FES with conventional therapy was helpful in improving the balance function of stroke patients [9].

A recent randomized controlled trial confirmed the effect of multi-functional electrical stimulation gait training for the peroneal nerve, knee flexor, and extensor muscles on improving gait among patients with subacute stroke within 30 days of onset. In another study, FES combined with transcranial direct current stimulation (tDCS) had a positive effect on gait regularity in patients with subacute stroke [10,11]. Likewise, recent gait-related FES studies have attempted to achieve better results by applying multi-channel approaches or incorporating therapeutic devices using neuromodulation.

Biofeedback for function of the lower limb

The most recent Cochrane review on biofeedback for function of the lower limb was published in 2007. Although it was reported that combining biofeedback with physical therapy led to significant improvements in muscle strength, functional recovery, and gait quality, the sample size of each clinical trial was small and the study designs were unclear, limiting the level of evidence [12]. A systematic review of 18 clinical trials concluded that compared to conventional treatment, biofeedback was more effective in improving the motor function of the lower extremities; however, the long-term effects of biofeedback were not confirmed [13].

A randomized controlled trial published in 2019 reported the effects of multimodal training using force sensor biofeedback. In total, 68 subacute stroke patients were allocated to a group performing 40-minute sessions of visual biofeedback training with cycling augmented by FES using a force sensor for 6 weeks or another group undergoing conventional balance training. A correlation was noted between the interventional treatment performed in the experimental group and improvements in gait speed and endurance [14]. As exemplified by that study, with the recent development of sensors, attempts have been made to use force sensors and force plates for treatment instead of electromyography biofeedback using surface electrodes.

rTMS

The effects of rTMS on improving lower extremity function are difficult to determine due to high heterogeneity among randomized controlled trials. According to a 2019 meta-analysis, rTMS could have positive effects on mobility and balance, but the level of evidence was low due to heterogeneity between studies and small sample sizes [15]. A network meta-analysis of 943 subjects in 26 randomized controlled trials showed that low-frequency rTMS was the most commonly adopted stimulation method, followed by high-frequency rTMS. Regarding the effect of stimulation, low-frequency rTMS had a significant effect on improving Fugl-Meyer evaluation scores, and high-frequency rTMS had a significant effect on increasing the magnitude of motor-evoked potentials [16].

A recent randomized controlled trial applied multimodal, multi-site stimulation combining rTMS with tDCS to patients with subacute stroke. The patients were randomly assigned to 4 groups: sham, low-frequency rTMS only, cathodal tDCS and low-frequency rTMS ($tDCS^-/rTMS^-$), and anodal tDCS and low-frequency rTMS ($tDCS^+/rTMS^-$). For multimodal stimulation, tDCS was first applied to the motor cortex on the affected or unaffected side, followed by rTMS. The treatment was performed for a total of 40 minutes (20 minutes in each session), 5 times a week for 4 weeks. At 8 weeks after the treatment, the $tDCS^+/rTMS^-$ group showed significant improvements in the National Institutes of Health Stroke Scale and the Barthel index compared to the sham group. The $tDCS^+/rTMS^-$ group also showed the most significant improvements in the Fugl-Meyer assessment score for the lower extremities, and the motor-evoked potential of the affected side and resting motor threshold also significantly improved. Therefore, the authors concluded that anodal tDCS and low-frequency rTMS were most effective for restoring motor function and modulating cortical excitability [17]. Likewise, recent neuromodulation studies on the lower extremities tried to maximize the effects of neuromodulation by combining multimodal and multi-site stimulation.

Robot-assisted therapy

The Clinical Practice Guideline for Stroke Rehabilitation in Korea recommends that robot-assisted therapy should be implemented in selected patients, in addition to conventional gait training, to improve the gait function of stroke patients [4]. In a Cochrane review, robot-assisted gait training was beneficial for recovering independent gait, especially in patients who were unable to walk on their own in the first 3 months after stroke onset. Gait speed immediately after treatment was superior to that after conventional rehabilitation; however, there was no significant difference in the long-term effects. A significant improvement was observed in patients within 3 months after onset, but not in patients more than 3 months after onset. The authors suggested that further studies should be conducted to assess its effects on activities of daily living and quality of life, the relationship of its effects with the duration and intensity of treatment, and its long-term effects [18].

In a meta-analysis of Nedergård et al. [19], it was possible to indirectly identify which specific gait factors contributed to the positive effects demonstrated in the Cochrane review. This meta-analysis investigated 13 studies on the effect of robot-assisted gait training on the biomechanical outcomes of stroke patients. The step length of the affected side significantly improved. In addition, positive effects of robot-assisted gait therapy were found in stride length and temporal symmetry. However, limitations were the small sample size and high heterogeneity of the included studies [19].

Kim et al. [20] reported the neuroplastic effects of end-effector robotic gait training. They divided hemiparetic stroke patients who were able to walk under supervision into an end-effector robot-assisted gait training group and a body weight support gait training group, and compared the results after a 4-week training period. The primary endpoint was regional cortical activity measured by functional near infrared spectroscopy (fNIRS), and the secondary endpoint was a gait-related variable. The activity of the primary sensorimotor cortex, supplementary motor area, and premotor cortex of the affected cerebral hemisphere significantly increased in the end-effector robot-assisted gait training group. The authors concluded that robot-assisted gait training influenced cortical reorganization. In the Fugl-Meyer assessment, the robot-assisted gait training group showed significant improvements, which were attributed to repetitive motor relearning; however, body-weight support gait training was associated with a lack of proper sensory input [20]. Another randomized controlled trial introduced assist-as-needed robotic gait training. The intervention involved a gait training robot with a high degree of freedom, which intervened as needed according to the patient's walking ability. The robot

 https://doi.org/10.12786/bn.2022.15.e12

used in the study connected and operated a shadow thigh and shank with the patient using the pelvis, knee joint, and ankle joint bars and supported the body weight with a pelvic strap and a harness. The study compared the therapeutic effects of assist-as-needed and conventional gait training in 34 subacute stroke patients. Compared with the control group, the experimental group showed significant improvements in step length and peak knee flexion of the affected lower limb in the swing phase [21].

A consensus exists that gait training robots have an advantage over conventional treatment methods in promoting the acquisition of independent gait and are more effective in patients with subacute stroke who are unable to walk. fNIRS and functional magnetic resonance imaging (fMRI) studies have shown that these effects are induced by promoting cortical neural reorganization through changes in cerebral cortical activity.

Virtual reality training

It is recommended to perform virtual reality training to improve walking function in addition to conventional treatment [4]. A Cochrane review published in 2015 did not confirm an advantage of virtual reality training over conventional treatment in improving gait speed [22]. However, a recently published meta-analysis reported that lower extremity function, balance, gait ability, and the activities of daily living were significantly improved after virtual reality training. For each functional evaluation scale, the lower-extremity Fugl-Meyer assessment, functional ambulatory category, Berg balance scale, timed up-and-go test, gait speed, and cadence significantly improved [23].

A recent randomized controlled trial investigated the treatment effect of virtual reality training combined with mirror therapy. Sixty-four chronic stroke patients were randomly assigned to a conventional treatment group or a combination treatment group (virtual reality training and mirror therapy), and 70 minutes of therapy per session was administered for 10 days. Compared to the control group, the experimental group had significant improvements in range of motion, manual muscle test, Fugl-Meyer assessment, and the functional reach test.

Virtual reality can provide repetitive, task-oriented training in an enriched environment. It can also simulate activities similar to those in the real world. Due to these features, virtual reality is being actively studied as an important adjuvant treatment tool for neurorehabilitation that induces patients' interest and encourages their participation in long-term treatment.

tDCS

Insufficient evidence exists regarding the association of tDCS with improvements in lower extremity function. A Cochrane review also reported that tDCS could be helpful in improving the activities of daily living, but the level of evidence was low [24]. A meta-analysis synthesized data from 10 randomized controlled trials to determine the effect of tDCS on balance and gait. The included studies generally applied tDCS to the lower-extremity motor area or supplementary motor area on the affected side at an intensity of 2 mA or more for 10 to 20 minutes to improve lower-extremity function. It was concluded that tDCS could help patients achieve independent gait, as the experimental group showed improved results in the functional ambulatory category and timed up-and-go test [25]. A systematic literature review also stated that tDCS could have a positive effect on gait ability and balance, but there was insufficient evidence on its long-term effects [26].

https://doi.org/10.12786/bn.2022.15.e12

In many tDCS-related clinical studies, tDCS was conducted together with body-weight support gait training, and some studies investigated the effect of combining tDCS with FES on recovery. In particular, performing tDCS in conjunction with FES had a positive effect on walking regularity and helped to improve gait ability [11]. However, its effect on the improvement of gait speed, which was the primary endpoint, was insignificant, indicating the limited effect of tDCS on lower-extremity function.

Whole-body vibration (WBV)

In 2 recent meta-analyses, WBV had positive effects on bone metabolism, spasticity, and the results of the 6-minute gait test, but the level of evidence was not high with regard to improvements in muscle strength, balance, and gait [27,28]. A recent randomized controlled trial reported that WBV reduced ankle plantar flexor spasticity and increased intramuscular blood perfusion in chronic stroke patients [29]. Based on the latest findings, WBV has a positive effect on the improvement of lower extremity spasticity in stroke patients, and this improvement can have a positive effect on some gait parameters.

MOTOR REHABILITATION FOR UPPER LIMB FUNCTION

CIMT

In the Clinical Practice Guideline for Stroke Rehabilitation in Korea, CIMT is recommended with a high level of evidence (recommendation level A, level of evidence 1++) [4]. The EXCITE trial reported that CIMT significantly improved stroke patients' motor function on the hemiplegic side and that the effect lasted for at least 1 year [30]. The most recent Cochrane review, published in 2015, stated that CIMT improved motor impairment, but there was limited evidence on its long-term effects [31]. Since the evidence is somewhat clear on the effectiveness of CIMT, recent randomized controlled trials explored the beneficial effects of CIMT combined with other treatments such as tDCS and botulinum toxin A injection, and all of these studies reported positive results [32,33].

Mirror therapy

Mirror therapy was reported to be effective in significantly improving the upper and lower extremity movements on the affected side and the activities of daily living in both subacute and chronic stroke patients in a 2018 Cochrane review. However, according to 3 meta-analyses published in 2020 and 2021, mirror therapy alone had little effect on the recovery of upper extremity function, although meaningful results could be obtained when it was used in combination with other treatment methods. Therefore, debate continues regarding the effect of mirror therapy performed alone [34-36].

MIT

MIT refers to the process of thinking about and practicing the movement to be trained in a state where there is no body movement. The Clinical Practice Guideline for Stroke Rehabilitation in Korea recommends using MIT in addition to rehabilitation involving actual movements [4]. A Cochrane review published in 2011 stated that there was insufficient evidence regarding the recovery of upper extremity function when a combination of MIT and other treatments was performed for stroke patients. However, a later Cochrane review reached a different conclusion, reporting a moderate level of evidence for positive effects [37,38]. According to a recent meta-analysis, the degree of upper extremity motor impairment significantly improved after MIT, and MIT produced a significant effect in patients with severe to moderate upper-extremity motor impairment (between 0 and 40 points on the Action Research Arm Test) [39]. In a study of chronic stroke patients, the upper extremity Fugl-Meyer assessment significantly improved compared to that in the control group. Furthermore, extensive reorganization of functional connectivity between both cerebral hemispheres was confirmed by resting-state fMRI; this reorganization was particularly prominent in the MIT- and learning-related brain regions on the affected hemisphere [40].

Functional electrical stimulation for upper extremity function

FES is strongly recommended because it helps to restore movement of the forearm and wrist on the hemiplegic side of stroke patients [4]. According to a recent meta-analysis, FES had a statistically significant effect on improving upper-extremity function compared to control groups [41].

Among recently published papers on FES, one exploratory study demonstrated the effect of wearable forearm neuromuscular electrical stimulation using a multi-electrode array to electrically stimulate individual forearm muscles to enable precise movements [42].

In light of the very extensive research on FES for functional recovery of the upper extremity, no relevant publications Hemiplegia due to stroke often leads to the development of subluxation of the shoulder joint, which causes functional and musculoskeletal problems that lower quality of life. FES is used as an interventional measure, and it is strongly recommended in the Clinical Practice Guideline for Stroke Rehabilitation in Korea. A Cochrane review reported that it had a significant effect on reducing shoulder pain, but the evidence was limited due to the small sample size [43]. In a meta-analysis published later, evidence was added, and it was concluded that FES was beneficial for reducing shoulder subluxation in acute and subacute stroke patients. It was advised to apply the treatment according to patients' compliance and conditions, as significant results were found in the acute phase rather than in the chronic phase, regardless of the treatment period [44].

rTMS

On the topic have been written since the last meta-analysis published in 2015. However, randomized controlled trials have combined FES with other treatment methods to improve the efficacy of treatment, and development efforts have been continued to enable precise movement control through selective muscle stimulation.

Functional electrical stimulation for shoulder subluxation

rTMS is a noninvasive brain stimulation method widely used to promote the recovery of upper extremity function after stroke. The level of evidence is rather limited, and the Clinical Practice Guideline for Stroke Rehabilitation in Korea specifies that it should be administered to selective patients by an experienced specialist who is familiar with contraindications and side effects. Several Cochrane reviews reported that there was low-quality evidence regarding its effect on the improvement of upper extremity function and activities of daily living [45,46]. In a meta-analysis published later, rTMS was reported to have both long- and short-term, effects on the improvement of upper extremity function in stroke patients. The effect size was larger and more significant in patients with acute and subacute stroke than in chronic patients. However, there were some problems related to heterogeneity in the treatment protocols used for rTMS among the included studies [47].

Recently published randomized controlled trials reported positive effects on functional recovery from simultaneously implementing theta-burst stimulation and low-frequency rTMS or applying rTMS together with FES and MIT [48,49]. The overall trend in research has been to apply rTMS as a dual-modulation protocol in a multi-modal framework, rather than as a single treatment.

Robot-assisted therapy

Robot-assisted therapy refers to the use of an electronic computer control system device for rehabilitation therapy. These robots can be divided into therapeutic and assistive. Unlike the existing therapist-centered approach to treatment, robot-assisted therapy can be performed repeatedly at a higher intensity, thereby promoting the brain plasticity and the recovery of upper extremity function [50,51]. In 2 Cochrane reviews published by Mehrholz et al. [52,53] at an interval of 3 years between 2015 and 2018, the level of evidence for robot-assisted therapy was changed from low or very low to high in terms of recovery in activities of daily living, upper extremity function, and upper extremity strength. Several randomized controlled trials have recently been published, and evidence is being established rapidly. A recent meta-analysis also reported that robot-assisted therapy is advantageous over conventional rehabilitation for improving upper extremity motor function [54].

Virtual reality training

Virtual reality is defined as the "use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events" [55]. Virtual reality is a relatively recent treatment tool that has the advantage of allowing repeated simulation practice of functional tasks, unlike conventional treatment. The Clinical Practice Guideline for Stroke Rehabilitation in Korea also recommends using virtual reality in addition to conventional rehabilitation, if the appropriate training equipment and skilled personnel are available [4]. Several review papers have also revealed that virtual reality training was helpful in improving stroke patients' upper-extremity Fugl-Meyer assessment and activities of daily living. There has recently been a directional change in the development of virtual reality therapy toward using it together with a brain-computer interface so that a patient's movement intention is detected and realized in virtual reality to give visual feedback [56,57].

Brain-computer interface

The brain-computer interface is a technology that allows a computer to recognize the intention of a patient through electroencephalogram signals; the interface produces output in various forms, and this method therefore has the potential to be applied to various fields. This innovative technology can restore or replace motor function and communication ability even in stroke patients.

A recent meta-analysis reported that brain-computer interfaces had significant effects on the recovery of upper extremity function in stroke patients. The treatment methods using brain-computer interfaces can be divided into motor imagery-based, movement attempt-based, and action observation-based, and a significant effect was noted with the motion attempt-based method. When the effect was analyzed according to the combined use of other treatment devices, a statistically significant effect was observed when a brain-computer interface was used together with FES [58].

tDCS

A Cochrane review published in 2020 stated that tDCS had very low-quality evidence for its effect on improvement in the activities of daily living [59]. A 2021 meta-analysis reported a positive effect on the improvement of upper-extremity function, but the level of evidence was limited due to the high heterogeneity among studies [60]. A subgroup analysis found that the effect was more significant in the chronic stage than in the acute stage, and in mild cases rather than in severe cases. In addition, the online effect was more significant than the offline effect, and a significant effect was noted at treatment intensities of 1.5–2 mA or higher. Meta-analyses have recently reported evidence on the combined application of tDCS with robot-assisted therapy for the upper extremities, and attempts are being made to implement therapy using virtual reality [61,62].

SUMMARY

Motor impairment in stroke patients reduces their activities of daily living, diminishes their quality of life, and imposes a substantial socioeconomic burden. In order to minimize these negative impacts, rehabilitation therapy that promotes the recovery of motor function is crucial.

Conventional treatments such as treadmill training, FES, and CIMT, which have been extensively studied, have been investigated as new types of treatment or in combination with other treatment modalities. These attempts have shown positive effects on increasing patients' motivation or enhancing functional recovery when compared to conventional treatment methods.

Recently, in the field of stroke rehabilitation therapy, various treatment methods using new technologies have been developed. The application of new technologies, such as brain-computer interfaces, to treatment is expected to promote brain plasticity and neural reorganization, thereby bringing about recovery in more patients. As technology advances, more stroke patients will have better recovery and improved quality of life. Therefore, clinicians should continue to research new technologies, obtain evidence, and apply these innovations in patient care.

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