# Stroke Rehabilitation from a Historical Perspective

**Monica Acciarresi and Mauro Zampolini**

**Abstract:** In western industrialized countries, stroke is one of the leading causes of acquired adult disability. Because of the recent advances in acute stroke treatment and neurocritical care, more patients survive stroke, with varying degrees of disability. Stroke rehabilitation is a dynamically changing field that is increasingly expanding. Advances in knowledge of mechanisms underlying stroke recovering and in technology are aiding the development of therapies that requires a multidisciplinary approach by physicians, therapists, biologists, physiologist and engineers working together with the aim of improve the quality of life of patients with stroke.

## 1. Introduction

Stroke is highly associated with acquired disability in developed nations [1]. Progress of late, in both acute stroke and neurocritical care, has led to greater numbers of stroke survivors; however, too often, survivors are burdened with acquired stroke disability [2].

It is widely known that observed neurological deficits are important for indicating the locations of damage done to tissue, as well as any associated neuronal loss [3], which, in turn, is responsible for the burden of disability [4].

## 2. Stroke Recovery and Stroke Rehabilitation

Generally speaking, stroke rehabilitation is commonly defined as any form of stroke care that seeks to reduce disability, while at the same time, foster more active participation in daily living activities. Achieving the highest possible level of independence is of paramount importance [2].

Stroke recovery focuses on striving to increase performance- and activity-based behavioral targets [2]. Recovery is recognized as being an articulated process, which can be successfully achieved when a combination of spontaneous and learning-dependent processes are improved upon. These include restitution, substitution and compensation. By definition, the first of these strives to regain functionality of any impaired neural tissue; the second reorganizes untouched neural pathways, so to regain functioning; whilst the third seeks to obtain betterment with regard to the issue of disparity between the impaired skills [5]. Despite the fact that patient outcome tends to be heterogeneous and individual recoveries differ widely due to varying patient features, results from several cohort studies [6] have reported that recovery can be predicted for the first few days post-event.

The ability to more accurately predict recovery on an individual level has been enhanced through the development of a multimodal biomarker-based algorithm based upon clinical results, for the most part made up of neurophysiological and brain imaging results [7]. Specifically, if patients exhibit the marked impairment of both shoulder abduction and finger extension, the functional integrity of the corticospinal tract can be assessed using transcranial magnetic brain stimulation. Whenever a motor-evoked potential is recorded, a good recovery can be predicted, as the tract will still be intact [8].

Currently, international guidelines recommend that any stroke rehabilitation regimen be performed under the direction of a qualified Stroke Unit, incorporating multidisciplinary rehabilitation strategies, within a few days of an event [9,10]. To this regard, the literature published to date suggests that intensive rehabilitation, when led by a structured multidisciplinary team, will more likely produce greater benefits, in terms of outcome and/or alleviating the burden of disability; in fact, results reported by less intense programs without the direction of a multidisciplinary team have failed to match these levels of benefit [11].

With regard to behavioral recovery, on average, it will occur within the first three months after stroke. In animal models, researchers have reported that any postponement in training after stroke, in animal models, was associated with attenuated effectiveness. However, results from clinical studies on this topic have not been so straightforward [12]. In fact, findings from human trials suggest that rehabilitation might be harmful when hastily initiated. The AVERT trial findings suggest that immediate mobilization, on average $\approx$ 18 h after stroke, was associated with a reduction in favorable outcome at 90 days [13].

To date, no moderate nonlinear association between impairment and function has been reported, particularly for motor impairment [5,6,14]. Moreover, evidence of neurological repair associated with the use of impairment-focused therapies has yet to be demonstrated. On the other hand, strong evidence exists supporting the role of task-oriented training. Here, the focus is on bolstering the natural pattern of functional recovery, driven mainly by adaptive strategies that make up for any impaired body functions [5,14,15].

Prior to current neurophysiological rehabilitation approaches, central nervous system damage had been treated via compensatory and orthopedic approaches: the stretching, bracing and strengthening of the affected side and by instructing patients to favor their sides unaffected by stroke [16]. A clearer understanding has been ascertained of the underlying mechanisms responsible for motor learning [17] and functional recovery post-stroke [5]. It seems that varying mechanisms trigger the nonlinear pattern of neurological recovery. To this regard, we mean the salvation of penumbral tissue surrounding the infarcted area; an elevation of cerebral shock, otherwise known as elevation of diaschisis; and finally, the ability of the brain to adapt via neuroplasticity [18].

Neuroplasticity, defined as changes in or a rewiring of the neural network, is held to be the main recovery process. The neural basis for post-stroke recovery relies on plasticity [19], namely, the ability of central nervous system cells to modify their structures and functioning in response to external stimuli [3]. Immediately following stroke, activation is decreased in the cortical areas afflicted, therein triggering changes in the localizations of certain tasks, such as movement.

During the acute and subacute phases, the neural networks will reconnect in the adjacent areas of the event site. However, in order to foster effective plasticity, rehabilitation interventions need to be task specific [2]. Recently developed neurorehabilitative approaches aim at stimulating cerebral plasticity through the employment of task-oriented models of motor learning [3,20–23].

## 3. New Neurorehabilitative Approches

Constraint-Induced Movement Therapy (CIMT) is a motor rehabilitation therapy technique that employs a mitt to constrain the unaffected limb, thereby the patient will favor the use of his/her affected hand. Clearly, the objective is to challenge the maladaptive "learned nonuse" of the paretic limb. This is achieved by not utilizing the compromised limb. Investigations made up of RCTs, along with a Cochrane review, have reported that CIMT played a role in augmenting the performance of motor skills [24,25], particularly with regard to arm function. It must be remembered that the routine use of CIMT is not without limitations. First of all, it is recognized as being labor-intensive, as well as being recommendable solely in those patients possessing discernable levels of conservation for motor skills performance. Moreover, any such candidates are required to have control over the functioning of their wrists and fingers.

Likewise, mirror therapy is an ulterior approach based on multisensory stimulation. This technique entails placing a mirror at a 90° angle in the midsagittal plane of the patient, so as to hide the paretic limb anterior to the mirror. Here, the unaffected limb is viewed, as if it were the affected arm, therein leading to the false perception on the part of the patient that the compromised limb is working regularly. Mirror therapy effects may influence the activity of mirror neurons [26]. A review [27] including 14 studies including 567 enrolled subjects who had utilized mirror therapy reported that, compared to other approaches, the former was associated with a greater impact with regard to benefiting motor function.

Virtual reality technologies are novel rehabilitation approaches utilizing interaction with virtual elements found in the environment [28]. A Cochrane review [29] reported a paucity of proof regarding the hypothesis claiming that virtual reality and interactive exercises might be associated with a greater benefit in daily functioning, compared to conventional treatments. Results from a meta-analysis on virtual reality [30] found that most of the included studies had reported evidence of significant motor recoveries after stroke for the upper limbs. Data from randomized controlled trials are needed to confirm this finding.

Robot-assisted rehabilitative devices have been shown to facilitate upper limb motor recovery in the absence of a significant benefit with regard to functional ability [31]. Specifically, in the UL-Robot Trial [32], one group received robot-assisted therapy, and the second group was prescribed standard physical therapy. The two groups were each compared to a cohort prescribed standard care. Whilst a superiority of the former therapy over the latter was not observed, both therapies did, however, prove to be better than standard care. Here, the authors suggested that the intensity of training might have acted decisively on motor recovery. Likewise, the Locomotor Experience Applied Post-Stroke (LEAPS) Trial, carried out by Duncan et al. [33], compared the impacts of robot-assisted rehabilitative devices through the employment of a body-weight-supported treadmill versus a standard home physical therapy program. The authors reported that most of the subjects (52%) referred to having improved walking function. However, no significant intergroup differences were recorded.

Concerning novel rehabilitation modalities, noninvasive brain stimulation techniques aimed at stimulating adaptative plasticity have produced beneficial early-phase results [34]. The theoretical model for brain stimulation is regarded as an "interhemispheric interaction" between the two primary motor cortices [35]. In healthy subjects, these cortices exert mutual inhibition at rest [8]. The interhemispheric competition model assumes that the unopposed excessive inhibition on the part of the healthy to the compromised hemisphere might hamper post stroke recovery. This theoretical model comprises (a) a post stroke imbalance of interhemispheric motor interactions, (b) diminished motor activity in the lesioned hemisphere and (c) overactive motor activity in the contralesional hemisphere.

The modulation of such an imbalance might foster motor recovery via brain stimulation in stroke survivors [34]. Presently, the two techniques for enabling enhancement and inhibition of a cortical nature [3] are repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS). In the former, a coil generates a focal magnetic field on the scalp, therein inducing, transiently, focally and reversibly, an electric current in the cortex below. Stimulation in the range of 1Hz alleviates cortical excitability, whereas greater frequencies raise cortical excitability. As for tDCS, weak direct currents are delivered to the cortex by way of two electrodes that aim to polarize the underlying tissue.

Correct electrode placement is required, so as to appropriately modulate both the current flow's distribution and direction. To this regard, anodal stimulation is associated with an excitatory effect through cortical neuron depolarization, whilst cathodal tDCS hyperpolarizes neurons via the suppression of cortical excitability.

Corti et al. [36] have suggested that rTMS is safe to use and could also be effective in facilitating motor recovery. Double-blinded, sham-controlled Phase II and Phase III clinical trials with larger sample sizes are needed to confirm this benefit. Hsu et al. performed a meta-analysis of 18 randomized controlled trials investigating rTMS benefit on upper limb motor impairment [37]. The authors, for motor outcome function, reported an associated benefit for subcortical stroke when low-frequency rTMS was applied to the unaffected hemisphere. Future well-designed randomized controlled trials are needed to confirm this finding. Results from a pilot randomized controlled trial performed by Kedhr et al. [38] showed that anodal and cathodal tDCS outperformed the sham stimulation with regard to the effects of rehabilitation of a training nature.

A review [34] of published tDCS studies reported positive stroke recovery results. However, albeit a large multicenter randomized study, most of the included studies were proof-of-concept investigations having limited sample sizes [35]. The current issues in current tDCS research for stroke recovery include the determination of optimal dosages and montages, the obtainment of reliable data able to predict long-term safety profiles, and finally, how to achieve a better estimate of the effect size of tDCS.

## 4. Conclusions

Stroke rehabilitation is a continuously evolving field. A greater understanding of the mechanisms underlying stroke recovery, along with advances in technology, are allowing for the development of more effective approaches able to effectively alleviate the burden of acquired stroke disability. In addition, when led by a structured multidisciplinary team, these regimens will more likely determine greater benefits.

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