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Rehabilitation Strategies and Key Related Mechanisms Involved in Stroke Recovery

Hideki Nakano

Abstract

Poststroke rehabilitation requires a thorough understanding of the neural mechanisms underlying motor function recovery. This chapter outlines these mechanisms and also discusses the corresponding rehabilitation strategies based on the functional characteristics of the brain. The main topics we discuss are as follows: Although ipsilateral brain region activity is inhibited when using the limbs under normal conditions, it is thought that a decrease in this inhibition and the subsequent increased ipsilateral brain area activity post-injury promote recovery in the damaged contralateral neural network. For optimal poststroke motor function recovery, it is important to normalize the resulting imbalance in brain activity. Therefore, increased corticomotor excitation in the injured hemisphere or decreased excitation in the non-injured hemisphere must be promoted. Rehabilitation strategies include reducing non-paretic limb somatosensory input to decrease excitation in the non-injured hemisphere, increasing paretic limb somatosensory input to increase excitation in the injured hemisphere, increasing excitation in the injured hemisphere through movement training of the paretic hand and anesthesia of the paretic upper arm, increasing excitation in the injured hemisphere, or reducing excitation in the non-injured hemisphere. Considering the functional characteristics of the primary motor area, during the early stages after stroke, it is important to increase the somatosensory input to the paralyzed side and combine mental practices using motor imagery.

Keywords: neurorehabilitation, stroke, brain injury, neural plasticity, functional recovery, motor imagery, mental practice

1. Introduction

Stroke is a central nervous system condition that is prevalent worldwide. According to a report from the World Health Organization [1], approximately 15 million people experience a stroke each year globally, and stroke is the third leading cause of death after heart disease and cancer. As impairment of motor function after a stroke drastically impedes activities of daily living (ADL) and reduces the quality of life [2], the development of effective rehabilitation methods, which encourage the recovery of motor function in patients who have sustained a stroke, is an important task.

Although the 2014 Cochrane Stroke Systematic Review reported several rehabilitation methods demonstrating moderate results in the recovery of upper limb motor function after a stroke, a highly effective method is yet to be established [3]. Understanding the neural mechanisms underlying motor function recovery after brain injury is indispensable for the development of highly effective poststroke rehabilitation strategies. Therefore, in this chapter we will outline these mechanisms and introduce strategies based on these mechanisms as well as on the functional characteristics of the brain.

2. Brain reorganization after brain injury

The brain is a highly plastic organ with the ability to reorganize as a result of learning or injury. In cases of injury in the motor cortex or corticospinal tract, the recovery of motor function is taken care of by the surviving brain regions. Dancause [4] has reported on cortical reorganization accompanying injury in the primary motor cortex. Neurons in the hand area of the primary motor cortex receive input from the fingers as well as the wrist/forearm, and signals are sent from the hand area of the primary motor cortex to the corresponding ipsilateral premotor area. If the hand area of the primary motor cortex is injured, elimination of the inhibitory neurons in the primary motor cortex leads to an increase in the input to the hand area from the wrist/forearm. This results in an enlargement of the wrist/forearm area and shrinking of the hand area of the ipsilateral premotor area. However, as inhibitory neurons at the non-injured side are eliminated, the hand area of the premotor area and the primary motor cortex at the non-injured side also enlarge. Subsequently, reorganization leading to functional recovery occurs through learning and practice. The hand area of the primary motor cortex continues to enlarge as networks are stimulated or adjacent areas are inhibited through changes in synaptic receptor density or the creation of new synapses due to neuroplasticity. Neural networks are also reorganized through the formation of new connections between neurons and axonal sprouting. Thus, brain areas in both the injured and non-injured hemispheres are involved in the functional repair process accompanying recovery after brain injury.

Premotor area activity is also important for the recovery of motor function after a brain injury. Apart from being responsible for certain functions of the motor network, the premotor area is also involved in the integration of sensory and cognitive information in the course of goal-oriented behavior (actions carried out with a clearly established goal or aim, such as ADL). It receives sensory information from the parietal lobe and cognitive information from the dorsolateral prefrontal cortex and the supplementary motor cortex, which are then integrated and sent to the primary motor cortex. This information is also sent directly to the spinal cord via the corticospinal tract. These neural network connections are highly susceptible to plastic changes resulting from injury, learning, training, or therapy. Kantak et al. [5] discuss the reorganization of the premotor area involved in promoting motor function recovery after a brain injury. Reorganization of the premotor area on the injured/non-injured sides in the context of motor function recovery is influenced by the extent and site of the damage. For example, in cases of localized damage to the primary motor cortex or corticospinal tract, patients experience mild functional impairment. In this event, the premotor area on the injured side assists in the recovery of motor function, simultaneously increasing direct input to the corticospinal tract and to the remaining area of the primary motor cortex on the injured side. In cases of extensive damage to the primary motor cortex or

corticospinal tract, patients exhibit severe functional impairment. In contrast to cases of localized injury, in these cases, the premotor area on the non-injured side increases input to the surviving sensorimotor area of the injured side. Thus, the premotor areas of the injured and non-injured sides are involved in reorganization contributing to motor function recovery post-brain injury by way of two different strategies.

It is known that reorganization of the brain after an injury changes over time along with recovery of motor function. Nishimura et al. [6] caused injury to the corticospinal tracts of monkeys and then carried out rehabilitation to examine the changes in brain activity during the initial phase (1 month) and the stable phase (3 months) of motor function recovery. The study confirmed activity in both the contralateral and ipsilateral primary motor cortices during the initial recovery phase, during which the pinching motion success rate was 80%. Meanwhile, when the success rate reached 100% for the same motion during the stable recovery phase, ipsilateral primary motor cortex activity decreased, while contralateral activity increased and the contralateral area expanded. Based on this study, although the activity of ipsilateral brain regions is inhibited when using the hands or feet under normal situations, it is thought that a decrease in this inhibition and the subsequent activity in the ipsilateral brain areas post-injury promote recovery in the damaged contralateral neural network. Furthermore, it can be concluded that when the injured neural network has recovered substantially, either through repair of the original network or the mobilization of an adjacent network, the ipsilateral brain area returns to a state of inhibition similar to that observed before the injury.

Similarly, the abovementioned phenomenon can be observed in the process of motor function recovery in stroke patients. Using functional magnetic resonance imaging (fMRI), Ward et al. [7] explored the correlation between stroke patient motor outcomes (motor function evaluations) 3 months after the onset and brain activity when performing a visually induced motor task with the paretic hand. The results demonstrated that the number of motor-related brain areas utilized during the motor task was higher in patients with a poor outcome, while patients with a favorable outcome utilized fewer of these areas—a pattern of brain activity close to that of healthy individuals. Further, a negative correlation between motor outcome and the activity of task-related brain areas, such as the supplementary motor area, cingulate motor area, premotor cortex, posterior parietal cortex, and cerebellum, was shown. This negative correlation was confirmed for both the non-injured and injured primary motor cortices. Thus, it was understood that when performing motions with the paretic hand, the worse a patient's poststroke motor function, the more bilateral their brain activity. In a similar study, Rehme et al. [8] used fMRI to investigate longitudinal changes in motor network activity during the recovery of motor function in the initial phase after stroke onset. The authors measured the motor function recovery score and brain activity during movement of the non-paretic and paretic hands in stroke patients 2, 5, and 10 days after onset. The results demonstrated activity of the bilateral primary motor cortex, dorsal and ventral premotor area, and supplementary motor cortex during movement of the paretic hand in stroke patients (**Figure 1B**). Further, when the results were compared by level of motor function impairment, patients with mild impairment showed activity resembling that of healthy individuals at 2, 5, and 10 days, whereas patients with severe impairment showed increased bilateral activity over time (**Figure 1C**). As this bilateral activity demonstrated a positive correlation with motor function recovery (**Figure 1D**), it is thought to reflect neural restructuring in the initial phase after a stroke.

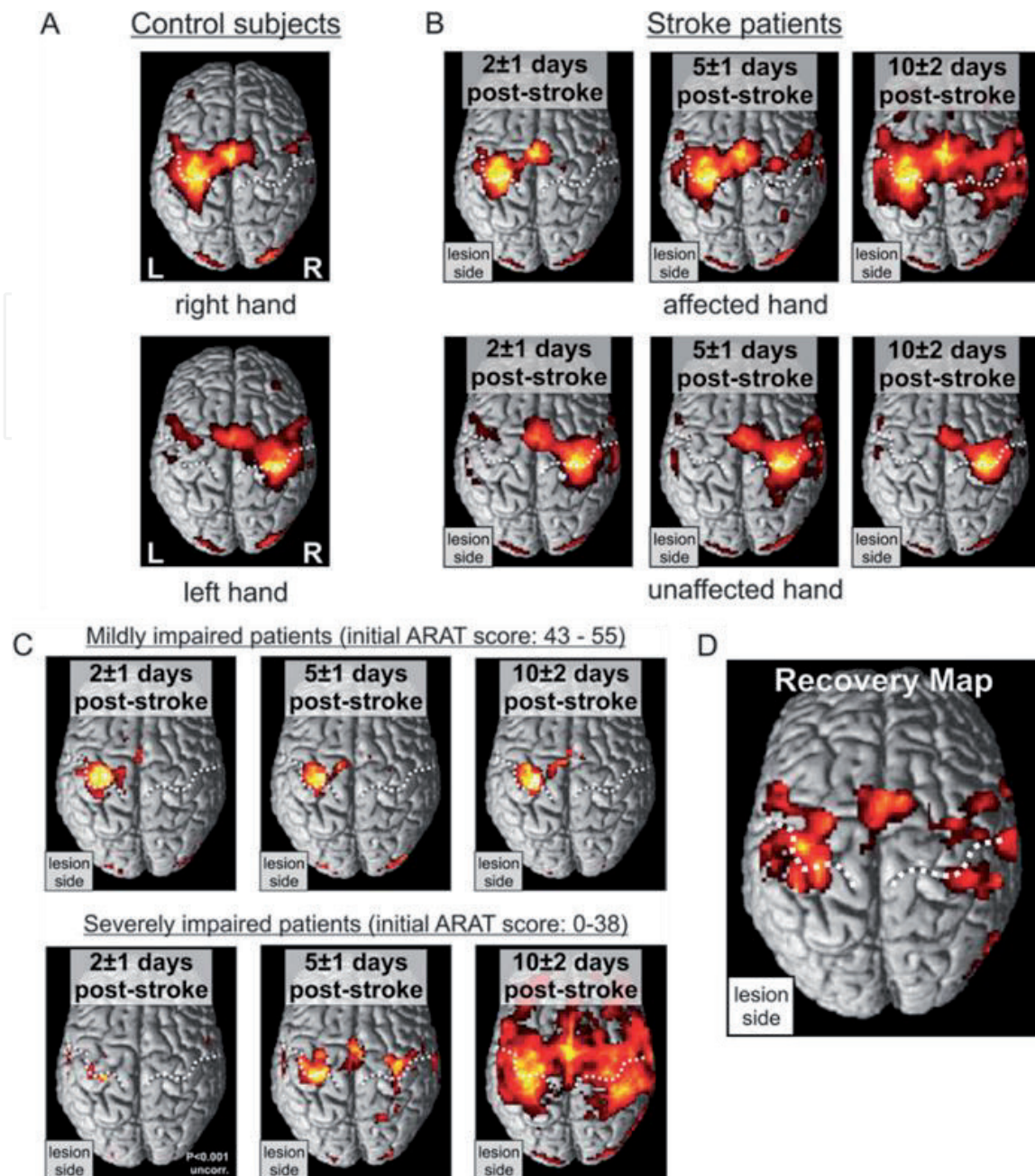


Figure 1. Longitudinal changes in motor network activity in the initial phase after stroke onset [8]. (A) Brain activity during right/left hand movement in healthy adults. (B) Brain activity during non-paretic/paretic hand movement in stroke patients (2, 5, and 10 days after onset). Bilateral activation is expanded for the paretic hand. (C) Brain activity during paretic hand movement for mild and severe stroke patients (2, 5, and 10 days after onset). In patients with mild functional impairment, only the contralateral hemisphere is active, whereas the activity in both hemispheres expands for severe patients. (D) Map of brain regions involved in favorable motor function recovery.

3. Interhemispheric inhibition imbalance after brain injury

Interhemispheric inhibition refers to the phenomenon in which activation of one side of the cerebrum inhibits the activity of neurons in the opposite side of the brain [9]. In humans, sensory information from the right half of the body is normally conveyed to the neocortex of the left hemisphere, while sensory information from the left half of the body is conveyed to the neocortex of the right hemisphere. The left and right neocortices are connected via the corpus callosum. The inhibition of information exchange between the left and right hemispheres allows humans to move the bilateral upper and lower limbs dexterously. Recent research has revealed the mechanism of this neural network of interhemispheric inhibition. Palmer et al.

[10] explored neuronal activity in the left and right brain of conscious rats with foot stimulation in order to observe nerve activity in a more natural setting. This study revealed the following series of events: when information is conveyed to one side of the neocortex, excitatory information is conveyed to the other side via the corpus callosum, activating the inhibitory nerve cells that exist on its surface and releasing gamma aminobutyric acid (GABA)—an inhibitory neurotransmitter—within the brain. GABA binds to GABA_B receptors on the dendrites of pyramidal neurons within layer V of the neocortex, thereby inhibiting nerve activity.

However, this interhemispheric inhibition between the left and right brain becomes imbalanced after a brain injury, leading to various dysfunctions. Grefkes et al. [11] investigated the functional intrahemispheric and interhemispheric connections of motor-related areas during voluntary hand movement in healthy individuals and stroke patients using fMRI. Interhemispheric inhibition functioned normally as described above for healthy individuals; it was found that in the resting condition, the left and right brain inhibited one another, while motor-related areas within each hemisphere stimulated one another (**Figure 2A**). It was further found that when healthy individuals moved the right hand, inhibition from the right hemisphere to the left hemisphere ceased, and inhibition from the left hemisphere to the right hemisphere was activated (**Figure 2B**). However, in contrast to healthy individuals, when stroke patients moved the paretic right hand, the right hemisphere (non-injured primary motor cortex) was found to inhibit the left hemisphere (injured primary motor cortex) (**Figure 2C**), such that the stronger the inhibition, the lower the motor performance in the paretic hand (**Figure 2D**). Use-dependent plasticity (use-dependent reorganization) is involved in this imbalance in interhemispheric inhibition in stroke patients [12]. Stroke causes paresis of the upper and lower limbs resulting in reduced motor function. As such, stroke patients commonly disuse the paretic limbs while overusing the non-paretic limbs. This poststroke disuse of the paretic and overuse of the non-paretic limbs—in other words, imbalance in the frequency of use for paretic vs. non-paretic limbs—is believed to influence the balance of the left and right cerebrum.

How does the disuse of the paretic limbs and overuse of the non-paretic limbs influence the left and right cerebrum in reality? Avanzino et al. [13] established an environment resembling that of a hemiplegic patient to explore the effect of restraining one-sided upper limb use in healthy individuals on interhemispheric balance using transcranial magnetic stimulation (TMS). To examine cortical changes due to abnormal unequal use of the hands, two experimental groups were compared: a group in which one hand (right) was fixed in place but the loose hand (left) could be moved freely and a group in which use of the left hand was also restricted. Note that the upper limbs were restrained for a period of 10 min. Despite the short restraint period, disuse of the right upper limb was found to decrease excitation in the left primary motor cortex and reduce interhemispheric inhibition from the left hemisphere to the right for both groups. Further, the group that not only disused the right upper limb but also overused the left upper limb showed increased excitatory activity in the primary motor cortex of the right hemisphere and increased interhemispheric inhibition from the right hemisphere to the left. Thus, it was revealed that disuse of one upper limb and overuse of the other—that is, imbalance in usage frequency between both upper limbs—causes imbalance between the cerebral hemispheres.

The hypothesis regarding the imbalance in interhemispheric inhibition post-brain injury is called the abnormal interhemispheric inhibition hypothesis [14, 15]. It states that in cases of subcortical brain injury, an abnormal inhibitory effect arises from the non-injured hemisphere, in which there is increased excitation, to the injured hemisphere. There are two conceivable strategies for

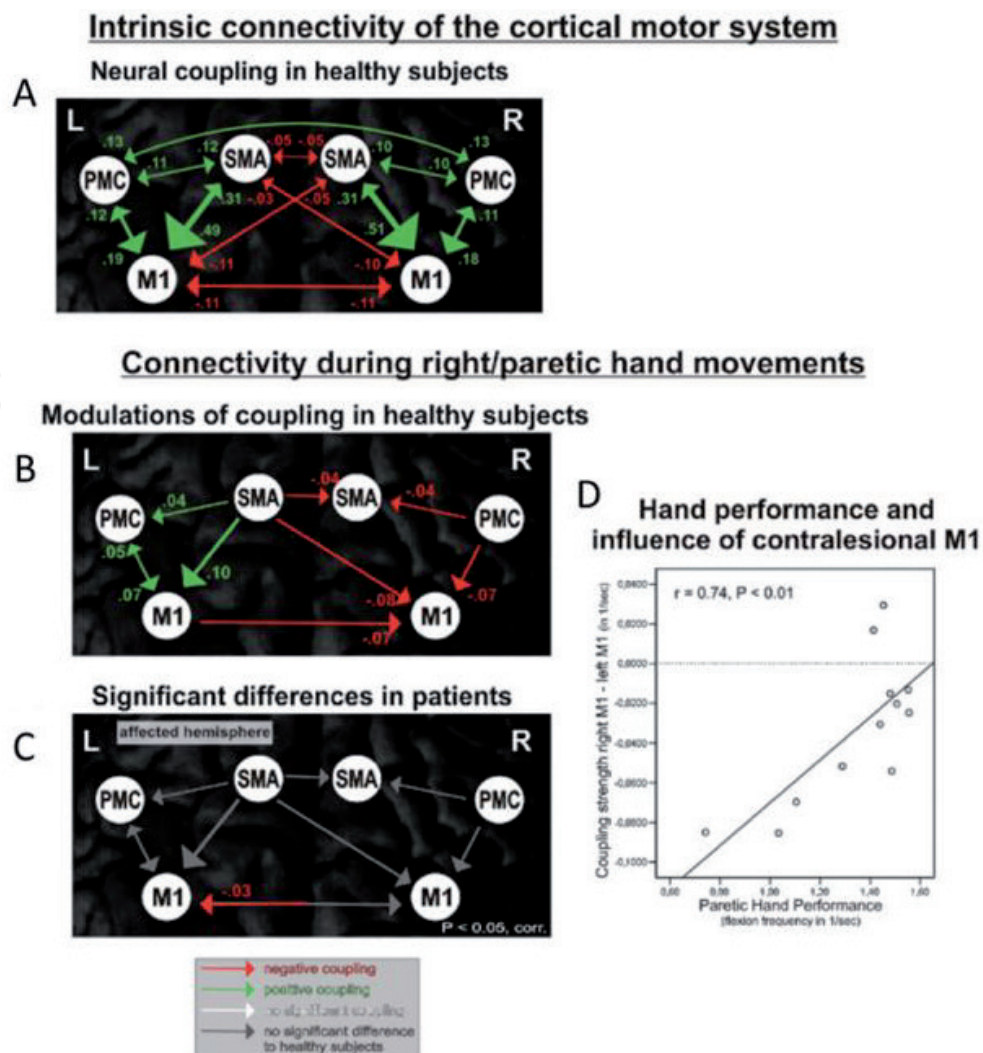


Figure 2.

Differences in cortical connectivity between healthy adults and stroke patients [11]. Green arrows represent excitation and red arrows represent inhibition. (A) Intra-/interhemispheric functional connectivity in healthy adults at rest. (B) Intra-/interhemispheric functional connectivity in healthy adults during voluntary movement of the right hand. (C) Intra-/interhemispheric functional connectivity in stroke patients during voluntary movement of the paretic hand (right hand). (D) Correlation between interhemispheric inhibition of the primary motor cortex and motor performance for the paretic hand (right hand) in stroke patients. The stronger the inhibition from the non-injured hemisphere to the injured hemisphere, the more the paretic hand motor performance was reduced.

treatment interventions corresponding to this hypothesis: increasing corticomotor excitation in the injured hemisphere or decreasing excitation in the non-injured hemisphere. Approaches for these strategies are known as hypothesis-driven approaches (**Figure 3**) [16]. Specifically, proposed methods include (1) reducing non-paretic limb somatosensory input in order to decrease excitation of the non-injured hemisphere, (2) increasing paretic limb somatosensory input in order to increase excitation of the injured hemisphere, (3) increasing excitation in the injured hemisphere through a combination of movement training of the paretic hand and anesthesia of the paretic upper arm, (4) directly increasing excitation in the injured hemisphere, or (5) directly reducing excitation in the non-injured hemisphere. With regard to procedures to directly manipulate excitation in one hemisphere, as in methods (4) and (5), effects can be exerted through the use of noninvasive brain stimulation methods such as transcranial direct current stimulation (tDCS) or repetitive transcranial magnetic stimulation (rTMS). These methods of stimulation bring about changes that are similar to long-term potentiation or long-term depression, resulting in increased or reduced excitation,

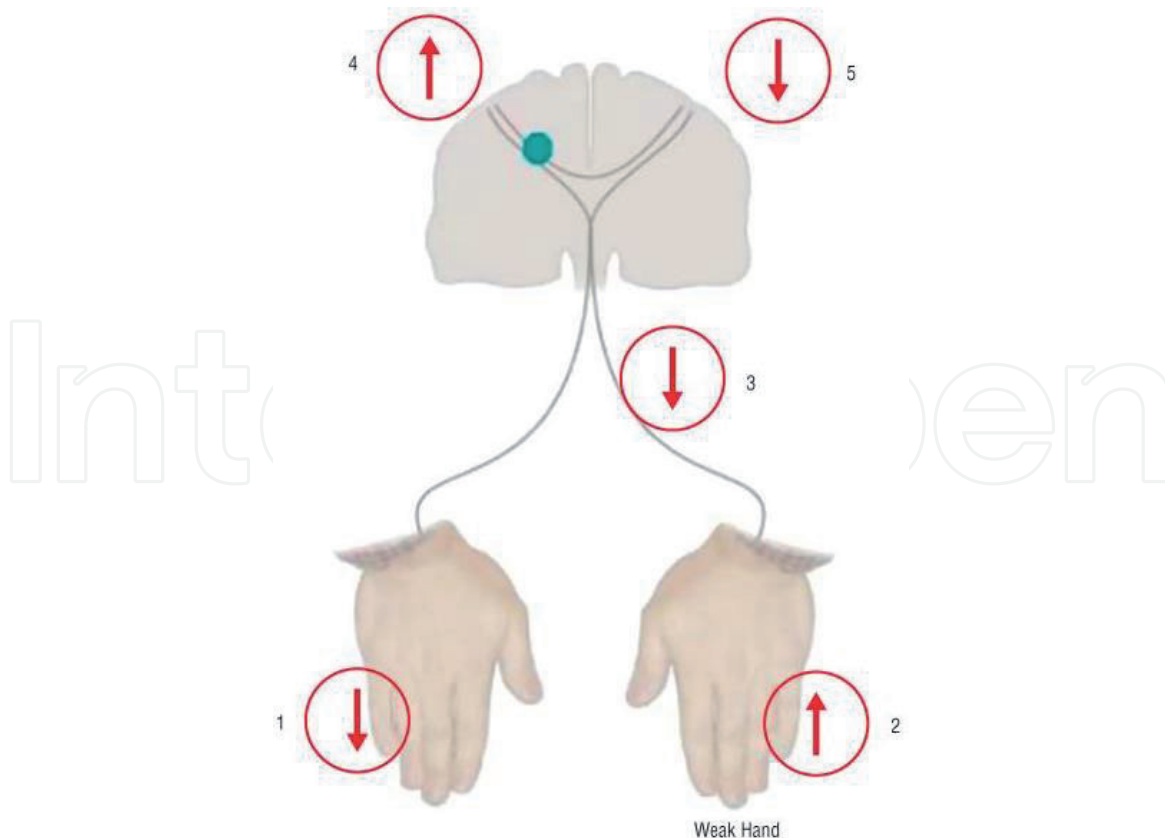


Figure 3.

Approach based on the abnormal interhemispheric inhibition hypothesis (hypothesis-driven approach) [16]. (1) Reducing non-paretic limb somatosensory input in order to decrease excitation in the non-injured hemisphere. (2) Increasing paretic limb somatosensory input in order to increase excitation in the injured hemisphere. (3) Increasing excitation in the injured hemisphere through a combination of movement training of the paretic hand and anesthesia of the paretic upper arm. (4) Directly increasing excitation in the injured hemisphere. (5) Directly reducing excitation in the non-injured hemisphere.

respectively, at the stimulation site. Regarding the efficacy of these methods, Hsu et al. [17] performed a meta-analysis that showed that rTMS was effective in motor function recovery in stroke patients. It was also reported in the 2011 Cochrane Review [18] that tDCS improved ADL function poststroke. At present, it has been established that the effects of rTMS and tDCS work on cortical neuromodulation and do not cause direct recovery from paresis. In other words, these methods are used for preconditioning to create a more plastic state in the brain or to stabilize the activity of the cerebral cortex. It is thought that these effects can be demonstrated with a combination of motor therapy, which is based on the process of motor learning. Constraint-induced movement therapy (CI therapy), established by Wolf et al. [19] and Taub et al. [20], is representative methods (1) and (2). In CI therapy, the non-paretic upper limb is first restrained in a sling or with a mitten to create a situation in which the patient is forced to use the paretic upper limb. Voluntary movement is then induced on the paretic side with intensive tasks of incremental difficulty levels leading to improvement in motor function. Regarding the results of this method, the 2009 Cochrane Review [21] confirmed the short-term effects on the recovery of motor function in stroke patients directly after CI therapy intervention. A meta-analysis by Langhorne et al. [22] about the effects of various rehabilitation methods on upper limb paresis in stroke patients also found that CI therapy had better intervention effects than other methods and that there was little variation among such effects. In addition, recent studies have used randomized comparative experiments to study the effects of behavioral strategies for the utilization of function acquired through CI therapy in daily life (transfer

package) [23, 24], as well as research examining the effects of motor therapy, which combines CI therapy with the abovementioned rTMS and tDCS [25, 26]. In this way, it is essential that motor therapy in the rehabilitation of stroke patients be developed with sufficient consideration to the imbalance in interhemispheric inhibition between the left and right cerebrum.

4. Rehabilitation strategies based on the functional characteristics of the brain and advances in clinical practice guidelines

Research by Geyer et al. [27] showed that the human primary motor cortex consists of two different regions: the anterior portion (IVa area) and the posterior portion (IVp area). These two regions differ in cell structure and receptor density. The IVa area is located in the anterior (rostral) portion of the primary motor cortex. This area is phylogenetically ancient and is thus referred to as the old primary motor cortex (Old M1). Outputs from the Old M1 control physical movement via the corticospinal tract and spinal interneurons. Meanwhile, the IVp area is found in the posterior (caudal) portion of the primary motor cortex and, being a newer section of the motor cortex compared to the IVa, is known as the New M1. New M1 includes cortical motoneurons, which synapse directly with spinal motoneurons. These synaptic connections are not mediated by spinal interneurons and are involved in the execution of extremely masterful and complex movements [28].

In light of the neural network functional disparity between the IVa and IVp areas of the primary motor cortex, Sharma et al. [29] proposed the somatosensory feedback for the paretic limb as one factor influencing the recovery of motor function after stroke (**Figure 4A**). The authors suggested that increased neural activity in the IVp area due to somatosensory input is involved in the recovery of motor function. Loubinoux et al. [30] investigated brain areas involved in motor function recovery for stroke patients using fMRI. They found that stroke patients with high neural activity in the IVp area had favorable motor function recovery in the hand and that neural activity in the IVp area predicted motor performance 1 year later. This suggests that early poststroke stimulation of neural activity in the IVp area of the injured hemisphere is critical for rehabilitation. As described above, the IVa and IVp areas are structurally disparate, but they are also functionally different with respect to afferent somatosensory information processing. Strick et al. [31] investigated differences in neural activity in the rostral (IVa) and caudal (IVp) areas of the primary motor cortex in monkeys using inputs from different sensory modalities. Their study found that the rostral primary motor cortex has plentiful cells that respond to the characteristic sensory input of muscles and joints, while the caudal area has an abundance of cells responding to cutaneous sensation input. Thus, it was suggested that providing cutaneous sensation to the paretic limb was important for increasing excitation in the IVp area. It was further found that neural activity in this IVp area was influenced by actively drawing attention. Binkofski et al. [32] examined the effect that directing attention to behavior had on neural activity in the IVa and IVp areas of the human primary motor cortex using fMRI. The authors found that the neural activity in the IVp area was affected by drawing attention to behavior, but this effect was not present in the IVa area. This suggested that apart from providing simple sensory stimulation, directing participants' active attention would also be beneficial for increasing neural activity in the IVp area. To summarize, for poststroke motor function recovery, it is considered important to increase the neural activity of the IVp area by providing somatosensory input to the paretic limb while capturing the patient's active attention.

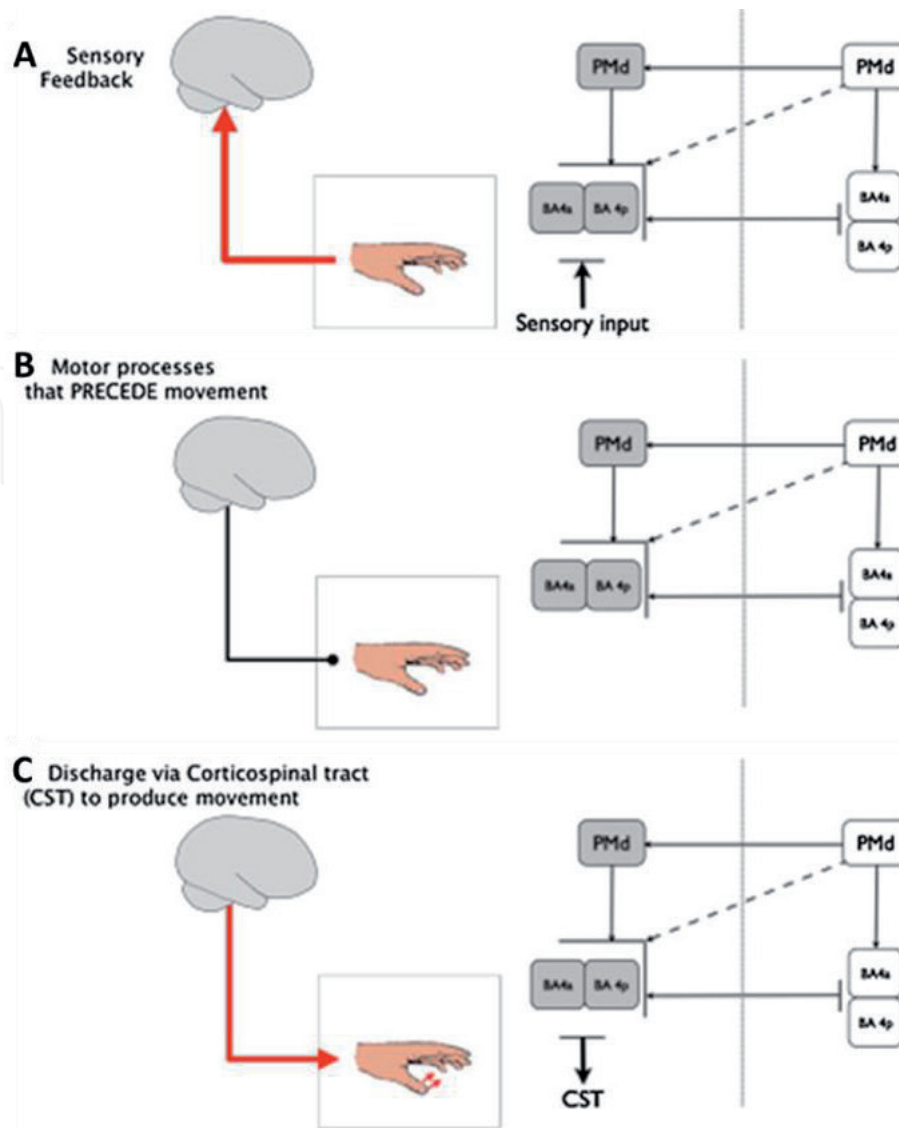


Figure 4. Three factors influencing motor function recovery after a stroke and the corresponding neural networks [29]. The injured hemisphere is shown in gray and the non-injured hemisphere in white. (A) Somatosensory feedback: This network can be accessed through somatosensory input such as peripheral nerve stimulation. (B) Processes preceding movement such as a movement plan: This network can be accessed through motor imagery or action observation. (C) Discharge via the corticospinal tract to produce movement: This network is involved in physical movement but predominantly through the combination of the other two (A and B).

Sharma et al. [29] proposed, as a second factor involved in poststroke recovery of motor function, activities preceding movement (**Figure 4B**). We know that the IVp area is excited in the same way by both the abovementioned somatosensory input and mental representations, such as motor imagery and preceding movement. Using fMRI and healthy adults, Sharma et al. [33] conducted a study of neural activity in the primary motor cortex (IVa and IVp areas) while the subjects imagined movement. The results demonstrated that the relative involvement of imagining movement was larger in the IVp area than that in the IVa area. Sharma et al. [34] then explored the relationship between neural activity in the primary motor cortex (IVa and IVp areas) in stroke patients, while imagining movement and motor performance using fMRI. The authors found that, while imagining movement of the paretic hand, the neural activity in the injured side of the IVp area of stroke patients was positively correlated with motor performance. These studies suggest that the neural activity of the IVp area, when imagining movement, can be used as a tool to predict motor function in stroke patients and, further, that intervention with tasks involving motor imagery may increase excitation in the IVp area.

A third factor influencing recovery of motor function after stroke suggested by Sharma et al. [29] is discharge via the corticospinal tract to produce movement (**Figure 4C**). This network is involved in all physical movement but predominantly through the combination of the other two. That is, this neural network for producing movement is predominantly utilized via the mutual involvement of the neural network based on somatosensory feedback and the neural network preceding movement. As a specific example, Nilsen et al. [35] and López et al. [36] conducted a systematic review and found that combining mental practice and the use of motor imagery with physical movement improved intervention effects. Further, a Cochrane Review [37] also reported that mental practice interventions combined with motor therapy, including physical movement, were more effective than mental practice alone. We also reported that neurofeedback-based motor imagery training combined with physical movement contributed to improving upper extremity function in stroke patients [38]. These findings indicate that somatosensory feedback accompanying physical movement promotes the effects of motor imagery interventions. In other words, the neural network preceding movement and that for somatosensory feedback may work together to enhance motor performance.

To summarize, the factors influencing motor function recovery accompanying the reorganization of the IVP area after a stroke are (1) somatosensory feedback to the paretic side; (2) movement-preceding activities, which utilize motor imagery and action observation; and (3) discharge via the corticospinal tract to produce movement. As (3) is ultimately effective through the combination of the neural networks involved in (1) and (2), information processing combined with somatosensory input to the paretic limb should take priority in motor therapy for hemiparetic stroke patients exhibiting motor paresis. Next, treatment should precede mental practice interventions utilizing motor imagery induction, based on estimations from that information processing and from motor practice producing movement through an exercise program based on those movement-preceding activities. This step-by-step intervention strategy is considered vital.

Nevertheless, according to the Guidelines for the Management of Stroke [39], the following therapies are recommended for rehabilitation for upper limb dysfunction—for patients with mild paralysis, a therapy that suppresses the non-paralyzed upper limb and forces the use of the paralyzed upper limb in life is highly recommended (grade A). For moderate paralytic muscles (such as wrist and finger extensors), electrical stimulation is recommended (grade B). For patients with mild to moderate paralysis, training should be performed with repetition of certain movements (reach movement of the upper limb on the paralyzed side, goal-oriented movement, repetitive movement of both upper limbs, mirror therapy, repetitive facilitation exercise, etc.) is recommended (grade B). rTMS and tDCS may be considered, but care must be taken in patient selection and safety (grade C1).

Moreover, the following therapies are recommended for rehabilitation for gait disorders—increasing the amount of limb training associated with walking or of walking itself is strongly recommended to improve walking ability (grade A). For stroke hemiplegic patients with equinovarus feet, it is recommended to use short leg braces to improve walking (grade B). Botulinum therapy and intramuscular nerve block to the tibial nerve or the lower leg muscle using 5% phenol is recommended when the spastic equinovarus foot hinders walking and ADL (grade B). Tendon transfer may be considered for patients presenting with spastic equinus and abnormal gait (grade C1). Biofeedback using electromyogram and joint angle is also recommended to improve walking (grade B). Functional electrical stimulation is recommended for chronic stroke patients with drooping foot, but the duration of treatment effect is short (grade B). Treadmill training is recommended because it improves walking speed and endurance in ambulatory stroke patients (grade B).

Walking training using a walking assist robot is recommended for those who cannot walk within 3 months of onset (grade B).

Furthermore, the following therapies are recommended for rehabilitation in cases of movement disorders and ADL. For stroke sequelae, active rehabilitation from the early stage is strongly recommended to promote the recovery of dysfunction and disability (grade A). It is strongly recommended to increase the amount and frequency of training early after onset to promote more effective recovery of disability in patients (grade A). For lower limb function and ADL, repeated task training is recommended (grade B).

Based on the above guidelines, it is necessary to consider three points: (1) dose dependency, (2) task dependency, and (3) neuroplasticity, in order to promote effective functional recovery in stroke rehabilitation.

In clinical practice, it is important to perform optimal rehabilitation for stroke patients while keeping the functional characteristics of the brain and the existing guidelines in mind.

5. Final remarks

In this chapter, we outlined the neural mechanisms underlying motor function recovery after stroke-related brain injury. We have also outlined the corresponding rehabilitation strategies based on the functional characteristics of the brain and advances in clinical practice guidelines. We discussed how, considering the functional characteristics of the primary motor area, it is important during the early stages after stroke to increase the somatosensory input to the paralyzed side and combine mental practices using motor imagery. The existing guidelines highlighted the importance of dose dependency, task dependency, and neuroplasticity, in promoting effective functional recovery in stroke rehabilitation. Understanding the rehabilitation strategies and key related mechanisms involved in stroke recovery is indispensable for the development of highly effective poststroke rehabilitation.

6. Future directions

Previous studies have shown that the recovery of motor function after stroke is acutely related to the functional replacement of damaged neuronal circuits and the interhemispheric imbalance model. Therefore, it is important to promote neuroplasticity related to motor function recovery in rehabilitation. In addition to the use of evidence-based clinical practice guidelines, rehabilitation strategies that take into account the functional characteristics of the brain may maximize the recovery of motor function in stroke patients. In the future, it is expected that improved intervention strategies will be widely applied in the clinical setting by accumulating knowledge about the pathology of relevant cases and brain areas.

Conflict of interest

The authors declare no conflict of interest.

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