# Application of Mirror Neuron System in Post Stroke Rehabilitation

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Abstract: Skill development by enhancing experience-dependent plasticity using mirror neuron system through motor imagery and or virtual reality approach has been increasing nowadays. Mirror neuron as a visuomotor neuron will activated in relation to movement of body parts or in observation of the actions. Several studies have examined this network and properties in humans and prove the mechanisms in enhancing neuroplasticity. Although there are many studies for on the mirror neuron system, several questions remain unanswered. The motor imagery and virtual reality as the practical approach studies in post stroke rehabilitation also showed none of this approach was absolutely superior to each other. To increase the comprehension of mirror neuron system involvement in post stroke rehabilitation, this article is try to focusing on the review of motor imagery and virtual reality approach that use the principle.

## 1 INTRODUCTION

Stroke is the most common acquired neurological disease in the adult population and a leading cause of disabilities worldwide (Aqueveque et al., 2017),(García-Rudolph et al., 2019). The prevalence of stroke in Indonesia reaches 10.9% in population according to the Indonesia basic health research in 2018 (Riskesdas, 2018). Increasing the number of stroke survivors make more survivors live with long-term disability. To manage the impact, interdisciplinary complex rehabilitation interventions were required and assumed to represent the mainstay of post-stroke care.

Optimal functional recovery of stroke is the ultimate goal of neurorehabilitation after acute brain injury. Optimizing sensorimotor performance in functional action is the main goal of rehabilitation. New brain imaging techniques are making it clear that the neurological system is continually remodeling throughout life and after damage through experience and learning in response to activity and behavior (Aqueveque et al., 2017). The potential ability of the brain to readapt after an injury is known as neuroplasticity, which is the basic mechanism underlying improvement in functional outcome after stroke. Therefore, one important goal of rehabilitation of stroke patients is the effective use of neuroplasticity for functional recovery (Winstein CJ et al., 2016).

The type and extent of neural plasticity are task-specific, highly time-sensitive and strongly influenced by environmental factors as well as motivation and attention. The recovery of function has been shown to depend on the intensity of therapy, repetition of specified-skilled movement directed toward the motor deficits and rewarded with performance-dependent feedback. Specifically, the exercise should be repetitive, task-specific, motivating, salient and intensive for neuroplasticity to occur (Aqueveque et al., 2017),(van Dokkum et al., 2015).

Evidence accumulated during the past 2 decades together with recent advances in the field of stroke recovery clearly shows that the effects of neurorehabilitation can be enhanced by behavioral manipulations. Recently, many training-oriented rehabilitation techniques have been developed, which allows the increase of independence and quality of life of the patients and their family (Aqueveque et al., 2017).

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Table 1: Classification according to ICF Model (Kwakkel, 2014).

| | Body Structure (i.e., the brain) | Body Function (i.e., upper limb) | Activity (a person) |
|---|---|---|---|
| Recovery | Any change in the structure that leads to improved function (includes restitution and substitution) | Improvement of the ability to perform a movement (includes compensation and restitution) | Improvement of the ability to perform a functional task (includes compensation and restitution) |
| Restitution | Repair: changes toward the original state | Identical employment of body components* as before the injury | Identical task performance as before the injury |
| Compensation/substitution | Alternative employment of body structures | Alternative employment of the same body components as before injury* | Task performance using alternative limbs and/or environmental adaptations |

* A body component is defined as a collection of body structures that contribute to a specific body function

Current resources today are unable to fulfill the intensity requirement for optimizing post-injury neuroplasticity, although standard rehabilitation helps improve motor function after stroke, only modest benefits have been shown. Limitation of conventional rehabilitation was including time-consuming, labor and resource-intensive, dependent on patient compliance, limited availability depending on geography, modest and delayed effects in some patients, requires transportation to special facilities, initially underappreciated benefits by stroke survivors and requires costs/insurance coverage after the initial phase of treatment (Saposnik et al., 2011).

As a result of the limitations of conventional rehabilitation, novel strategies targeting motor skill development and taking advantage of the elements enhancing experience-dependent plasticity have recently emerged. In the last 20 years, neuroimaging techniques and the discovery of mirror neurons system have brought about a deeper understanding of brain function, that turn has led to the design of new treatment approaches such as mirror-symmetric bimanual movement priming (motor imagery/MI) and virtual reality (VR) technology (Saposnik et al., 2011),(García Carrasco and Aboitiz Cantalapiedra, 2016). This article focuses on the review of both techniques in post-stroke rehabilitation.

# 2 DISCUSSION

## 2.1 Motor Recovery Through Cortical Plastic Reorganization

One of the most important areas affected by stroke is motor skills. Stroke usually results in injury to the cerebral cortex, most of the sensory-motor apparatus in the forebrain including the frontal and parietal cortex and/or subcortical structures in the striatum and thalamus, which then produces a deficit of motor function in the contralateral parts of the body (Selzer et al., 2014). Improvements in bodily functions and activities can generally occur spontaneously or as a result of the learning process. These include processes of restitution (restoring damaged nerve tissue function), substitution (reorganization of nerve pathways to relearn lost functions), and compensation (new motor patterns resulting from adaptation or motor substitution remaining) (table 1).

Weakness and paresis are the most important impairments in the early stages after stroke as they lead to learned nonuse of limbs. Immobility, chronic pain, and some sensory impairments can also contribute to the learned non-use state. As the recovery progresses, spasticity and spastic co-contractions can induce some compensatory movements, which if are persistent in time and repeated may contribute to a learned bad use (Aqueveque et al., 2017).

Understanding the ability of the motor cortex to carry out functional and structural reorganization is very important to know because many studies in experimental animals and humans have shown that the functional and structural motor cortex can be modified by utilization. The principle of *use-dependent plasticity* occurs not only in the brains of healthy individuals to learn new motor skills but also in injured brains in re-learning motor skills. To understand the mechanism of plasticity (the brain's ability to reorganize by making new neural connections) post-injury, it is necessary to study the normal structure and function of the motor cortex area that functions to control movement. Rehabilitation approach using either MI or VR technology was intended to prevent the condition through a focused and repetitive exercise.

## 2.2 Mirror Neuron System

Mirror neurons system is a group of specialized neurons that “mirrors” the actions and behavior of others. It will discharge both when individuals perform a given motor act and when they observe others perform the same motor act (a movement that has a specific goal). The involvement of MNS is implicated in neurocognitive functions (social cognition, language, empathy, the theory of mind) and neuropsychiatric disorders (Rajmohan and Mohandas, 2007).

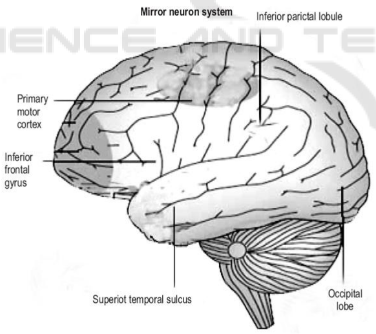

Figure 1: Mirror neuron regions in humans (Rajmohan and Mohandas, 2007).

Neuroimaging demonstrated the existence of 2 main networks with mirror properties: one residing in the parietal lobe and the premotor cortex plus the caudal part of the inferior frontal gyrus (parietofrontal mirror system), and the other formed by the insula and the anterior mesial frontal cortex (limbic mirror system)(figure 1). The parietofrontal mirror system is involved in the recognition of voluntary behavior, while the limbic mirror system is devoted to the recognition of affective behavior (Cattaneo and Rizzolatti, 2009).

Brain imaging studies reveal that action observation in humans activates the inferior frontal gyrus lower part of the precentral gyrus, the rostral part of the inferior parietal lobule and also the temporal, occipital and parietal visual areas. The frontal and the parietal mirror neuron regions are somatotopically organized. The activation of pars opercularis of the inferior frontal gyrus reflects the observation of distal hand and mouth actions, whereas the activation of the premotor cortex reflects proximal arm and neck movements. The mirror neurons will be firing on the frontal and temporal nodes with an observation of transitive actions, while that of intransitive (meaningless) actions result in the firing of the frontal node only.

## 2.3 Motor Imagery

Various definitions of motor imagery have been coined by experts. Sharma states that motor imagery is a dynamic state in which a representation of motor activity inactivated in memory without any motor output. Meanwhile, according to Mcavinue, the concept of motor imagery is a motor representation or prototype of the movement that is connected with the memory process. In short, motor imagery can also be interpreted as “activities to imagine the movement of the body”(Garcia-Rudolph et al, 2019).

Annett affirmed the importance of volunteer control of the imagery performers when doing motor imagery. Two perspectives can be used when imagining movement, internal perspectives, and external perspectives. In the internal perspective (or kinaesthetic), subjects imagine the sensations of motion in their bodies. External imagery or perspective was used visual component, in which subjects imagine seeing themselves from the viewpoint of an external observer. Therefore, the activity of imagining a movement from both an internal or external perspective that involves manipulating an object can be called motor imagery (García Carrasco and Aboitiz Cantalapiedra, 2016). Studies using Transcranial Magnetic Stimulation (TMS) show an increase in motor-evoked potential (MEP) amplitude which is a marker of corticospinal excitability. When motor imagery is performed there is an increase in MEP amplitude compared to at rest, MEP amplitude increases only in the muscles involved in imagined movements and when performing MI (figure 2). In general, kinesthetic imagery activates the cortical motor better than visual imagery (Ruffino, et al, 2017).

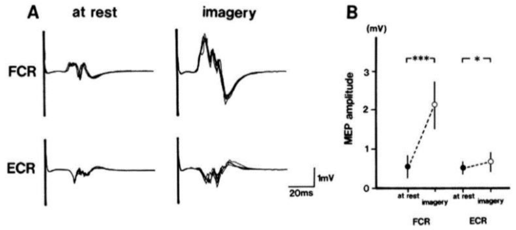

Figure 2: The specificity of corticospinal excitability in motor imagery. Increased MEP occurs in the flexor carpi radialis muscle (FCR) and not in the extensor carpi radialis (ECR) when imagining flexion movements of the hand (Ruffino et al, 2017).

The observation of other individuals performing skilled movements, as well as MI was proved effective for motor training. Neuroimaging studies have shown that the primary motor cortex (M1) and secondary motor areas, including the premotor cortex, supplementary motor area, and the parietal cortices, are activated during M1 tasks and motor execution (Lotze et al., 1999). Functional imaging is used to find out the involvement of primary cortex motor in motor imagery and compare it with real movements. Based on several previous studies, there are different conclusions regarding the involvement of the motor cortex, especially Broadmann area 4 (BA 4) in motor imagery. In primates and humans, BA 4 cam be divided into two, BA 4 anterior (BA 4a) and BA 4 posterior (BA 4p). BA 4a is thought to have more role in the execution of movements than produce a real movement. Whereas BA 4b is more involves in cognitive tasks and non-execution functions. Besides, BA 4b is also activated by sensory input and can be modulated by attention. Because motor imagery does not principally involve motor execution, it is suspected that activation of BA 4 when imagery is carried out is more inclined to BA 4p. However, Sharma's study shows that activation occurs in both BA 4p and BA 4a when performing motor imagery with B4p activation which tends to be stronger when compared to BA 4a. When compared to the execution of real movements, these two parts of the BA 4 area are relatively weaker when doing the motor imagery. Meanwhile, when viewed from its distribution, the activation of BA 4 between motor imagery and movement execution has a similar pattern. Cortex activation when motor imagery still adheres to the principle of motor lateralization in the brain similar to the execution of movements. The things above are proof of the relationship between the movement being executed and the motor imagery.

Motor imagery could also divide based on the motor representation involved whether it is done consciously (explicit motor imagery) or unconsciously (implicit motor imagery). The main difference between explicit and implicit motor imagery is the level of awareness involved in doing imagery. Explicit motor imagery can be measured by an independent questionnaire or by the mental chronometry paradigm. In this measurement, subjects are asked to do motor imagery and consciously imagine their movements. Whereas the implicit motor imagery measured is the prospective action decision or the motor perception of the participants. Participants are asked to make decisions based on the visual stimulus provided. For example, participants are asked to choose a picture of the position of the hand that is most comfortable holding a log in a certain position. When doing this task, participants are unconsciously asked to do motor imagery.

The following is a summary of changes or adaptations to the central nervous system that are triggered by motor imagery exercise (figure 3) (Ruffino et al., 2017):

a. At the cortical level, both cortical mapping that represents the muscles being trained and the excitability of the corticospinal pathway will increase in the first week of exercise. Furthermore, it will decrease when it reaches performance stabilization in the automation phase. In the initial phase of corticocerebellum tissue and corticostriatal tissue will be activated. Next, when achieving automation, only corticostriatal will be activated to recall the stored motor patterns.
b. At the cortical and spinal level, a long-term potentiation process can occur and synapses strengthen. Motor imagery will produce a subliminal motor signal that will run along the corticospinal tract until it reaches the structure in the spinal cord without activating alpha motor neurons. This subliminal motor signal will play a role in increasing the sensibility and conductivity of synapses on the corticospinal tract.
c. At the spinal level, there is a reduction in presynaptic inhibition which increases signal conductivity which is thought to be caused by descending motor output resulting from motor imagery exercise.

d.

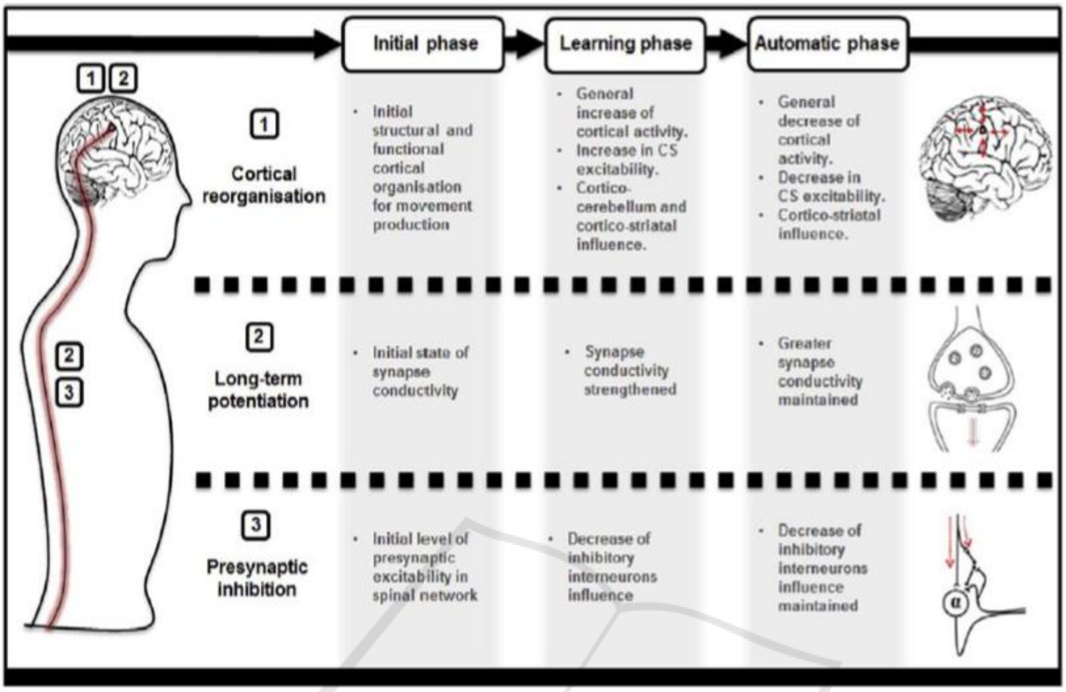

Figure 3: Neural Adaptation Model After Motor Imagery Exercise (Ruffino C, et al, 2017).

## 2.4 Virtual Reality

Virtual reality (VR) is a computer-based technology that allows users to interact with the multisensory simulated environment and receive “real-time” feedback on performance by computer software and experienced by the user through a human-machine interface (Calabrò et al., 2017a). VR is the stimulation of a real-time environment, scenario or activity that generated. VR is made using hardware and software that allows users to interact with objects and events that appear and sound, and in some cases can be felt, like those in the real world. These two environments communicate and exchange information through a barrier called interface. The interface can be considered as a translator between the user and the VR system. The user performs an action (e.g. movement, speaking) as input, this interface will translate this action into a digital signal that can be processed and interpreted by the system. The system will do a reaction that will be translated by the interface into something that users can feel physically (e.g. pictures, sounds, touching sensations, and so on). Finally, the users will interpret the information and react to the system. A stronger sense of “presence” in the virtual world can be achieved because of different feedback modalities including visual and audio feedback and less frequent haptic and vestibular feedback (Reinkensmeyer DJ et al., 2016).

VR provides the patient with multisensory feedbacks that can potentiate the use-dependent plasticity processes within the sensory-motor cortex, thus promoting or enhancing functional motor recovery through visuomotor cortical facilitation. Furthermore, VR can increase patient’s motivation during rehabilitation by decreasing the perception of exertion, thus allowing patients to exercise more effortlessly and regularly (Calabrò et al., 2017b) The use of an avatar may strengthen the use-dependent plastic changes within higher sensory-motor areas belonging to the mirror neuron system (MNS). The observation of an action, even simulated (on a screen) allow the recruitment of stored motor programs that would promote movement execution recovery. (Modroño et al., 2013) These processes are expressed by wide changes in α and β oscillation magnitude at the electroencephalography (EEG) across the brain areas putatively belonging to the MNS (including the inferior frontal gyrus, the lower part of the precentral gyrus, the rostral part of the inferior parietal lobule and the temporal, occipital and parietal visual areas). (Laver et al., 2015) Broadband involvement may be due to the recruitment of multiple brain pathways expressing both bottom-up (automatic recruitment of movement simulation) and top-down (task-driven) neural processes within the MNS implicated in locomotion recognition. Recent work has shown that observed, executed, and imagined action representations are decoded from putative mirror neuron areas, including Broca's area and ventral premotor cortex, which have a complex interplay with the traditional MNS area generating the rhythm (Filimon et al., 2015).

Training in VR is beneficial for restoring neural function through several neurophysiological processes that enhanced the potential for neuroplastic changes early in the recovery phase and stimulation of sensorimotor areas that may otherwise undergo deterioration due to disuse. Many of motor learning principles that become part of VR in successfully motor skill development such as massed repetition practice, task-specific practice, goal-directed task, and meaningful practice. This principle boosts the motivation of patients and serves as a pleasurable experience during treatment by controlling the level of difficulty and the variability of the task (Brunner et al., 2014). With VR, there also a potential mechanism of action that works in enhancing skill motoric development, such as augmented feedback that importance in motor learning. At the behavioral level, movement errors in the visual domain can influence motor cortical areas during moor learning and active/rewarded practice. Feedback can be used to reduce movement errors and can shape neural activity in motor and premotor areas. Even observation of actions was done in VR, if performed repetitiously an intentionally, it can facilitate the magnitude of motor evoked potential (MEPs) and influence corticocortical interactions (both intracortical facilitation and inhibition) in the motor and premotor areas (Fu et al., 2015).

## 2.5 Implications For Practice Of VR

Virtual reality-based interventions have been used for almost 2 decades, but there is still controversy regarding the efficacy of using virtual reality in stroke rehabilitation. Cochrane review conducted in 2017 concludes that the use of virtual reality and interactive video gaming is no more useful in improving function in the upper limbs when compared to conventional therapy. Virtual reality can improve upper limb function and activities of daily life if used in addition to previous therapies (to increase therapy time) (Laver KE et al., 2017). Meanwhile, a study by Maier et al evaluated the efficacy of 2 types of VR systems, named Specific VR (SVR) and Non Specific VR (NSVR) with Conventional Therapy (CT) for rehabilitation of upper limb function and activity after stroke with the results showed that SVR is more beneficial than CT in the recovery of upper limb function, whereas in the use of NSVR it does not show benefits (Maier M et al., 2019).

The VR system to train balance and the ability to walk in post-stroke patients needs special requirements that require greater technical space related to patient safety issues. In contrast to VR therapy in the upper limb which allows the patient to sit while doing movements with upper extremities, while for patients who have problems with balance and walking patterns require patients to walk upright. Systematic reviews and meta-analysis of randomized controlled trials conducted by Li et al and de Rooji et al, showed that VR can improve balance and ability to walk after a stroke. Llorens et al conducted a study with the result that exercise with virtual stepping can improve balance when compared to conventional therapy. Participants are required to step on items that appear around the circle with the nearest foot while maintaining the other foot in the circle. This intervention also encourages an increase in walking speed. The system is also used in home-based intervention with the same results as those done in the clinic (Maier M et al., 2019). The results of this study differ from the Cochrane review which shows that there is not enough evidence about the effectiveness of virtual reality and interactive video gaming on walking speed, balance, participation or quality of life for post-stroke patients (Laver KE et al., 2017).There is low-quality evidence that VR is a safe and effective method of improving function and activities of daily living function following stroke. Patients in the acute and subacute phases with milder severity strokes appear to be most likely to benefit from this technique. However, there is a lack of information regarding the most effective types of programs and even whether programs specifically designed for rehabilitation settings are more effective than commercial gaming console.

# 3 CONCLUSIONS

MI technique or VR systems can be applied as a single technique or combination for driving neuroplasticity and lead to benefits in motor function improvement after stroke. The use of MI or VR in post-stroke proved that it can facilitate cortical reorganization. Future studies need to be done to determine whether the combination of MI and VR with also conventional therapy will enhance stroke rehabilitation.

# REFERENCES

Aqueveque P, Ortega P, Pino E, Saavedra F, Germany E, Gómez B. After Stroke Movement Impairments: A Review of Current Technologies for Rehabilitation. In: Uner T, editor. 2017. Physical Disabilities-Theurapeutic Implications. Turkey:Intechopen;.p.95-116. Available from : https://doi.org/10.5772/67577

Brunner I, Skouen JS, Hofstad H, Strand LI, Becker F, Sanders AM, et al. 2014.Virtual reality training for upper extremity in subacute stroke (VIRTUES): study protocol for a randomized controlled multicenter trial. BMC Neurol. 2014 Sep 28;14:186.

Calabrò RS, Naro A, Russo M, Leo A, De Luca R, Balletta T, et al. 2017. The role of virtual reality in improving motor performance as revealed by EEG: a randomized clinical trial. J Neuroeng Rehabil. 2017 Jun 7;(14)1:53.

Calabrò RS, Russo M, Naro A, De Luca R, Leo A, Tomasello P, et al. 2017. Robotic gait training in multiple sclerosis rehabilitation: Can virtual reality make the difference? Findings from a randomized controlled trial. J Neurol Sci. 2017 Jun 15;377:25–30.

Cattaneo L, Rizzolatti G. 2009. The Mirror Neuron System. Arch Neurol. 2009 May;66(5):557–560.

de Rooij GLI, Meijer J. 2016. Effect of Virtual Reality Training on Balance and Gait Ability in Patients with Stroke: Systematic Review and Meta-Analysis. Phys Ther.2016 Dec;96(12):1905-18.

Diers M, Kamping S, Kirsch P, Rance M, Bekrater-Bodmann R, Foell J, et al. 2015. Illusion-related brain activations: a new virtual reality mirror box system for use during functional magnetic resonance imaging. Brain Res. 2015 Jan 12, 1594:173–182.

Filimon F, Rieth CA, Sereno MI, Cottrell GW.2015. Observed, Executed, and Imagined Action Representations can be Decoded from Ventral and Dorsal Areas. Cereb Cortex. 2015 Sep;25(9):3144–58.

García Carrasco D, Aboitiz Cantalapiedra J.2016. Effectiveness of motor imagery or mental practice in functional recovery after stroke: a systematic review. Neurologia. 2016 Jan-Feb;31(1):43–52.

García-Rudolph A., Sánchez-Pinsach D, Salleras EO, Tormos JM. 2019. Subacute stroke physical rehabilitation evidence in activities of daily living outcomes: A systematic review of meta-analyses of randomized controlled trials. Medicine (Baltimore) 2019 Feb;98(8): e14501.

Kwakkel G, Buma FE, and Selzer ME. 2014. Understanding the mechanisms underlying recovery after stroke. In Selzer ME, Clarke S, Cohen LG, Kwakkel G, Miller RH., Textbook of Neural Repair and Rehabilitation Vol 2(2). Cambridge University Press; 2014 .p.7-24.

Laver K, George S, Thomas S, Deutsch JE, Crotty M.2015.Virtual reality for stroke rehabilitation: an abridged version of a Cochrane review. Eur J Phys Rehabil Med, 2015 Aug;51(4):497–506.

Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M.2017.Virtual reality for stroke rehabilitation. Cochrane Database Syst Rev. 2017;11: CD008349.

Maier M, Rubio BB, Duff A, Duarte OE, Verschure P.2019. Effect of Specific Over Nonspecific VR-Based Rehabilitation on Poststroke Motor Recovery: A Systematic Meta-analysis. Neurorehabil Neural Repair. 2019 Feb;33(2):112-29.

Modroño C, Navarrete G, Rodríguez-Hernández AF, González-Mora JL.2013.Activation of the human mirror neuron system during the observation of the manipulation of virtual tools in the absence of a visible effector limb. Neurosci Lett. 2013 Oct 25;555:220-4.

Prochnow D, Bermúdez i Badia S, Schmidt J, Duff A, Brunheim S, Kleiser R.2013. A functional magnetic resonance imaging study of visuomotor processing in a virtual reality-based paradigm: Rehabilitation Gaming System. Eur J Neurosci. 2013 May;37(9):1441–7.

Reinkensmeyer DJ, Dietz V.2017. Neurorehabilitation Technology: Springer International Publishing; 2016.

Ruffino C, Papaxanthis C, Lebon F.2017. Neural plasticity during motor learning with motor imagery practice: Review and perspectives. Neuroscience. 2017 Jan 26;341:61-78.

Saposnik G, Levin M, Outcome Research Canada (SORCan) Working Group.2011. Virtual reality in stroke rehabilitation: a meta-analysis and implications for clinicians. Stroke. 2011 May;42(5):1380–6.

Selzer M, Clarke S, Cohen L, Kwakkel G, Miller R.2014. Textbook of Neural Repair and Rehabilitation Vol 1: Neural Repair and Plasticity: Cambridge University Press; 2014.

van Dokkum LEH, Ward T, Laffont I.2015.Brain-computer interfaces for neurorehabilitation – its current status as a rehabilitation strategy post-stroke. Ann Phys Rehabil Med. 2015 Feb;58(1):3-8.

Winstein CJ, Stein J, Arena R, Bates B, Cherney L, Cramer SC, et al.2016. Guidelines for Adult Stroke Rehabilitation and Recovery. Stroke. 2016 Jun;47(6):e98-e169.