

Review



Brain-machine Interface in Robot-assisted Neurorehabilitation for Patients with Stroke and Upper Extremity Weakness – the Therapeutic Turning Point

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Highlights

- Robot with BMI therapy for arm after stroke has closed feedback and more chance of neural plasticity.
- Understanding of the new rehabilitation technologies such as robot with BMI therapy for arm after stroke shall give the therapeutic turning point.

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Conflict of Interest

The authors have no potential conflicts of interest to disclose.

ABSTRACT

Activity and participation after stroke can be increased by neurorehabilitation of upper extremity. As the technology advances, a robot-assisted restorative therapy with/without a brain-machine interface (BMI) is suggested as a promising therapeutic option. Understanding the therapeutic point of view about robots and BMIs can be linked to the patient-oriented usability of the devices. The therapeutic turning point concept of robot-assisted rehabilitation with BMIs, basics of robotics for stroke and upper extremity weakness and consequent neuroplasticity/motor recovery are reviewed.

Keywords: Robotics; Brain-machine Interfaces; Rehabilitation; Stroke; Neuroplasticity

INTRODUCTION

Stroke is a sudden neurologic deficit caused by disturbance of vascular supply to the brain by ending up ischemic/hemorrhagic lesions on it. A large proportion of disease burden of stroke can be explained by the loss of motor function causing decreased activity of daily living and participation restriction for the patient. Affected brain regions in stroke, especially in sensorimotor areas, could show various kinds of motor deficits such as weakness, incoordination and changes of muscle tone. For the execution of activity of daily living, those motor deficits need to be properly intervened, which would be the reason why we claim an intensive neurorehabilitation for the recovery of functions during long survival period after stroke [1-3].

In Merriam-Webster (<http://merriam-webster.com>; accessed on 26 August 2016), one simple definition of robot is a machine that do the work of a person and that works automatically or is controlled by a computer. Some kinds of a robot can move human body parts, and the purpose of the robot can be the neurorehabilitation and the improvement of the function of that body parts.

Robot-assisted arm rehabilitation can give the patient repetitive, controlled motion of upper extremity without exhaustion of therapist. Level of difficulty for the training task can be

adjusted according to the status of the patient [4]. Through robot-assisted upper extremity training of movement, neural plasticity and motor recovery can be facilitated [5].

The motivation for the use of devices and the study of psychological stability would be important in terms of efficacy in all kinds of therapies, including robot therapy. Closed feedback during the robot therapy can elevate the patient's emersion to the task and increase the motivation. Among many methods of closed feedback, brain-machine interface (BMI) system can give the direct and immediate feedback to the patient [5]. The BMI is a system that picks up the brain signal, by extracting a useful characteristic, and develop some logics to control other devices using that characteristic, which ideally congruent with the patient's intention [6]. Many logics of current BMI are used for controlling robots. Through such robot-assisted rehabilitation with BMI system, closed feedback from patient's immediate, not preprogrammed, intention can be completed. Even though robotic devices or do not give any haptic sensory feedback, visual or proprioceptive observation of the robotic arm to perform the intended movement will give the BMI-controlling patients more appropriate feedback. In this review, non-invasive electroencephalogram based BMI combined with robot-assisted rehabilitation technique is considered.

THE CURRENT CLINICAL STATUS OF ROBOT-ASSISTED NEUROREHABILITATION OF UPPER EXTREMITY WITH/WITHOUT BMIS

There have been several studies reporting favorable results about the robot-assisted training in stroke patients [7-14]. Using robots, upper extremity passive or active/assistive training can be done with the patient cooperation. Many reviews deal with the efficacy of robot-assisted therapy. In the meta-analysis of the Cochrane review of 2015 with inclusion of 34 trials (involving 1,160 stroke patients), the arm function was improved by the robot-assisted therapy (standardized mean difference 0.35; 95% confidence interval 0.18 to 0.51, $p < 0.0001$). However, more qualified evidences would be necessary due to its overall low quality of evidences [15].

Recent guidelines for stroke rehabilitation describes that robot-assisted therapy for upper extremity gives some benefits for arm motor function and for participation, but the superiority of robot-assisted rehabilitation to dose-matched conventional one is not proven yet [16]. For relatively more functional patients, with not severe but mild impairment, more options of various therapist-driven conventional therapies exist, and robot-assisted therapy cannot be universally justified currently. For persons with moderate to severe motor impairment of upper limb, robot therapy is a reasonable option, maybe due to the more intensive nature of therapy assisted by robots, which do not feel any fatigue [16]. So, the robot-assisted rehabilitation is accepted as beneficial for the upper extremity functional recovery, which increases almost proportional to training intensity [17].

But there is some cautions that the robot-assisted rehabilitation cannot be a substitute for the patient-therapist interaction [18]. The robot-assisted therapy can be accepted at least as an add-on therapy, when the therapist-driven one is formally saturated and the patient needs more intensive therapy.

BMIs interpret the patient's brain signals as the own intention and can move robotic arm accordingly [19]. The robot used in the clinical fields, can move the patient's arm as a

dynamic orthosis, which means that the patient’s cooperation would be essential. If the situation, that the patients do not interact with the robot, exists like a sleeping condition, the efficacy of the robot may be compromised. BMIs will give a promising route for the patient engagement increment during therapy, because the robot could freeze and give negative feedback for the low engagement when the participant do not express motor intention via BMIs, for example during sleeping or dozing. Completion of movement, according to the intention of the patient, will give the BMI-controlling patient closed feedback and this feedback can be associated with more favorable motor recovery, especially reported in chronic stroke [20-23]. Current BMI therapy have broad indications or therapeutic rationales for the patients even with severe motor impairment, but other new therapy of constraint-induced movement therapy has narrow indication, for example that one who has severe impairment and cannot extend own hemiplegic wrist may not have benefit from it [24]. A patient, with severe paresis for which constraint-induced movement therapy cannot be applied, can imagine the movement of paretic hand and even try to move the hand without muscular recruitment, and for this patient the BMI can be applicable [25]. Therapeutic efficacy of BMI system may be relatively elevated than that of constraint-induced movement therapy for the patients of severe motor impairment, according to the above simple comparison between target populations [25]. However, only a few randomized control trials have been published regarding BMI-assisted robot therapy with comparison of robot therapy without BMI, which showed that both kinds of therapies improved motor function in severe stroke patients without the significant difference between them [25,26]. It warrants further study related with closed feedback [27] of BMI or other BMI-assisted facilitation of neural plasticity, which would show more favorable results. Understanding BMI- and robot-technology in terms of plasticity enhancing effects would be prospectively more important as a therapeutic turning point.

STRUCTURE OF ROBOT AND ROBOT-ASSISTED THERAPY

For understanding about the nature of BMI-assisted system in the circumstances of robot-assisted rehabilitation, thorough understanding of robots is a prerequisite. In clinical situations, patients and therapists, who prescribe therapies or set up robotic and/or BMI devices for the therapies, encounter various problems, including selecting from many robot control modes. Robot training mode for range of motion exercise can be passive, active assistive, active, and resistive. Mode of action in robot for neurorehabilitation can be gravity or resistance overcoming type, which can give non-actuator driven active assistive range of motion training. Preprogrammed excursion type can induce a patient passive range of motion training. And motion-responsive type can give patients mainly actuator driven active assistive range of motion training and some active or resistive training. Other combinations including game mode can also give the patients more motivation.

One physical type of robot for neurorehabilitation can be end-effector based type, which gives less interaction than exoskeleton one, more free body area and so less modified arm status than exoskeleton one. Exoskeleton based type provides more interaction points than end-effector type, so more precise controls are needed for imitating natural body movement. In case that the natural movement was achieved, exoskeleton type should give more potential adjustment points to the human body. Introduction for the body motion and the types of robots are explained in other reviews [28,29].

For the application of robot-assisted rehabilitation, many things should be considered.

External force can make further injury to the body parts, which warrants these points to be considered [30]. The bony integrity, bone density, tenderness of the body parts and limitation of range of motion should be carefully checked. A neurorehabilitation robot should be safe and in the normal or reasonable range of motion. While there are limitations of range of motion, patient specific joint/soft tissue range of motion should be considered. Considering speed and range of motion altogether, the power should be in the safe range. Pain and fear sensitivity in each patient should be monitored if it is possible. Even those factors including the noise of the machine operation and the cultural variability also should be considered.

If the mechanism of the robot is not understandable in clinical spectrum, application of the robot to the patient could be ineffective and potentially harmful [30]. Monitoring/measuring function of robots should be always considered for patients and clinicians. Current robots are beneficial but are immature yet. So, measurement of the patient's response and real action kinematic/kinetic data of body parts of patients could also be considered for further analysis of immediate use for the professionals [31].

CONCEPT OF BMI-ASSISTED NEUROREHABILITATION

Current BMI-assisted rehabilitation mainly depends on the event-related desynchronization (ERD) of mu rhythm. In human, 7–14 Hz rhythmic electroencephalogram wave is observed during idling at around primary sensory motor area, which is converted to relatively flat wave by the movement of muscles or by the imagination of the same movement without actual motion [32]. It is interpreted as synchronized power decrease, ERD, of mu rhythm, and interpreted as a marker of movement intention [33]. Slow cortical potentials (motor related cortical potentials [MRCPPs]) [34] with negative polarity can be depicted as another marker of motor intention, before the movement [33]. They are called also readiness potentials and conscious confirmation of movement is associated with these potentials but whether a real movement exists or not is not associated with these potentials [35]. The speed or accuracy of slow cortical potentials is less than that of the ERD. So many algorithms use only the ERD or hybrids of ERD and slow cortical potentials. Beta range or other waves are also used for the analysis of ERD but the accuracy is less than the mu rhythm [36]. Feature extraction from electroencephalogram, for example ERD or slow cortical potentials, gives the logics that participants have the motor intention, which can be used for driving movement of robot arms. The observation of contingent execution by the robot arm linked to the participant's brain status can give the participant's brain positive feedback [37], which can be associated with favorable outcomes. Selection of adequate brain signal for proper movement and its fine tuning may have favorable influences to the neural plasticity [33,38].

PRINCIPLES OF NEURAL PLASTICITY

Post-infarct cortical plasticity is influenced by many endogenous and exogenous conditions [39]. Spontaneous recovery and rehabilitation-driven neural plasticity both can occur. Plasticity mechanisms basically rely on the receptor remodeling by protein formation at dendrites in synapse [40]. However, when it comes to plasticity in systemic level, there would be various kinds of plasticity mechanisms involved in recovery from stroke including peri-lesional reorganization and interhemispheric interaction [41]. There are plenty of evidences of showing peri-lesional reorganization of motor network associated with functional gain by

'use of hand' [42-44]. So among many events influencing plasticity, behavioral experience is one of the most salient determinants for recovery [42-44]. In addition to above local neural plasticity, robotic training may have influence on the plasticity through remote interhemispheric and intrahemispheric neural network [45,46]. As robotic control is precise and repeatable, this sensorimotor synchronization may have more effects on the neural plasticity thereby achieving functional gain [47].

There have been plenty of neuroimaging studies supporting the biologic neural plasticity. Interventional study showed that the increased fractional anisotropy was obtained in longitudinal stroke study using diffusion tensor imaging, in which other motor tract, rather than the corticospinal tract, was increased almost proportion to training intensity in accordance to functional gain over time [17].

Active assistive range of motion training may have an influence on neuroplasticity and it has been done by therapist conventionally [48]. Now it can be done by the robot. In task-oriented active assistive training, therapist or robot can assist to complete the intended movement. Active assistive training gives patients novel somatosensory experience that otherwise would not be achieved. This additional somatosensory input, especially in repetitive robotic therapy manner with stretching synergistically reduced impairment and increased participation, in some proportion via neural reorganization, thereby enhancing motor planning [49]. Even passive movement has the effects on sensorimotor cortical representation [50,51], which is also activated possibly via enhanced movement planning [49,52]. For application of robot, task-oriented repetitive robot-assisted training of the upper extremity is currently the most agreed and salient approach as well as the paradigm of importance of distal movement [16,53]. Usually proximal upper extremity function improves early and distal one improves later. Vigorous training of proximal arm rather than training of distal portion could aggravate the natural recovery of distal upper extremity, and this phenomenon can be explained as interference principle of neural plasticity [16,53,54].

Immediate feedback during a therapy could enhance more recovery via Hebbian neural plasticity [38] as well as partially due to more engagements in the therapy. As the brain naturally seeks hedonia, it can be beneficial for deeper emersion to the therapy that BMIs give the patient more immediate feedback [55]. especially as positive feedback. Immediate feedback can be contingent when the stimuli and the response are paired within a short time range, such as milliseconds to seconds [33]. Although currently this gold standard is not determined, latency between the participant's intention and the response of a few milliseconds was related with more neuroplasticity of motor recovery and delayed movement feedback resulted as inefficient learning [33]. Appropriate BMIs can give patients the positive feedback [56-58]. This operant conditioning associated with the contingent reward via BMI can be linked to the positive feedback [33,37,38,59], which will lead to the increment in motivation of the participants. When the motivation of the patient is high, the chance of reward-based reinforcement learning will also have the chance to be increased [24].

CONCLUSIONS AND FUTURE PERSPECTIVES

For more activity and participation, restorative to compensatory therapy can be helpful. Traditional occupational and physical therapy with sensorimotor approach and more recent robot/BMI-assisted therapy can be the examples of restorative to compensatory therapy, in

which the associated recovery mechanisms of neural plasticity are supported. These basic principles of neural plasticity can be more quantified prospectively and then systematic comprehensive approach based on the quantified mechanisms shall be possible [60,61].

Robot/BMI-assisted rehabilitation market is still in a growing stage, which needs to be improved a lot. For example, robot-assisted therapies are less responsive than those by skillful therapists now. Fundamental knowledge about robots and BMIs is needed as the technology grows up. What are needed are not the myth but the balanced understanding about the rehabilitation technology of healthcare personnel and subsequent the balanced patient education by the professionals.

The BMI-assisted neurorehabilitation, especially based on electroencephalogram, is also a newly focused method of rehabilitation. Electrophysiological phenomena of brain are always observable during every brain activity and electroencephalogram can be measured without additional body energies of participants, but only with some bothersome uses of electroencephalogram devices. Using appropriate electroencephalogram signals, the measurement of that brain activity will give much additional information about the intention of that person, so appropriate logics based on the intention of that person will give many conveniences in the future. For example as an assistive device, BMI-driven robot arm can pick up a cup of water and carry it to the patient's mouth and consequently he or she can drink a cup of water not using his or her arm but using the own brain and the BMI-controlled robot arm [62]. This use of BMIs can be called assistive BMIs. Training such an activity with the own arm attached to the robot, as a dynamic orthosis, repeatedly can make an internally favorable brain circumstance for the neural plasticity, and consequently more motor recovery can occur. Although restorative BMIs are the focus of this review, in the future assistive BMIs can be partially integrated in restorative BMIs. The technology developers for assistive BMIs should consider this restorative point of assistive devices.

Motor control theory which is being proved can be applied in robot therapy with/without BMI approach, and future study of robotics should involve the detailed treatment paradigm, massed vs. distributed training, continuous vs. discrete tasks, training specificity according to patient's conditions and etc. [63-66].

Now the application of BMIs for a rehabilitation purpose is near the practice level. Sound understanding of the technology is important for the all involved people, including patients, health personnel and the technology developers.

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