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Review Article

A review: Motor rehabilitation after stroke with control based on human intent

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Abstract

Strokes are a leading cause of acquired disability worldwide, and there is a significant need for novel interventions and further research to facilitate functional motor recovery in stroke patients. This article reviews motor rehabilitation methods for stroke survivors with a focus on rehabilitation controlled by human motor intent. The review begins with the neurodevelopmental principles of motor rehabilitation that provide the neuroscientific basis for intuitively controlled rehabilitation, followed by a review of methods allowing human motor intent detection, bio-feedback approaches, and quantitative motor rehabilitation assessment. Challenges for future advances in motor rehabilitation after stroke using intuitively controlled approaches are addressed.

Keywords

Stroke rehabilitation; Motor rehabilitation; Human motor intent; Brain computer interface; Neuroplasticity

Abbreviations

ADLs	activities of daily living
ARAT	action research arm test

BCI	brain-computer interface
BMI	brain-machine interface
BP	Bereitschaftspotential
BWST	body weight supported treadmill training
CNS	central nerve system
ECoG	electrocorticography
ED	extensor digitorum
EEG	Electroencephalogram
EMG	Electromyography
ERD	event-related desynchronization
ERS	event-related synchronization

FGA	functional gait assessment
FMA	Fugl-meyer assessment
fMRI	functional magnetic resonance imaging
fNIRS	functional near-infrared spectroscopy
MAS	modified Ashworth scale
MEG	magnetoencephalography
MEP	Motor-evoked potential
MI	mental imagery
MP	mental practice
MRC	Medical Research Council Scale
MRCPs	movement-related cortical potentials

mVEP	motion visual evoked potential
NMES	neuromuscular electrical stimulation
OWS	Over-ground walking speed
PADAUAP	peak dorsiflexion angle during swing phase
PHFADSP	peak hip flexion angle during swing phase
PKFADSP	peak knee flexion angle during swing phase
PNF	proprioceptive neuromuscular facilitation
RAGT	robot-aided gait training
SCP	slow cortical potential
SPECT	single photon emission computed tomography
SSMVEP	steady-state motion visual evoked potential

SSVEP	steady-state visual evoked potential
tDCS	transcranial direct current stimulation
TMS	transcranial magnetic stimulation
TST	triple stimulation technique
TUG	timed up and go
WMAFT	wolf motor assessment function test
VR	virtual reality
6MWT	six minute walk test

Introduction

Strokes are a common global health problem, and are a leading cause of acquired disability.[1] Strokes, which occur when blood vessels in the brain burst or when the blood supply to the brain is blocked, cause brain cell death and disrupt the internal intricate circuits of the brain.[2,3] Depending on the lesion locations, strokes may damage the motor and sensory neural system, block the closed loop between the brain and the body, and thus frequently lead to permanent neurological impairment associated with significant physical and cognitive dysfunction.[2,3] Stroke-related motor impairments affect survivors' activities of daily living (ADLs) at home and in the community, and only a minority of patients with motor impairment can resume their professional lives. More than 30% of all stroke survivors are left with some degree of functional impairment, and still require assistance to manage their ADLs.[4,5]

The goal of stroke rehabilitation is to maximize patients' recovery, allow functional independence, and improve the quality of life. To promote the functional recovery of motor deficits from strokes, it requires interdisciplinary collaborative work in the fields of neuroscience, robotics, computer science, and clinical rehabilitation to create innovative rehabilitation training approaches.[6,7] Brain plasticity and the mechanisms controlling brain plasticity are considered critical to the functional recovery after strokes.[8] Inducing the activity of the primary motor cortex by active motor intent training is a promising approach for motor recovery.[9] Using brain-machine interface (BMI) techniques, the impaired movement execution of stroke patients is bypassed through peripheral stimulation;[10] by linking the intent to execute a movement with sensorimotor feedback, this approach has greater potential to induce neuroplasticity in the motor cortex, allowing better rehabilitation results compared to passive movements or stimulation of the limbs alone.[11–13]

Stroke rehabilitation was reviewed by de Vries et al. [14] in 2007, Daly et al.[15] in 2008, Johansson et al. [16] and Silvoni et al. [17] in 2011, and Takeuchi et al.[11] in 2013 with a focus on motor imagery, neural plasticity, or BCIs. However, more new information has become available in the recent five years. Moreover, human intent-controlled motor rehabilitation has not been fully reviewed, such as, quantitative motor assessment for human intent-controlled rehabilitation, which has yet to been reviewed. In this study, we review recent technologies in motor rehabilitation related to using patients' intent for movement control and address their benefits and limitations. The neurophysiological principles of motor rehabilitation are introduced first, providing the neuroscientific basis for rehabilitation using patient's movement intent control. Next, we review methods on patient's intent detection, feedback approaches, and quantitative motor rehabilitation assessment. We hope the information provided in this study can be used as a starting point for scientists to become familiar with potential neurophysiological mechanisms that can promote motor function recovery for stroke patients.

Neurophysiological mechanisms of human intent-controlled motor rehabilitation

Neuroplasticity, which is central to the recovery of functions after strokes, describes an intrinsic property of the human central nervous system (CNS) that can structurally and functionally adapt to acquire new skills, in response to experiences on the scale of the entire brain, as occurs with cortical remapping.[8,16,18,19]

Recovery or functional improvement after a stroke is a complex process that includes three phases: restitution, substitution, and compensation.[2,11,18,20,21] During phase one, the regenerative processes of brain cells, which normally occur at a very low rate in the adult human brain, are activated creating new neurons and glia.[2] The last two phases are also involved in normal learning and are the "driving force" of functional recovery.[18] Because of redundancies created by a significant degree of functional overlap within and across brain regions, it is possible to recruit motor areas that did not contribute much to the lost function before a stroke, to compensate for neuronal death in the infarcted tissue caused by a stroke.[22] Unfortunately, not all changes in plasticity are beneficial, and some may lead to maladaptive reorganization (for example, flexor/extensor synergies).[15,23–26] Therefore, rehabilitation training is required to guide adaptive plasticity.[27]

It is essential to make sure the patient is actively involved in the motor training process to induce activity-dependent neuroplasticity.[3] Stroke patients would benefit from peripheral stimulation that quantifies their active motor attempts, since the brain reward system is implicated during motor learning and neuroplasticity.[28–30] Moreover, detecting and assisting the patient's attempted movements, namely coupling voluntary cortical activity, task-related motor execution, and movement-rated feedback, may be an effective way to guide adaptive plasticity, which could be beneficial for the control of movement and improve functional recovery.[31–35] Besides, closing the sensorimotor feedback loop can further facilitate decoding of movement intent.[36]

Mirror neurons, which link vision and motion, can be activated either when an individual acts, mentally rehearses an action (motor imagery (MI) or mental practice (MP)), or observes the same action performed by another human, robotic actions, or virtual characters in a virtual reality (VR) environment.[37] Neurorehabilitation methods based on mirror neuron system theories have positive impacts on the rehabilitation of motor functions after strokes.[14,38–45] However, it is difficult to assess the performance of these neurorehabilitation methods. BCIs can quantitatively measure cerebral functions modulated by MI in real time and the introduction of BCI technology in assisting MI practice can result in better motor functional outcomes compared to MI training without BCI support.[46]

For rehabilitation with sensory motor integration, accurate matching between movement intent and sensory feedback is important to facilitate neuroplasticity.[11] Additionally, the timing of paired human movement intent and associated feedback is critical to induce neuroplasticity, which means that the sensory feedback needs to be synchronized with movement intent.[47,48] However, future study is required to clarify which applications pose which requirements on maximum feedback delays, and whether less time between the movement intent and the associated feedback certainly induces facilitating effects.

Consequently, rehabilitation training that involves repeatedly performed task-related skilled movements, movement intent detection, and appropriate multisensory feedback can induce neuroplasticity and thus enhance motor recovery. Fig. 1 shows the schematic diagram of human intent-controlled motor rehabilitation.

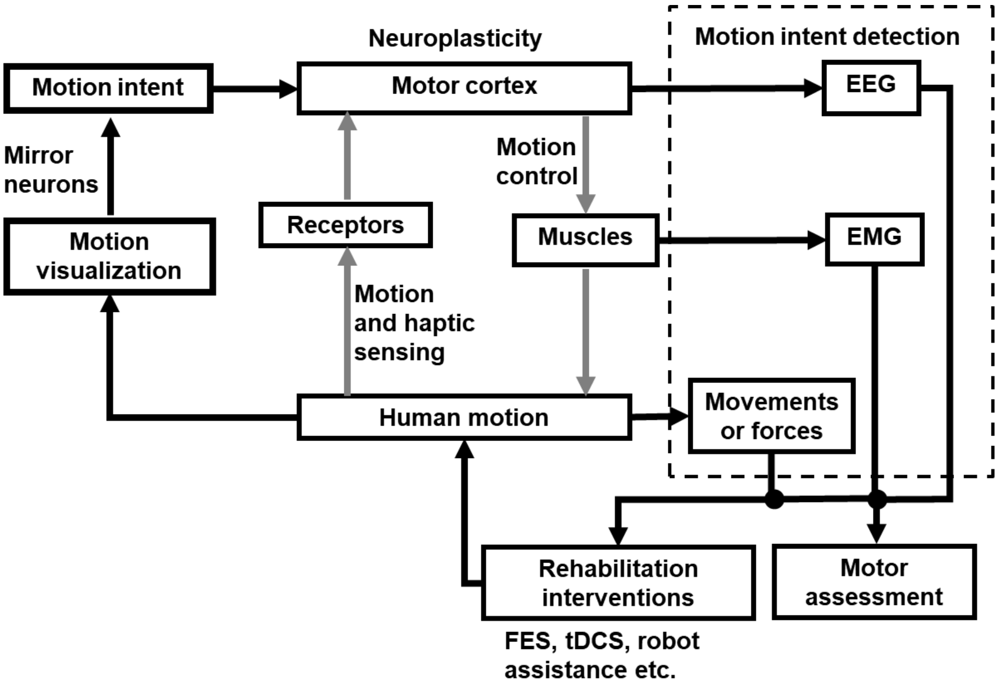

Fig. 1 Schematic diagram of human intent-controlled motor rehabilitation for stroke survivors (grey arrows represent weakened connections because of stroke).

Human movement intent detection

Human movement intent can be detected by monitoring human-machine interactive movements and forces[49–51], analyzing electromyographic signal (EMG), or using BCI methods. Since human movement intent detection based on human-machine interactive movements and forces has been used for decades, in this section, we focus on EMG and BCI based human movement intent detection methods that have drawn more recent research attention.

Human movement intent detection based on EMG signals

EMG signals reflect muscle motion status. The well-accepted feedback latency of EMG-based neuroprosthesis control is less than 200 ms.[52] Thus, this technique ensures the timeliness of neuroplasticity. Moreover, use of the EMG signal can identify finer movements than using BCI methods.[53] Substantial research efforts have been made to effectively extract motor control information from EMG signals[54], and several rehabilitation devices were developed that are controlled by EMG signals.[55–59] However, the EMG of stroke patients may have been weakened. Additionally, many stroke patients have conditions such as paralysis and abnormally co-activated muscles[60], and there is a concern that continuous EMG control may reinforce pathological movement rather than encouraging the recovery of normal motion patterns.[61] Therefore, only relying on EMG to detect movement intent is unreliable for stroke patients. EMG has been combined with human-machine interactive force detection[62] or electroencephalography (EEG)[12,63–66] to improve the recognition of movement intent.

Human movement intent detection based on brain-computer interfaces

BCI or BMI uses neural activities from the brain to provide direct communication between the external device and the brain, independent of the normal neuromuscular pathways (peripheral nerves and muscle tissue).[3,67,68] Since BCI technology exploits learning mechanisms, it can also be used for neurorehabilitation that facilitates the relearning of lost motor function, promotes brain reorganization for functional compensation, guides brain plasticity, and works as a neuro modulatory system, with the aid of the sensory feedback or stimulation.[15,17,63,69] For stroke rehabilitation applications, neuromodulation BCI systems that can be implemented in a fully asynchronous (self-paced) paradigm based on online motor imagination-triggered peripheral interventions can be applied continuously, providing a more engaging human–machine paradigm.[63,70]

Several neuroimaging modalities are available for acquiring brain signals, including invasive methods such as electrocorticography (ECoG) with subdural electrodes[71] and intracortical neuron recording, and non-invasive methods such as EEG performed with electrodes on intact scalp, functional imaging techniques (functional magnetic resonance imaging fMRI, single-photon emission computed tomography SPECT, positron emission tomography PET), magnetoencephalography (MEG), and functional near-infrared spectroscopy (fNIRS).[15,17,72] Ease of use, device cost, and resolution of states are the main factors to consider during the selection of the measurement modalities.[73] MEG and fMRI require bulk devices, but fNIRS has better usability and is less sensitive to head motion artifacts.[74,75] Importantly, MRI-compatible rehabilitation devices are not required for fNIRS. Other advantages of NIRS include a more natural setting of the examination, high sensitivity, and low operational cost.[76] However, there was little subsequent study of the use of fNIRS-BCI for rehabilitation, except the study reported in [74] in 2014. EEG is considered suitable for the general public and has become the most commonly used method in BCI research, since the method is non-invasive, easy to use, and portable in comparison to other methods.[77]

Several types of neurophysiological signals and EEG features have been used to detect movement intent. The time needed to detect movement intent using EEG features is shown in Table 1. MI can cause event-related desynchronization/synchronization (ERD/ERS) of the sensorimotor rhythm.[78] MI allows online classification of neuroelectric brain activities, which can predict the onset of the upcoming movement, its direction, and even the involved limb. However, it is considered a drawback of MI-based BCI that subjects need training before their brain signals can be used in a MI-based BCI system[77] and the accuracy of decoding user intent using MI greatly depends on the attention of patients and their ability to perform mental imagery.[79] Accordingly, object-oriented MI may enhance activation in the mirror neuron system and improve MI ability.[79,80] Strokes may alter patients' ERD/ERS responses and thus limit the potential for survivors to engage in MI-based training.[81] Researchers showed that neuromodulatory techniques such as transcranial direct current stimulation (tDCS) may potentiate ERD responses leading to better MI accuracy.[82,83]

Movement-related cortical potentials (MRCPs) are proposed as immediate and reliable indicators of cortical reorganization during motor learning.[84] Bereitschaftspotential (BP) is one of the important components of movement-related cortical potentials (MRCPs) and normally starts 1-2 s before motion onset.[85] By monitoring BP signal, the onset of the upcoming movement can be predicted and ensures the timeliness of neuroplasticity during rehabilitation.[85] Peripheral electrical stimulation triggered by MRCP-based BCI for ankle dorsiflexion[70] and an exoskeleton controlled by MRCP-based BCI for upper limb rehabilitation[86] have been reported. How to further improve the detection accuracy and reduce the latency is a current research focus.[87] Although naive subjects can generate MRCP in the first session without training,[66] it is also considered a drawback that calibration (training) is required for MRCP-based BCI, because of trial-to-trial variability.[86] To allow the use of BCI methods in clinical settings, it is essential to minimize the time for system preparation, calibration, and training. Instead of using individual training for each subject, Niazi et al.[88] proposed to calibrate MRCPs-based BCI with an ensemble dataset of previously collected signals from a population of subjects. Bhagat et al.[86] proposed an adaptive window technique to compensate for trial-to-trial variability.

Human movement intent can also be evoked by external visual stimulations. Motion visual evoked potential (mVEP), which can be recorded in the visual areas following the presentation of visual stimuli, has important research value for understanding of how humans process motion information.[89] Stimulation paradigms of steady-state motion visual evoked potential (SSMVEP) were designed for BCI applications.[90–93] A visual movement stimulus in the stimulation paradigm occurs first, followed by visual perception of the movement by a person. SSMVEP-based BCIs estimate the stimulus that the human subject is staring at, by comparing the frequency information carried by brain signals and the motion frequency of the stimulus. The motor intent of this person can then be detected. This type of BCI can achieve detection accuracy higher than 85%.[90]

Table 1 Time needed to detect movement intent

Methods	Detection time	Reference
MRCP	Detection latency from movement onset is from about -600 ms to 500 ms	[70,86,87]
ERD/ERS of sensory motor rhythms	ERD/ERS-based neuromodulation studies rarely reported the timing of motor intent detection.	[66]
SSVEP	Stimulation duration (about 300 ms), visual latency (about 140 ms), online computation time (about 80 ms)	[94]

Hybrid-BCI uses at least two types of neurophysiological signals, for example, one BCI that simultaneously combines ERD and SSMVEP BCIs. Compared to conventional BCIs that use only one type of neurophysiological signal, this approach can achieve more control target options, higher information transfer rates, and higher robustness.[95] EEG has also been combined with motion capturing[96] and eye-tracking[97] for movement intent detection.

Human intent-controlled neuro stimulation and sensory feedback

The correspondence between human motion intent and peripheral stimulation is an important factor in promoting recovery.[98] This section reviews feedback modalities that can be used as peripheral stimulation for motor rehabilitation with control based on human intent.

Human intent-controlled motor rehabilitation for stroke survivors has drawn much research attention in the past five years. Table 2 provides a summary of the studies. The literature review was restricted to articles published from 2012 to the present in the following databases: PubMed, Web of Science, IEEE Xplore, SpringerLink, ScienceDirect, Elsevier, Scopus, Wiley Online Library, and Tayler & Francis Online. The search terms were *rehabilitation* AND *stroke* AND (*movement intent* OR *EMG* OR *EEG* OR *fMRI* OR *fNIRS)*. Searches in Google Scholar and the references listed in primary findings were also conducted to find additional relevant studies. Inclusion criteria were (1) English-based articles about, (2) human intent-controlled interventions, (3) that aimed to or claimed to have potential to be used for motor rehabilitation, and (4) of stroke survivors. Exclusion criteria were studies only reported as: (1) conference abstracts, (2) conference posters, (3) theses, or (4) dissertations. Note that we also included studies that conducted experiments only on healthy subjects, but aimed to or have potential to be used in human intent-controlled motor rehabilitation for stroke survivors.

Table 2 Studies of human intent-controlled motor rehabilitation for stroke survivors (from 2012 to present).

Human intent-controlled electrical and magnetic stimulation

Neuromuscular electrical stimulation (NMES) is widely used for motor rehabilitation of stroke survivors, and works by inducing the depolarization of peripheral neurons to elicit muscle contractions and facilitate plastic changes, leading to improvement of motor functions.[99] Similarly, functional electrical stimulation (FES) aims to generate movements that mimic normal voluntary movements by directly stimulating the nerves or their motor points in a specific sequence and magnitude.[100] Takahashi et al.[101], Ono et al.[102], and Cincotti et al.[65] used BCI-controlled FES for active rehabilitation training for stroke survivors, to enhance neuroplasticity and achieved good rehabilitation results. Hara et al.[76] proposed an EMG-controlled FES and found that the EMG-FES had more influence on ipsilesional brain cortical perfusion than voluntary muscle contraction and simple electrical muscle stimulation. Hong et al.[103] combined EMG-triggered FES with MI training and observed an advantage over FES alone.

Transcranial direct current stimulation (tDCS) delivers a weak polarizing electric current to the cortex through a pair of electrodes, to modulate cortical activity by increasing or decreasing brain excitability.[104] Ang et al.[3] proposed combining tDCS with MI-based BCI and robotic feedback for upper limb stroke rehabilitation, and the results suggested the tDCS helped modulate MI in stroke. However, a drawback of tDCS is that it is challenge to properly position electrodes over multiple sessions.[105,106]

Transcranial magnetic stimulation (TMS), which can modulate cortical excitability, is a therapeutic approach to improve rehabilitation efficacy for motor recovery after a stroke. This technique is used to increase excitability within the ipsilesional motor cortex and reduce the excitability of the contralesional motor cortex, to balance interhemispheric inhibition after a stroke. Kraus et al.[107] proposed a closed-loop single-pulse TMS controlled by MI (ERD) of finger extension, and proved the effects of repetitive MI (ERD)-controlled TMS of the precentral gyrus on corticospinal excitability. The disadvantage of TMS is that the cranial anatomical target for TMS must be reestablished at each therapeutic session.[105]

The combination of epidural electrical stimulation (EECS) and task-oriented upper limb motor rehabilitation showed better outcomes when compared to patients treated only with rehabilitation.[105] To the best of our knowledge, use of this invasive method in combination with a neuro-computer interface has not yet been reported.

Human intent-controlled sensory stimulation

Visual stimulation has been used for stroke rehabilitation. By visualizing the output force or EMG, a patient may feel more confident in performing these exercises and motor learning may be facilitated. As described in section 2, both abstract and natural motor visualizations can activate the mirror neural system, recruit action observation networks, and activate the human premotor and motor cortex.[44,108–110]

For patients whose vision has been damaged, visual stimulation will not work. Alternatively, auditory stimulation can be used to provide feedback and enhance stroke rehabilitation.[5] Compared to visual feedback, auditory feedback can reduce perceptual and cognitive workload as well as distraction.[111,112] There is research on electronic textile sensors and auditory feedback used in lower limb monitoring and interactive biofeedback.[113] To the best of our knowledge, use of this feedback method in combination with a neuro-computer interface has not yet been reported.

The bidirectional property of the haptic sense allows us to interact with the simulated world, simultaneously perceive these interactions, and thus, induce neuroplasticity and enhance motor learning.[114] Simple position control, haptic guidance strategies, and a haptic-augmented environment are used in motor rehabilitation to strengthen muscles and connective tissue, generate somatosensory stimulation, reinforce the movement pattern by movement repetitions, and increase patients' motivation.[115] Narrowly defined haptic feedback devices have been designed to generate somatosensory feedback.[116] Haptic feedback provided by a WAM robot arm (Barrett Technology, Inc.) has been combined with an MI-based BCI for stroke rehabilitation.[36] Without the use of haptic devices, force can also be used to provide visual feedback during rehabilitation tasks.[49] Generalized haptic feedback also includes physical guidance and physical assistance that is normally created by robots.[117] This will be discussed in detail in section 3.4.

Stroke patients may have different degrees of brain damage, weakening their sensory abilities. The human brain processes and integrates sensory information automatically and simultaneously.[16] Multisensory influences are essential to both primary and higher-order cortical operations.[16] Multimodal feedback can take advantage of each modality to enhance motor learning.[117–124] Therefore, multimodal stimulation and multisensory training protocols are more effective for learning in healthy subjects.[16,119,125] Visual, auditory, and haptic feedbacks, as well as other stimulations, can be combined to form multisensory feedbacks to promote motor recovery in stroke survivors. Virtual reality and robots are useful tools to provide those feedbacks.

Human intent-controlled virtual reality-mediated motor rehabilitation

Virtual reality (VR) allows the user to interact with a multisensory simulated environment that mimics real-world scenarios and receive real-time feedback on performance, confirming their own movements without the assistance of a therapist.[30,126,127] Additionally, VR offers a high level of tunable control of the parameters, to adjust them to create individualized treatments.[128] VR can also be easily combined with other interventions.

Although some provide additional sound information or haptic feedback that enhances the experience, most current VR systems are primarily visual experiences.[129,130] VR-mediated motor rehabilitation has been proved to be effective for stroke survivors.[126] Neuroplasticity, the brain reward system, and the mirror neuron system may be involved in VR-mediated motor rehabilitation.[29,30] VR itself may lead to benefits in stroke patients, irrespective of the specific device (including off-the-shelf virtual reality gaming devices).[131] However, patterns of improvement may depend on the specific interface systems used.[131]

By detecting the patient's movement intent, VR systems can react accordingly, creating a more engaging experience. For example, Biswas et al.[132] proposed an EMG-based biofeedback system with VR for gait rehabilitation, using an avatar to mimic the gait of the user, with joint trajectories estimated based on a standard kinematic curve and gait parameters like strike time and gait phase obtained from EMG data. Luu et al.[96] proposed a closed-loop BCI-VR system that translates neural activity acquired from scalp EEG into lower limb movements during treadmill walking, to control an avatar in a virtual environment.

Berkeleymudez et al.[133] proposed and validated an MI-driven BCI-VR system to promote cortical reorganization for motor rehabilitation.

Human intent-controlled robot-assisted motor rehabilitation

Robot-assisted motor rehabilitation uses devices with sensory, actuation, and intelligence capabilities.[7] Some rehabilitation robots provide kinematic and kinetic measurements during rehabilitation training, allows for assessment of patient's participation and can adjust their motion according to movement intent detected via parameters such as force, torque, and joint angle and position.[134,135]

EMG-based, robot-assisted rehabilitation has achieved promising results in clinical trials using triggering-type control [136] and proportional control.[137] Motion pattern classification based on EMG was also proposed to control robot-assisted rehabilitation.[58] Paredes et al.[138] reported that EMG-based robot-assisted rehabilitation achieved a significantly higher completion rate, compared to torque control for the severe-to-moderate group.

For BMI-based robot-assisted rehabilitation, Ang et al.[139] showed that EEG-based MI-BCI with robotic feedback was effective in facilitating the motor recovery of upper extremities in stroke patients. Moreover, Varkuti et al.[140] conducted a comparison study between MI EEG-BCI-based robotic rehabilitation and pure robot-assisted rehabilitation, and found that the MI-BCI group exhibited higher Fugl-Meyer (FM) gain and higher functional connectivity changes. Since subjects require training before their EEG could be used to control robots based on ERD/ERS from MI, in recent years, there have been attempts to use other extracted EEG features (SSVEP[141], SSMVEP[142], and MRCP[66,86]) for robot-assisted rehabilitation.

Motor assessment for human intent-controlled rehabilitation

Measurement of functional outcomes is essential to assess the quality of rehabilitation. Evaluation scales are subjective, and may not be sufficiently sensitive to detect slow improvement in the complex motor function.[143] The multitude of different clinical scales used to evaluate rehabilitation effects limits comparison between systems.[135]

Human intent-controlled motor rehabilitation requires automatic, continuous, and quantitative measurement and assessment. More quantitative assessment methods may better describe stroke-induced motor deficiencies and improvements.[49,144] With the development of motion-capturing technology, quantified human movement information and kinematic analysis becomes an important tool to evaluate the abnormal neuromuscular execution caused by strokes.[144,145] Parameters such as range of motion (ROM)[59], walking speed[59], gait symmetry ratio[96], pinch force[49], joint synergy index[143], jerk metric and normalized jerk of standard movements[146] have been used.

EMG provides information on the extent of neuromuscular disorder for stroke patients.[147] The EMG signal features that have been used to evaluate motor functions of stroke survivors include muscle activation level[148], activation pattern[149], co-contraction level[56], complexity[144], time-to-peak contractions[150], and RI index (indicates the overall muscle activity).[55]

The above methods, including conventional behavioral measures may mask individual variability in cortical reorganization during recovery.[151] Therefore, in recent years, there is a trend to directly measure physiological parameters of the motor system via EEG features or radiologic methods such as fMRI and NIRS to evaluate patient motor function. EEG features of stroke patients can be significantly different across individuals even when the patients scored similarly for conventional behavioral measures.[151] ERD power of the motor-related cortex from MI[152], power spectral density analysis, and connectivity estimation[46], as well as Limpel-Zic complexity analysis[153] have been used to evaluate functional states of the brain for motor rehabilitation assessment. Hara et al.[76] evaluated rehabilitation effects by analyzing brain cortical perfusion using NIRS during rehabilitative training of a paretic upper limb. Ono et al.[102] analyzed changes in cerebral blood volume through fMRI before and after rehabilitative training.

EEG and sEMG can be used together to assess motor rehabilitation by providing muscle functional response information to the brain. Xu et al.[154] used a cortico-muscular coherence analysis method with time lag to compensate for the time delay between the two signals, to enhance the cortico-muscular coherence. However, the phase frequency correlation acquired by this analysis is complex and linear, thus, non-linear coupling correlation is lost. This cortico-muscular coherence analysis method may have the potential to assess motor rehabilitation.

Electrodiagnosis assesses the nervous system using EMG, nerve conduction velocity, and evoked potentials. Motor-evoked potential (MEP) elicited by transcranial magnetic stimulation (TMS) has been used to assess the motor cortex excitability.[46,66,107] The triple stimulation technique (TST) is an improved method of MEP.[155] TST uses TMS and peripheral electric stimulation to measure the percentage of the activated spinal motor neurons, allowing quantification of the integrity of the conduction function of nerve center.[155] Although TST can accurately measure the level of motor nerve conduction, it has disadvantages including high device cost, use of electromagnetic radiation, and limits to suitable patients.

Discussion

As demonstrated in section 2, the timing of paired human movement intent and associated feedback is critical to induce neuroplasticity (estimated to be within 300 ms).[47,48] Which applications pose which requirements on maximum feedback delays and whether less time between the movement intent and the associated feedback certainly induces facilitating effects must be clarified. As shown in Table 1, ERD/ERS-based neuromodulation studies rarely reported the timing of motor intent detection. Researchers need to pay more attention, to determine the time needed to detect the movement intent and the time needed for the system to react accordingly for human movement intent-controlled rehabilitation.

There is a trend to combine different stimulations for multimodal feedback, for example, combining tDCS with robot-assisted rehabilitation[83], visual feedback with exoskeleton-assisted rehabilitation[57,64], and robot-assisted rehabilitation with visual feedback as well as FES.[59] These stimulations should be provided in an understandable way and should not overwhelm the patient.[156] In other words, the amount of information should not exceed the capacity of the individual to process the information efficiently. [156] However, this could be highly subjective, patient-dependent, and case-dependent. Questionnaires such as in Shah's study[157] could be used to find the optimal amount of information combination and design parameters of multimodal feedback in motor rehabilitation for a specific patient. Use of methods with these stimulations demonstrated motor ability improvements, but careful comparisons between methods have not been performed.

Most current BCI studies for motor rehabilitation used EEG-based BCI, with little investigation of other BCIs like fNIRS-based BCI to detect movement intent for rehabilitation other than the study by Rea et al.[74]. This illustrates that the use of other BCI methods to detect movement intent for rehabilitation needs more research attention.

Currently, SSMVEP-based BCIs use stimulation paradigms such as oscillatory and continuous unidirectional random-dot motion,[158] or Newton's rings with oscillating expansion and contraction motions[90]. Since point-light biological motion can both activate human premotor cortex[108,109] and carry motion frequency information, it may be more suitable to use the stimulus of SSMVEP-based BCI than current stimulation paradigms to evoke patient's movement intent, thus requiring more attention in future studies.

Current BCI approaches and devices are financially expensive. For example, a g. tec instrument (g.tec medical engineering GmbH, Schiedlberg, Austria) costs more than $20,000. Moreover, the preparation time required to use BCI devices is relatively long. Subjects must wear an electrode cap filled with conductive gel. The long preparation time and high price means that most current BCI devices are more suitable for research purposes than clinical practices. Although cheaper devices are available, concerns about their accuracy still remain. Therefore, non-invasive, low-cost, and easy-to-install BCI that are convenient to use with acceptable accuracy are needed for use in clinical practice.

EEG signals vary from patient to patient and recording channels are often manually selected. Therefore, an important challenge is determining the best strategy to personalize EEG methods for each patient. EEG signals may be influenced by other internal states of the subjects such as attention, fatigue, and motivation, therefore, these global states should be quantified in future studies. Finally, BCIs must consider the difference in EEG patterns between stroke survivors and healthy subjects to ensure the system's effectiveness for diagnosis and to promote recovery.[151]

Compared to EEG, EMG provides increased user control over movements. However, EMG-controlled rehabilitation is only appropriate for users able to generate voluntary muscle bio-electricity in a normative pattern.[159] Moreover, the quality of EMG signals can vary across patients. Thus, a process of adjustment to a specific user is required. Besides, there is a concern that continuous EMG control may reinforce pathological movement rather than encouraging the recovery of normal movement patterns.[61] How to avoid pathological movement reinforcement associated with EMG-controlled rehabilitation needs more further research.

Most human intent-controlled motor rehabilitation techniques are still at the laboratory stage. Currently, there are relatively more studies on healthy subjects than stroke patients. Since results from healthy subjects may not be directly generalized to a stroke population, future studies with larger sample size and longer duration of training are needed. In 2016, Donati et al.[10] proved that long-term BMI usage (12 months) can trigger both cortical and spinal cord plasticity for paraplegic patients. Similar long-term studies are also desired for human intent-controlled motor rehabilitation for stroke patients.

Systematic, automatic, continuous, and quantitative motor assessment using the combination of cortical, muscular, and behavioral information may be more useful for human intent-controlled motor rehabilitation, since the combined information reflects the function of motor neural circuits and links cortical changes in excitability to changes in functional parameters. However, EEG, sEMG, and quantified motion information are currently used separately to assess patient's rehabilitation. Since cortico-muscular coupling is mutual, some researchers introduced information theory to cortico-muscular coherence analysis. Transfer entropy, which does not rely on a postulated model and is a non-linear quantitative analysis approach to identify the function coupling strength and information transfer direction[160] may have potential to be used to analyze the combined information of EEG and sEMG to assess motor rehabilitation.

Conclusion

In this study, we summarized motor rehabilitation methods for stroke survivors, with a focus on human movement intent-controlled rehabilitation based on neurodevelopment and neuroplasticity. Movement intent detection methods and feedback modalities are also introduced. Recent research has focused on increasing patient engagement during rehabilitation training, which is important for inducing neuroplasticity to facilitate motor recovery. Use of these methods demonstrated improvements in functional outcomes. Future work will include minimization of the time needed to detect the movement intent and the time needed for the system to react accordingly, evaluation of the efficacy of different methods for patients with different abilities, and systematic motor assessment using the combination of cortical, muscular, and behavioral information.

Declaration of Conflicting Interests

The authors declare that they have no conflict of interest.

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1 **Table 2 Studies of human intent-controlled motor rehabilitation for stroke survivors (from 2012 to present).**

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
Ang et al.[83]	2012	EEG (MI)	Upper limb	tDCS, robot-assisted movements	EEG (Accuracy of detecting MI versus the idle condition)	19 patients	2 weeks	No	The results suggest the tDCS effect in modulating MI in strokes, but more data are needed for a more conclusive result.
Cincotti et al.[65]	2012	EMG, EEG (MI)	Hand	FES	ESS, MRC, FMA	29 patients	1 month	Yes	Rehabilitation with BCI-mediated neurofeedback allows a better engagement of motor areas, compared to MI alone.
Hong et al.[103]	2012	EMG	Upper limb	FES	FMA	14 patients	4 weeks	Yes	MI training combined with EMG-triggered FES, increased metabolism in the contralesional motor-sensory cortex and improved motor function of the paretic extremity in stroke survivors.
Mrachacz-Kersting et al.[12]	2012	EMG, EEG (CNVs from MRCPs)	Lower limb	TMS, PNS	MEP elicited by TMS, CNV	24 healthy subjects	21 days	Yes	Only when the afferent inflow arrives during the highest activation phase, the excitability of the neural connections between the relevant brain areas and the target muscle is increased. The changes are specific to the task and the brain-muscle neural connections involved in the task.
Frisoli et al.[97]	2012	Eye-tracking for target selection,	Upper limb	Exoskeleton-assisted movements	Movement classification error rate	3 healthy subjects and 4 patients	40 trials × 2 conditions	No	All subjects were able to operate the exoskeleton movement by BCI with a classification error of 89.4±5.0% in the robot-assisted condition, with

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
		EEG (MI) movement control of the exoskeleton							no performance difference observed in stroke patients compared with healthy subjects.
Bermúdez et al.[133]	2013	EEG (MI)	Upper limb	Visual feedback	Mean activity brain maps (power) and statistics for each frequency band (α/μ,β,γ)	9 healthy subjects	24 min	No	To a larger extent, simultaneous motor activity and MI is more effective in engaging cortical motor areas and related networks.
Cesqui et al.[161]	2013	EMG	Upper limb	Visual and auditory feedbacks	EMG classification accuracy of the movement direction	9 healthy subjects and 7 patients	60 movements for healthy subjects and 80 movements for patients	No	Statistical classifiers-based EMG pattern recognition approaches to decode subject's intent worked well for healthy subjects but did not perform well on patients.
Fan et al.[62]	2013	EMG and human-machine interactive force detection	Lower limb	Exoskeleton-assisted gait training and EPP feedback	Joint ROM, Active joint force, force error and angle error	3 healthy subjects and 3 patients	Up to 14 days	No	Valuable information on the safety, feasibility, and effectiveness of the human intent-controlled exoskeleton-assisted training.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
Hara et al.[76]	2013	EMG	Upper limb	FES	NIRS (Brain cortical perfusion)	16 patients	5 months	No	The sensory motor integration during EMG-FES therapy might result in functional improvement of the hemiparetic upper extremity.
Hu et al.[162]	2013	EMG	Upper limb	Exoskeleton-assisted movements	FM, ARAT, WMFT, MAS, muscle co-ordination between FD and ED, ED EMG level, ED and FD co-contraction, excessive muscle activities	10 patients	20 sessions (4-6 weeks)	No	Upper limb training, incorporated with the EMG-driven robot hand, could improve the muscle coordination between the antagonist finger muscle pair.
Ono et al.[102]	2013	EEG (ERD from MI)	Upper limb, finger	NMES	fMRI, EMG (Cortico-muscular coherence evaluation), FMA score and MAS	1 patient	9 weeks	No	The superiority of closed-loop training with BCI-driven NMES is superior to open-loop NMES.
Seel et al.[163]	2013	Inertial sensors	Lower limb	FES	Foot-to ground angle	Patients and healthy subjects (numbers was not mentioned in the paper)		No	Using the measured foot-to-ground angle to adapt the stimulation profile can produce a constantly physiological and symmetric gait.
Song et al. [137]	2013	EMG	Wrist	Robot-assisted movements	Range of motion, RMSE between the actual wrist angle and target angle, muscle strength and clinical scales	16 patients	20 sessions/5-7 weeks	No	There were significant improvements in muscle strength and clinical scales after EMG-controlled robot-aided therapy.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
Várkuti et al.[140]	2013	EEG (MI)	Upper limb	Robot-assisted movements	Resting state functional connectivity changes based on RS-fMRI, FM	9 patients	4 weeks	No	Both the FM gain and functional connectivity changes were numerically higher in the MI-BCI group.
Watanabe et al.[164,165]	2013	Inertial sensors	Lower limb	FES	Angular velocity, stride time, angle range, and inclination angle	3 healthy subjects and 1 patient	1 session	No	Inertial sensor-based FES is useful for rehabilitation.
Bhagat et al.[64]	2014	EEG (MRCPs), EMG	Upper limb	Robot-assisted movements (upper-limb exoskeleton MAHI Exo-II) and visual feedback	Movement intent classification accuracy	3 healthy subjects and 1 patient	80 movements × 4 modes	No	Experimental results (median classification accuracy around 75% for the stroke participant) provide initial evidence for the potential applicability of MRCP-based robotic training for stroke survivors.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
Fluet et al. [166]	2014	Force and motion tracking	Upper limb	Visual feedback and haptic feedback (Haptic Master)	WMAFT, FMA, distal kinematics, proximal kinematics and force, MEP elicited by TMS	5 patients	8 sessions/two weeks	No	This study showed the feasibility of adding one hour of intensive robotic/virtual reality (VR) therapy in the acute phase of recovery of stroke survivors.
Genna et al.[55]	2014	EMG	Shoulder	Robot-assisted movements	RI index (indicates the overall muscle activity)	4 healthy subjects and 1 patient	1 hour	No	All subjects could produce continuous EMG activation in target muscles, in order to smoothly control the robot. However, in the stroke patient, an abnormal activation (loss of selective recruitment of some muscles) was observed.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
He et al.[167]	2014	EEG	Lower limb	Exoskeleton-assisted movements	Pearson's correlation coefficient between the measured kinematic/ EMG signal and the predicted output from EEG	2 healthy subjects and 1 patient	5 min× 3 conditions	No	Kinematic and surface EMG patterns could be decoded from scalp EEG during walking of both healthy and post-stroke subjects with a powered robotic exoskeleton.
Lechner et al.[168]	2014	EEG (MI	Hand	FES and visual feedback	Time needed for 9-hole Peg test	1 patient	14 sessions in 6 weeks	No	The experimental results proved the effectiveness of the proposed method.
Munoz et al.[169]	2014	EEG, motion capturing sensor (Kinect)	Hand, upper limb, and	Visual feedback	Range of motion	700 patients with motor impairments	4 months	No	Significant improvements in the mobility of affected joints, improved adherence to treatments by patients, and high acceptability by therapists and end-users.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
			lower limb			(including stroke patients)			
Xu et al.[66]	2014	EEG (MRCPs) and EMG	Ankle	Robot-assisted movements	MEP elicited by TMS (to assess the excitability of the motor cortex before and after the intervention)	10 healthy subjects	15 min	No	MRCP-based BCI system provides a fast and effective approach to induce cortical plasticity through BCI, and has potential in motor function rehabilitation for stroke patients.
Zhang et al.[142]	2015	EEG (SSMVEP)	Lower limb	Visual feedback, robot-assisted movements	Movement intent classification accuracy	3 healthy subjects	5 min	No	This asynchronous EEG-driven lower limb rehabilitation system obtained accurate classification of 76.7%- 96.7% with information transfer rates ranging from 6.82- 16.11 bits/min.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
Kwak et al.[141]	2015	EEG (SSVEP)	Lower limb	Exoskeleton-assisted movements	Accuracy, response time, information transfer rate	11 healthy subjects	50 trials of offline experiment, 70 trials of task 1 and 17m walking of task 2 in online experiment	No	The feasibility of this SSVEP-based lower limb exoskeleton for gait assistance was proved.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
Hu et al.[56]	2015	EMG	Wrist	NMES	FMA, MAS, ARAT, co-contraction index from EMG	26 patients	3 months	Yes	The additional NMES application could bring more distal motor function improvements and faster rehabilitation progress.
Zhou et al.[57]	2015	EMG	Ankle	Robot-assisted movements and visual feedback of the processed EMG	Passive and active properties of ankle joint	5 patients	6 weeks	No	The proposed robotic ankle-foot rehabilitation can improve ankle spasticity and /or contracture.
Leonardis et al.[58]	2015	EMG of free hand	Hand	Exoskeleton-assisted movements	The correction between the grasping pressure estimation and reference	6 healthy subjects and 2 patients	3 conditions ×10 repetitions	No	The study confirmed the advantage of driving robotic assistance by the healthy hand in bilateral training.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
Pichiorri et al.[46]	2015	EEG (MI)	Hand	Visual feedback of virtual hands	FMA, MRC, MAS, oscillatory activity and connectivity at rest based on EEG recordings, MEP elicited by TMS	28 patients	1 month	Yes	The introduction of BCI technology in assisting MI practice demonstrated significantly better motor functional outcomes.
Jiang et al.[152]	2015	EEG (ERD/ERS from MI)	Upper limb	FES	ERD power of motor related cortex	2 healthy subjects and 2 patients	2 weeks	No	The ERD power of the motor-related cortex was improved significantly using BCI-FES system.
Luu et al. [96]	2016	EEG (SCPs in the delta band), goniometers,	Gait	Visual feedback of a walking avatar	Gait symmetry ratio	4 healthy subjects	8 days	No	Using the closed-loop BCI can control a walking avatar under normal and altered visuomotor perturbations, which involved cortical adaptations.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
		accelerometers							
Vourvopoulos et al.[170]	2016	EEG (MI)	Upper limb	Visual feedback (Oculus Rift DK1 Head mounted display) and sound feedback	The different EEG rhythms, the classification score, and the hemispheric asymmetry and subjective data on workload, kinesthetic imagery and presence	9 healthy subjects	3 days	No	Both VR and particularly motor priming can enhance the activation of brain patterns present during overt motor-execution.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
Bhagat et al.[86]	2016	EEG (MRCPs)	Upper limb	Robot-assisted movements (upper-limb exoskeleton MAHI Exo-II) and visual feedback	Movement intent classification true positive rate and false positive rate	4 patients	5 days	No	The closed-loop EEG (MRCPs)-based BMI for detecting movement intent of chronic stroke patients can work across multiple days without system recalibration.
Srivastava et al.[59]	2016	EMG	Lower limb	Robot-assisted movements, visual feedback, and FES	FMA, FGA, TUG, 6MWT, OWS, PHFADSP, PKFADSP, and PADAUAP	12 patients	5 daily training sessions × 3	No	Assist-as-needed robot-assisted gait training has similar effects as body weight support treadmill training on improvements of gait pattern in stroke survivors.

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
							weeks with 2 weeks off		
Kraus et al.[107]	2016	EEG (ERD from MI)	fingers	TMS	EEG (MEP amplitude)	17 healthy subjects	40 min	No	Corticospinal excitability was increased by TMS of the motor cortex during β-ERD, and the corticospinal excitability persisted beyond the period of stimulation and the depotentiation task.
Sarasola-Sanz et al.[171]	2017	EEG and EMG	Upper limb	Robot-assisted movements	FMA, robot control performance	1 healthy subject and 1 patient	1 session	No	This method constantly requires the active participation of central and peripheral structures of the nervous system. The experimental results

Study	Year	Movement intent detection	Target	Feedback modality	Assessment method and indicator	Subjects	Duration	Randomized controlled?	Findings
									showed encouraging results for its application to a clinical rehabilitation scenario.

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