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Review on Motor Imagery Based BCI Systems for Upper Limb Post-Stroke Neurorehabilitation: From Designing to Application

Muhammad Ahmed Khan[a,*], Rig Das[a], Helle K. Iversen[b], Sadasivan Puthusserypady[a]

[a]Department of Health Technology, Technical University of Denmark, 2800 Kgs. Lyngby, Denmark
[b]Department of Neurology, University of Copenhagen, Rigshospitalet, 2600, Glostrup, Denmark
*Corresponding Author: mahkh@dtu.dk

Abstract:

Strokes are a growing cause of mortality and many stroke survivors suffer from motor impairment as well as other types of disabilities in their daily life activities. To treat these sequelae, motor imagery (MI) based brain-computer interface (BCI) systems have shown potential to serve as an effective neurorehabilitation tool for post-stroke rehabilitation therapy. In this review, different MI-BCI based strategies, including "Functional Electric Stimulation, Robotics Assistance and Hybrid Virtual Reality based Models," have been comprehensively reported for upper-limb neurorehabilitation. Each of these approaches have been presented to illustrate the in-depth advantages and challenges of the respective BCI systems. Additionally, the current state-of-the-art and main concerns regarding BCI based post-stroke neurorehabilitation devices have also been discussed. Finally, recommendations for future developments have been proposed while discussing the BCI neurorehabilitation systems.

Keywords: Stroke; Brain-Computer Interface (BCI); Motor Imagery (MI); Neurorehabilitation Devices; Virtual Reality; Electric Stimulation; Robotic Assistance.

1. Introduction

Stroke occurs when the blood flow to the brain is disrupted and subsequently causes long-term disabilities to the survivors. A recent (2016) study shows that there were approximately 5.5 million deaths and 116.4 million DALYs (disability-adjusted life-years) due to stroke [1]. Among the stroke survivors, the specific manifestations are determined by the upper limb hemiparesis, i.e., weakness or inability to move the upper limb in one side of the body [2]. Studies have shown that up to 55 – 75% of stroke patients with a hemiplegic arm still had impaired function in arm movement activities after three to six months of rehabilitation, thus indicating the need for improved rehabilitation techniques/strategies for stroke patients [3].

Presently, the primary approach used to induce motor recovery in stroke patients involves active motor training via physical and occupational therapy [4]. Moreover, new strategies are needed to speed-up the motor recovery along with providing physical assistance to stroke patients during rehabilitation therapy. Hence in this regard, the mental rehearsal of physical movement tasks, or in other words, the motor imagery (MI) can be seen as an approach to access the motor system and rehabilitation at all stages of stroke recovery [5 - 7]. This opens up the opportunity to explore the use of brain-computer interface (BCI) systems with its neuro-feedback ability as an innovative and practical approach to neuro-rehabilitation. A BCI is a computer-based system that records, decodes and translates measurable neurophysiological signals into computer-readable commands for controlling single or series of output devices. These devices assist in performing different tasks based on the required application [8].

BCI based systems are widely categorized into invasive and non-invasive systems depending on the methodology adopted for the measurement of brain activities. Invasive BCI systems comprise either electrode arrays placed directly on the brain surface for electrocorticography (ECoG) recordings or microelectrode arrays implanted in the brain cortex. Brain surface electrodes have been tested in BCI systems research by using epidural electrodes [9] and subdural electrodes [10-12], whereas in [13-15], microelectrode arrays have been successfully used for designing BCI systems. Invasive systems however, have problems regarding long-term robustness of acquired signals [16] and therefore are usually investigated in in-vitro experiments, having limited success in in-vivo conditions [17]. On the other hand, non-invasive systems, due to their portability, safety, comfort, and low cost are the more preferred ones to acquire the relevant brain signals (electroencephalogram (EEG)). In such systems, multiple electrodes are placed on the scalp for acquiring the EEG signals. From the acquired signals, relevant features regarding the user's movement intention are extracted and used to control specific actuating devices depending on the patient's intended motion [18–20]. Nowadays, wireless EEG systems are preferred, as they are more user-friendly and have reduced noise/artifacts that are produced by wired movements of the EEG setup [21]. Moreover, semi-dry and dry electrodes have also been proposed to minimize the signal acquisition time [22, 23]; however, their performance is not significant in comparison to the gel-based electrodes and needs further improvements in the future [24].

For BCIs, the brain activities are recorded via EEG acquisition systems, which are then analyzed for interfacing computers with the brain. Depending on the way the brain signals are extracted, EEG based BCI systems are divided into four paradigms [25]: (a) Steady State Visual Evoked Potential (SSVEP), (b) P300, (c) Slow Cortical Potential (SCP) and (d) MI. The SSVEP is generated by a visual stimulus when the user is exposed to flashing light with specific frequencies. This potential is generated at the visual cortex area of the brain and the EEG system records the triggered brain activities at corresponding frequencies [26]. The P300 is an event-related potential (ERP) that is acquired from the parietal lobe and measures the brain evoked response approximately 300 ms after the onset of the somatosensory stimulus (such as visual, auditory, or somatosensory) [27]. The SCP is another event-related brain potential that is represented by the gradual changes in the membrane potentials of cortical region and can last from one to several seconds. SCP might be self-induced or externally triggered. Positive SCPs are related to the decreased activity in neurons, whereas negative SCPs are associated with neuronal activity [28]. The major difference between SSVEP and ERP is that SSVEPs are a response to the complete stimulation duration, whereas ERPs are a response to a specific event of stimuli. The fourth BCI paradigm is the MI, which is a type of intervention that uses visuo-motor imagination to visualize the execution of motor tasks (for instance, hand, arm or foot movements). Unlike the other paradigms, MI is stimulus independent (i.e., it does not require any external stimulus and control actions are executed as a result of neural activity) [29]. Hence, in this regard MI-BCI systems have an advantage over other paradigms because stroke patients may not be adequately responsive against the provided stimulus. For instance, if someone has a hearing issue, then auditory stimuli would not be effective for him/her. Similarly, individuals with vision problems would not be able to respond to visual stimuli appropriately and can also get eye fatigue [30]. Additionally, research has shown that in contrast to other strategies, MI possesses the same activation of the motor area during the task movement execution and task movement imagination [31]. Upon imagination, event-related synchronization (ERS) and desynchronization (ERD) are produced over the sensorimotor cortex region. These are processed by the BCI system, which then infers the user intent of action based on the recorded EEG events [32]. Thus, this MI attribute provides a unique opportunity to study and analyze movement related brain activities in patients as well as in healthy people [33, 34]. Therefore, the MI has been widely used in BCI systems for neurorehabilitation applications, ranging from individuals with motor disability, severe muscular disorders, and paralysis to the restoration of limb movements [35-37]. Due to the bidirectional interaction between the brain and the computer, MI-BCI systems are used to alter brain functions of stroke patients [36, 38] through neural plasticity (i.e., the reorganizational processes in the brain) [39-41].

The MI based BCI controlled neurorehabilitation therapy assists the stroke patients in restoring their impaired motor functions. Several BCI based strategies have been used to design a neurorehabilitation system for stroke patients (Figure 1). These approaches vary in terms of the methodology adopted to convert the participant's movement intention into real actions. These methods involve:

i. ***Functional Electric Stimulation (FES):*** In this method, the BCI system is connected with the FES device, which uses electrical currents to activate nerves innervating extremities affected by paralysis [42].

ii. ***Robotics Assisted Systems*:** In the BCI-Robotics systems, robotic hardware assists the patient/subject in performing the intended movements, which further enhances motor learning abilities [43].

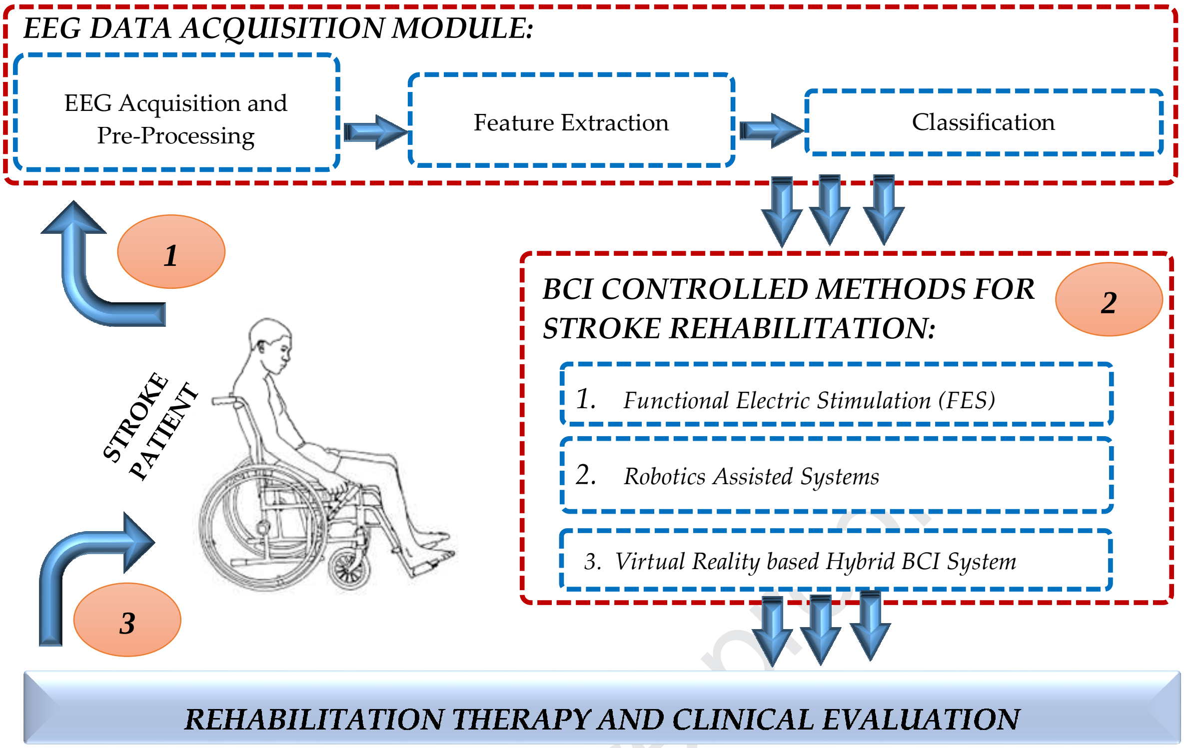

Fig.1. Research Methodology for Designing BCI Based Rehabilitation System

iii. ***Virtual Reality (VR) based Hybrid Models***: In this approach, VR is coupled with haptic, FES or robotics feedback to develop a hybrid system. With VR, the patient can see the movements of his/her paralyzed limb, which further causes activation of neurons in the premotor cortex and helps in fast recovery of stroke patients [44].

Regarding neurorehabilitation systems, many review papers have been published [45-51]; however, none of the studies have presented the in-depth description and comparison of different types of BCI controlled methods adopted to the design of stroke rehab systems. Hence, in this review paper, these methods are comprehensively presented and compared in terms of their usage, efficacy, and their future implications for stroke patients.

2. Materials and Methods

In order to perform this systematic review, we searched for articles in Scopus, PubMed, IEEE, and ScienceDirect databases using the keywords: stroke, rehabilitation, brain-computer interface, motor imagery, neurorehabilitation devices, FES, robotics systems, and virtual reality. While searching, no year restriction was applied and only articles that met all the following criteria were considered :

- The scientific paper was written in English.
- The study was focused on the rehabilitation of stroke patients.
- The study reported information about any of the following: stroke rehabilitation therapies, rehabilitation systems for stroke patients (either conventional or BCI based), case studies for post-stroke rehabilitation, possibility to improve stroke rehabilitation and future perspectives of neurorehabilitation.

Initially, 242 relevant studies were selected based on their title. Then, 37 articles were excluded after examining the abstracts and finally, 188 manuscripts were found most relevant and are included in this review article. As the main focus of the presented review paper is to provide a wide range detailing of different BCI based neurorehabilitation systems, the manuscript has been divided into two main sections. The first section focuses on describing various methods of BCI based rehab systems and their stroke application. The second section on the other hand, emphasizes more on discussing the comparison of available rehabilitation systems, hence exploiting the advantages and shortcomings of each system along with their future implications.

3. PART I: BCI Controlled Methods for Post-Stroke Rehabilitation Therapy

Generally, the therapist's assistance is used in the conventional rehabilitation therapy of stroke patients, but one of its significant drawbacks is that there is no quantified method for the exact measurement of the patient’s MI pattern. The patient might receive positive feedback even when they do not imagine the instructed movement properly and when unable to produce necessary MI signals. As a result, neural plasticity will be induced at a slower pace and the patient will not attain the desired results of recovery [52].

Thus, a new technology known as the “paired associative stimulation (PAS)” has been introduced in the post-stroke rehabilitation system, which uses BCI for evaluation of MI activities [53-60]. The recorded MI is then used to control the feedback and stimulation, such as avatar movements, FES activation, and robotics assistance for producing the required movements. Recent researches not only confirm the feasibility of BCI based rehab systems in clinical trials but also validate the hypothesis that rehabilitation recovery outcome could be improved by using PAS [61-63].

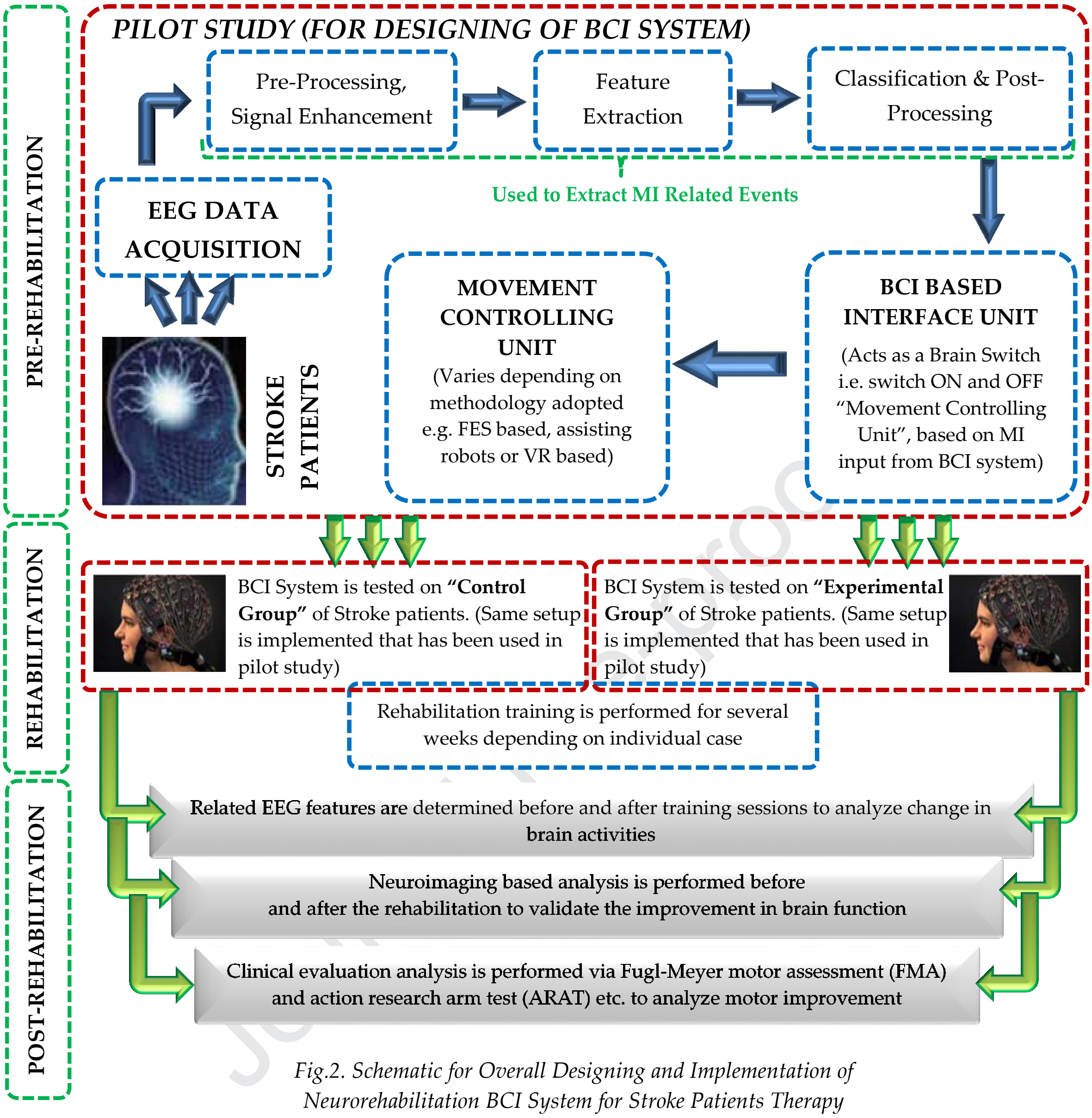

Fig.2. Schematic for Overall Designing and Implementation of Neurorehabilitation BCI System for Stroke Patients Therapy

BCI systems for stroke rehabilitation are mostly coupled with one of the three output controlling/feedback units: (i) FES, (ii) Robotics system, and (iii) VR based hybrid BCI systems. The overall methodology of BCI based rehab system, starting from system designing to its implementation mainly involves the following three phases (Figure 2):

i. ***Pre-Rehabilitation Phase:*** Firstly, a pilot study is conducted on stroke patients to design and develop an MI-based BCI system. It utilizes MI rhythms generated by imagining the intended movements. The common patterns of MI activation are determined by the specific brain stimulation, which is characterized by the EEG as features. Once the features corresponding to the required movements are obtained, it is classified and used for the development of the BCI setup for stroke rehabilitation.

ii. ***Rehabilitation Training Phase:*** Developed BCI system is tested by performing rehabilitation training sessions on an "Experimental Group", and its performance is compared with a "Control Group" of stroke individuals. The experimental group undergoes BCI controlled rehabilitation whereas the control group performs rehabilitation without the BCI system. The control group is selected using different possible ways i.e., it can be randomly selected by randomized control trials (RCTs) or can also act as a sham control group. In [42], the FES unit of the experimental group was driven by the user's intention (motor imagery BCI). Meanwhile, the sham control group received the same process as the experimental group except the FES stimulation was delivered randomly and not controlled by neural activity.

iii. ***Post-Rehabilitation Phase:*** After rehabilitation therapy, clinical evaluation is the primary and most important criteria to evaluate the efficacy of BCI based rehabilitation. The clinical assessment is performed (both on the experimental and control groups) by estimating different test scores, such as FMA, ARAT, 9-Hole Peg Test, and others. These scores identify the level of significant motor improvements and recovery of upper-extremity function in stroke patients [64-66]. Secondly, to investigate electrophysiology outcomes, neuroimaging modalities are used that validate the improvement of the brain functions. It also helps in understanding how well the rehabilitation paradigm performs on the patients. These functional imaging techniques mainly include positron emission tomography (PET), functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), transcranial magnetic stimulation (TMS), and near-infrared spectroscopy (NIRS) [67].

In the latter section of the manuscript, different BCI controlled methods for post-stroke rehabilitation (FES, Robotics assistance and VR hybrid model based) have been discussed in terms of their "Pre-Rehabilitation, Rehabilitation Training and Post-Rehabilitation" phases (Table I, II and III).

3.1. BCI- FES Rehabilitation Systems:

Post-stroke neural injuries usually disrupt the muscle activation of different body areas. Hence to restore muscle activation, an effective method using "Functional Electrical Stimulation" has been adopted. FES offers a non-invasive solution for re-establishing the connection in motor pathways by stimulating the nerves, thereby causing muscular movement of the affected limb [65-67]. Research has shown that FES has been implemented in several clinical practices to restore walking [68-70], standing [71-73], hand grasp [74-76], arm reaching [77, 78] and other post-stroke rehabilitation [79]. However, some key parameters including dosage [80, 81] and onset time of therapy [82, 83] should be taken into consideration for the efficacious implementation of FES in clinical rehabilitation.

According to Hebb's principle ("cells that fire together wire together" [84, 85]), the pairing of peripheral and cortical activities could strengthen and improve the impaired motor function, which will remain persistent after a rehabilitation therapy has been completed [86–89]. Thus, it would be beneficial to couple FES systems with some external system responsible for recording and monitoring cortical activities to enhance the efficiency of FES based systems. Thus in this regard, BCI systems are used, which are capable of measuring brain activities caused by the imagination of the intended movement [89-93].

The general system architecture of the BCI-FES device comprises of several sub-units (Figure 3). First, the predetermined task appears on the screen and the subject tries to perform that task by imagining the task execution. The process of thinking stimulates a series of MI events, which are then recorded by the EEG acquisition system. System

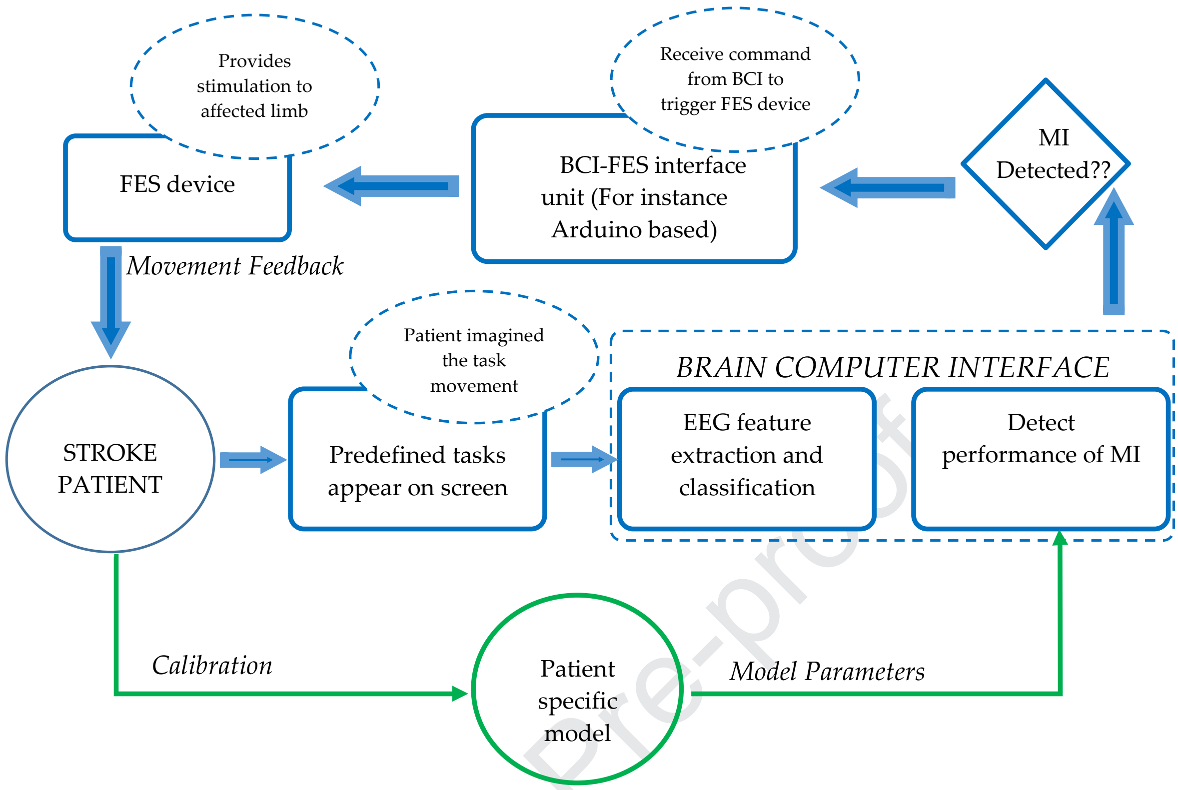

Fig.3. Schematic Representation of BCI-FES Neurorehabilitation System

calibration is done via a specific model designed for each patient. Thus, once the required MI events are detected, the trigger command is sent to the BCI-FES interface unit, which then switches ON the FES device. The interface module is a microcontroller-based hardware unit that controls the ON/OFF state and stimulation parameters of the FES device, depending on the received brain input/control signal. Lastly, the FES device provides the required stimulation to the affected region/muscles with controlled stimulation parameters which are adjusted according to the patient's state. Hence, the desired movements are achieved and its accuracy relies on the designed system and training sessions given to the patients regarding BCI-FES system usage.

3.1.1. BCI-FES Systems for Stroke Rehabilitation

BCI-FES systems are widely used for stroke rehabilitation, comprising both customized and commercially available BCI controlled stroke rehab systems. Fabricio et al. [94] designed a BCI rehabilitation system for post-stroke therapy. In this study, FES has been used as a movement assisting unit, which is coupled with the MI-based BCI system and allows the patient to perform the required motion with provided support. EEG data acquired during the experiments (between 8 and 30 Hz) are processed and used to produce topographic maps of brain activities recorded against each performed task. The topographic representation of MI events corresponds to the imagination of right, left and both hands movements. Results show that Event-Related Desynchronization (ERD) patterns for all the imagery tasks are visualized differently, which reveals the activation of different cortical areas in response to different imagery tasks. In another work, Daly et al. [95] tested a customized BCI-FES system on a stroke patient with a problem in index finger joint extension. Rehab training was conducted for 3 weeks, with 3 sessions per week. The result shows that during the first therapy session, the subject exhibited high accuracy in imagined movements (83%) and attempted movements (97%), whereas encountered some difficulties in attempted relaxation (deactivation of brain signal-65%). However, by 6 sessions, relaxation control improved to 80% and after completion of 9 sessions, index finger extension was completely recovered. In [96], Leeb et al. designed a BCI based FES controlled hand neuroprosthesis, which was tested by Tevella et al. [97] in a handwriting task. It involves the user performing multitasking, i.e., simultaneously performing a handwriting task and controlling the BCI. Very low numbers of erroneous trials are observed during the experiments, which illustrate how flawlessly the subjects were able to control the movement according to their intention. Pfurtscheller et al. demonstrated the restoration of hand grasp function by using the BCI-FES system [98]. The MI events for the patient's imagination to perform the desired motion were recorded, analyzed and classified by the BCI system and the obtained output was used to control the FES stimulation. Results show that the patient was able to perform grasp movement through his affected limb. Likewise, Cincotti et al. [99] also illustrated the application of a BCI-FES rehabilitation device to restore hand grasping movements. This research was conducted on 29 stroke patients and the spectral changes in their brain activities during imagery and hand grasping movements have been reported. Moreover, system performance was evaluated using the FMA (Fugl-Meyer Assessment), MRC (Medical Research Council) and ESS (European Stroke Scale) scores. Additionally, in [100-103], the clinical application of a custom made BCI-FES rehabilitation system has been proposed to improve the upper extremity movements and promote motor recovery after stroke. Sabathiel et al. [104], Cho et al. [105], and Qiu et al. [106] have conducted experiments using the RecoveriX system to regain wrist dorsiflexion. In another study, Irimia et al. [107] have used RecoveriX to recover the affected limb movement of stroke patients by performing rehabilitation therapy of 120 left and 120 right-hand movements. It has been found that a high accuracy has been achieved in task execution via the RecoveriX System. Moreover, significant improvement in different evaluation scores were reported, which shows the enhanced motor function recovery of stroke patients by RecoveriX. A detailed list of BCI-FES stroke rehabilitation research works is provided in Table I.

Table I. Research studies and their outcomes for BCI-FES neurorehabilitation systems

FES BASED BCI SYSTEMS FOR UPPER LIMB NEUROREHABILITATION						
Selection Criteria for Included Articles: Only those studies are included in this section which fulfills the following criteria: (1) Manuscript is related to an MI-based BCI controlled system with the FES control unit. (2) Study possesses real-time online testing of the system, i.e., must be tested on either stroke patients or healthy subjects. Article that contains only offline analysis is excluded. (3) Scientific paper is related to BCI application for upper-limb neurorehabilitation.						
	PRE-REHABILITATION		**REHABILITATION TRAINING**			**POST-REHABILITATION**
Study	**Commercialized/Customized Rehabilitation System**	**BCI Methodology/ EEG Acquisition Method**	**Experimental Group (EG) and Control Group (CG)**	**Therapy per Participant (i. Total Sessions, ii. Runs/Session, iii. Trials/Run or Trials/Session)**	**Targeted Areas**	**Outcome Measures/Clinical Scores**
Daly et al. (2009)	Customized	58 channels (SynAmps,	EG: 01 stroke	i. 09 ii. N/A	Index finger joint extension	High accuracy in imagined movements

[95]	System	Compumedics, El Paso, TX)	patient CG: N/A (Stroke Severity: 10 months post-stroke: Chronic of moderate to severe level)	iii. 150 (per session)	(FES provided to isolated index finger extension)	(83%) and attempted movements (97%). Participants were able to execute 26 degrees of isolated index finger metacarpophalangeal joint extension
Tavella et al. (2010) [97]	Customized System (contains FES stimulated orthosis) [96]	16 channels (g.tec system)	EG: 04 healthy subjects CG: N/A	i. N/A ii. N/A iii. N/A	Grasping and handwriting movement (FES only to targeted hand)	Only tested working performance of a system
Pfurtscheller et al. (2010) [98]	Customized System	4 channels	EG: 01 stroke patient CG: N/A (Stroke Severity: Chronic of severe level)	i. N/A ii. N/A iii. N/A	Hand grasp function (FES to paralyzed hand)	Only tested working performance of a system
Cincotti et al. (2012) [99]	Customized System	32 channels	Randomized Control Trial (RCT) EG: 08 stroke patients CG (with conventional FES therapy): 08 stroke patients	i. 12 ii. 04 iii. 20 (per run)	Hand grasping movement (FES to paralyzed hand)	FMA, MRC and ESS score shows a good recovery of hand function with BCI system as compared to the control group. Exact values of these scores has not been reported
Li et al. (2014) [100]	Customized System	16 channels (G.tecGuger Technologies, Graz, Austria)	EG: 08 stroke patients CG (with conventional FES therapy): 07 stroke patients (Stroke Severity: subacute of severe level)	i. 24 ii. N/A iii. 20 (per session)	Upper extremity movements (FES stimulated the affected hand)	FMA and ARAT score shows significant motor improvement ΔFMA (EG) = 12.7, ΔARAT (EG) = 18.0; ΔFMA = 6.7 (CG), ΔARAT = 7.6 (CG)
Mukaino et al. (2014) [101]	Customized System	N/A	EG: 01 stroke patient CG (with conventional FES therapy): Same patient (Stroke Severity: Chronic of severe level)	(Total there are 4 phases) i. 10 (for each phase) ii. N/A iii. 600 (for each phase) (per session)	Finger movement (FES applied to the paralyzed finger)	BCI-FES system efficacy reported via FMA and MAS score ΔFMA = 3.5 (EG); ΔFMA = 0.5 (CG)
Sabathiel et al. (2016) [104]	RecoveriX System (g.tec GmbH, Austria)	24 channels (g.Hiamp device by g.tec GmbH, Austria)	EG: 02 stroke patients CG: N/A (Stroke Severity: Chronic of severe level)	i. 24 (patient 1) and 10 (patient 2) ii. N/A iii. N/A	Wrist dorsiflexion (FES applied to both affected and unaffected hands)	Higher classification accuracy obtained. Moreover, Nine-Hole Peg Test (9-HPT) is performed only of patient 1 and result shows steady improvement over about three months
Kim et al. (2016) [102]	Customized System	16 channels (PolyG-I by Laxtha Inc., Daejeon, Korea)	EG: 15 stroke patients CG (with conventional FES therapy): 15 stroke patients (Stroke Severity: Chronic of	i. 20 ii. N/A iii. N/A	Shoulder and wrist movement (FES stimulated the affected hand)	Improvement in FMA, MAL, MBI, and ROM was found. ΔFMA = 7.9 (EG); ΔFMA = 2.9 (CG)

			moderate level)			
Irimia et al. (2017) [107]	RecoveriX System (g.tec GmbH, Austria)	45 channels (g.tec GmbH, Austria)	EG: 03 stroke patients CG: N/A (Stroke Severity: Chronic of severe level)	i. 24 ii. 06 iii. 40 (per run)	120 left and 120 right hand movements (FES applied to both affected and unaffected hands)	High accuracy in task execution achieved (95% in at least one session) and Nine-Hole Peg Test (9-HPT) shows improved motor function.
Cho et al. (2017) [105]	RecoveriX System (g.tec GmbH, Austria)	16 channels (g.LADYbird by g.tec GmbH, Austria)	EG: 02 stroke patients CG: N/A (Stroke Severity: Chronic of severe level)	i. 25 ii. 04 iii. N/A	Left or right wrist dorsiflexion (FES applied to both hands)	Improved performance observed via FMA score (pre and post BCI) Patient 1: ΔFMA = 21 Patient 2: ΔFMA = 11
Qiu et al. (2018) [106]	RecoveriX System (g.tec GmbH, Austria)	16 channels (Guger Technologies, Graz, Austria)	EG: 10 stroke patients CG: N/A (Stroke Severity: Chronic of different levels)	i. 12 ii. 02 iii. 30 (per run)	Left or right wrist dorsiflexion (FES applied to both hands)	System accuracy of more than 95%. FMA score shows enhanced motor function recovery among 5 patients (pre and post BCI)
Tabernig et al. (2018) [103]	Customized System [94]	08 channels (Wireless EMOTIV by Epoc headset)	EG: 08 stroke patients CG: N/A (Stroke Severity: Chronic of severe level)	i. 20 ii. N/A iii. Between 20 and 30 (per session)	Different tasks from right/left hand (FES applied to the affected hand)	Significant improvement in FMA, mMAL and VAS scores (before and after the BCI intervention)

FMA = Fugl-Meyer Assessment; **MRC** = Medical Research Council; **ESS** = European Stroke Scale; **ARAT** = Action Research Arm Test; **MAS** = Modified Ashworth Scale; **MAL** = Motor Activity Log; **MBI** = Modified Barthel Index; **ROM** = Range of Motion; m**MAL** = Modified Motor Activity Log; **VAS** = Visual Analog Scale

3.2. BCI- Robotics Rehabilitation Systems:

Robotics systems were introduced in stroke rehabilitation in the 1990s, and use devices with actuation, sensory, automation and intelligence-based capabilities [108]. There are different types of robotic modes available in clinical trials of post-stroke rehabilitation,such as active, passive and assistive [109]. The selection of the modes to be used is done by the therapist depending upon the condition and impairment level of the patient. For instance, in passive mode, the movement of the paretic limb is entirely controlled by a robot and no motion is performed by the patient. Meanwhile in assistive mode, the robot helps the subject in performing the desired movements of the affected limb. These robots carry out kinetic and kinematic measurements of patient movements and adjust their actions via several control parameters such as torque, force, position and joint angle [110, 111]. Thus, the primary objective of robotic stroke rehabilitation is to restore impaired limb movements by providing sensorimotor feedback and research has shown that when compared to the conventional rehabilitation methods, robotic interventions enhance upper limb motor functions [112-116].

In recent years, several robot-assisted neurorehabilitation systems have been designed to improve post-stroke rehabilitation of hand movements, arms, and gait. Some of the robotic systems used in conventional rehabilitation therapies include MIME (Mirror Image Motion Enabler) [117], MIT-MANUS (Massachusetts Institute of Technology Manus) [118], ARM (Assisted Rehabilitation and Measurement) Guide [119, 120] and WAM (Whole Arm Manipulation) robotic arm [121]. MIME was presented by Burgar et al. [122], containing wrist-forearm orthosis and a robot connected with the affected arm. The healthy forearm is connected to a 6-axis digitizer and its motion commands the robot to execute mirror image movements (master/slave mode), thus allowing the subject to perform shoulder and elbow movements in the horizontal plane. The system has been tested on 21 hemiparetic patients and the results show improvement in the FMA score of motor functions in terms of shoulder and elbow mobility. In the early 1990s, MIT-Manus has been developed by Hogan et al. [123-125], which is a robotic platform with 2 degrees of freedom and offers horizontal plane movements of the elbow and shoulder joints. Volpe et al. [126] analyzed the data from 96 subacute stroke patients, who underwent rehab therapy either by MIT-Manus or by conventional rehabilitation methods. Their results showed that patients with robot-assisted therapy possessed high motor power and FMA score for the elbow and shoulder joints. Similarly, ARM Guide is another well-known robot-based system that has been designed at the Rehabilitation Institute of Chicago [119, 120]. It allows the patient to perform "reaching tasks", both in a vertical and horizontal motion. The patient's hand/forearm is connected to a splint and a robotic motor resists or assists the impaired arm actions accordingly. ARM Guide has been tested by David et al. [127] on 3 stroke patients and their preliminary results demonstrate that robot-assisted therapy can produce positive results in restoring chronic hemiparetic arm movements. Another robotic system is the Barrett WAM robotic arm, which is an adaptive robotic arm with standard 4 degrees-of-freedom and contains torque-controlled actuators. Phan et al. [121] designed an adaptive rehabilitation system based on WAM robot for guided physical therapy. The proposed system permits simultaneous active/passive control of a robotic arm and allows data recording regarding motor function assessment of the patient.

Although the robot-aided rehabilitation systems have shown potential for stroke rehabilitation and provide an effective as well as convenient tool for stroke patients, their use in conventional therapies however provides no direct connection between the patient's MI pattern and executed movements. Most of the actions are performed according to a predefined program set by the therapist [128] and therefore in such conditions, the patient's attention state and motor initiatives may not be fully explored. To overcome the aforementioned shortcoming, BCI systems are combined with robotic rehab systems, in which the robot is controlled by a patient's own intention (MI) extracted from the EEG signals [129, 130]. The system architecture of the BCI-Robotics is similar to that of the BCI-FES system, just replacing the FES module with the robotic controlling unit.

3.2.1. BCI-Robotics Systems for Stroke Rehabilitation

BCI-Robotics rehab systems have played a very vital role in post-stroke rehabilitation therapy. The summary presented in Table II shows the extensive study of several BCI controlled robot-assisted neurorehabilitation systems used for rehabilitation of post-stroke patients. Broetz et al. [131] presented a case report for a combination of robotics controlled BCI training and goal-directed physical therapy in chronic stroke. The study shows a significant improvement (mean 46.6%) in hand and arm movements. Thus, the presented case study suggests that the combination of physical therapy with BCI training may improve the motor functionality of chronic stroke patients. In [132], the robotics-assisted BCI neurorehabilitation system has been designed using the MIT-Manus robot in which robotic assistance is triggered by an MI-based BCI system. Their results indicate that robotic feedback was effectual in motion assistance, as well as in the motor recovery of impaired extremities of stroke patients. Gomez et al. [133, 134] and Meyer et al. [135]

performed research on stroke rehabilitation via WAM robot arm assisted BCI system. They demonstrated the system efficiency in assisting the flexion/extension of the forearm and elbow joint. Va′rkuti et al. [136] compared the performance of the MIT-Manus based robotic rehabilitation system with and without BCI for shoulder and elbow movement of stroke patients. Results exhibit that the MI-BCI based robotic system presents a greater change in functional connectivity and achieves a higher FM gain. Similarly, Ang et al. conducted comprehensive research using MIT-Manus [137] as well as haptic knob [138]. They confirmed that the BCI-Robotic neurorehabilitation system is a great tool to be used for the upper limb motor recovery of post-stroke patients. Moreover, Xu et al. [139] proposed a novel design of a robotics-assisted BCI neurorehabilitation system in which the Barrett WAM Arm has been used as a motion controlling unit during functional recovery therapy. They developed a fuzzy logic-based PD controller for the WAM robot to introduce more stability in executing the defined movements during the exercises. The performance of the BCI robotics system was evaluated by assessing the recognition rates (83.00% and 93.00%) of the movements against imagination tasks. Furthermore, the position control performance of the fuzzy PD controller was also compared with that of a conventional controller for controlling the WAM robot. Hence, higher movement accuracy was achieved while using the proposed fuzzy PD controller for maneuvering WAM motion. Likewise, Sarac et al. [140] tested customized Assist-On-Mobile rehabilitation robot [141], Bhagat et al. [142] and Pehlivan et al. [143] operated MAHI Exo-II exoskeleton, Frolov et al. [144] employed robotic hand exoskeleton (Neurobotics, Russia) and Jessica et al. [145] used customized robotic hand orthosis [146] for different kinds of BCI based post-stroke upper extremity rehabilitation studies (table II for details).

Table II. Research studies and their outcomes for BCI-Robotics neurorehabilitation systems

ROBOTICS ASSISTED BASED BCI SYSTEMS FOR UPPER LIMB NEUROREHABILITATION

Selection Criteria for Included Articles: Only those studies are included in this section which fulfills the following criteria:

(1) Manuscript is related to an MI-based BCI controlled system with the robotics control unit. (2) Study possesses real-time online testing of the system, i.e., must be tested on either stroke patients or healthy subjects. Article that contains only offline analysis is excluded. (3) Scientific paper is related to BCI application for upper-limb neurorehabilitation.

	PRE-REHABILITATION		**REHABILITATION TRAINING**			**POST-REHABILITATION**
Study	**Commercialized/Customized Rehabilitation System**	**BCI Methodology/ EEG Acquisition Method**	**Experimental Group (EG) and Control Group (CG)**	**Therapy per Participant (i. Total Sessions, ii. Runs/Session, iii. Trials/Run or Trials/Session)**	**Targeted Areas**	**Outcome Measures/Clinical Scores**
Broetz et al. (2010) [131]	Rehabilitation robot (Motorika, Israel)	N/A	EG: 01 stroke patient CG: N/A (Stroke Severity: Chronic of severe level)	i. N/A ii. N/A iii. N/A	shoulder flexion, elbow flexion/ extension, forearm supination/pronation, wrist and finger extension/flexion	Improvements are analyzed based on FMA, WMFT, Ashworth, and GAS scores

Ang et al. (2010) [132]	MIT-Manus robot	27 channels (Nuamps acquisition by Neuroscan)	Randomized Control Trial (RCT) on 25 stroke patients EG: 11 stroke patients CG (Only MIT-Manus): 14 stroke patients (Stroke Severity: Chronic of severe level)	i. 12 ii. N/A iii. 160 (per session)	Different tasks for stroke-affected limb	FMA shows higher motor improvement via BCI-Robot rehabilitation ΔFMA = 4.5 (EG); ΔFMA = 6.2 (CG); After 2- month spost-rehabilitation ΔFMA = 5.3 (EG); ΔFMA = 7.3 (CG);
Gomez-Rodrigue z et al. (2011) [133]	WAM robot arm (by Barrett Technology, Inc.)	35 channels (Electro-Cap International, Inc.)	EG: 06 healthy subjects CG: N/A	i. N/A ii. N/A iii. N/A	Flexion/extens ion of the forearm	Power spectrum and statistical analysis reported
Gomez-Rodrigue z et al. (2011) [134]	WAM robot arm (by Barrett Technology, Inc.)	35 channels (Electro-Cap International, Inc.)	EG: 06 healthy subjects and 03 stroke patients CG: N/A (Stroke Severity: Chronic)	i. N/A ii. N/A iii. N/A	Flexion/extens ion of the elbow joint	Power spectrum analysis reported
Meyer et al. (2012) [135]	WAM robot arm (by Barrett Technology, Inc.)	128 channels (Brain Products, Gilching, Germany)	EG: 02 stroke patients CG: 06 healthy control subjects (Stroke Severity: Chronic)	i. 01 ii. N/A iii. 50 (per session)	Upper extremity movements	Analyzing frequency bands related to motor processes
Va´rkuti et al. (2012) [136]	MIT-MANUS robot-assisted rehabilitation	27 channels (Nuamps acquisition by Neuroscan)	EG: 06 stroke patients CG (Only MIT-Manus): 03 stroke patients (Stroke Severity: Chronic of moderate to severe level)	i. 12 ii. N/A iii. Variable in EG and 960 fixed in CG (per session)	Shoulder and elbow movement	FM gain and FCC were numerically higher in the MI-BCI group
Sarac et al. (2013) [140]	Customized AssistOn-Mobile rehabilitation robot [141]	3 channels (Biosemi ActiveTwo EEG System)	EG: 09 healthy subjects CG: N/A	i. N/A ii. 05 iii. 40 (per run)	Right Arm movement	High classification accuracy and overall system performance obtained.
Ang et al. (2014) [138]	Haptic knob (two-degree-of-freedom robotic hand interface)	27 channels (Nuamps acquisition by Neuroscan)	Randomized Control Trial (RCT) on 21 stroke patients EG (BCI with haptic knob): 06 stroke patients CG1 (Only haptic knob): 08 stroke patients CG2 (Standard Arm Therapy (SAT)): 07 stroke patients (Stroke Severity: Chronic of moderate to severe level)	i. 18 ii. 04 iii. 30 (per run)	Hand and wrist movement	FMA shows improvement in patient performance of all groups ΔFMA = 9.7 (EG); ΔFMA = 8.3 (CG1); ΔFMA = 3.6 (CG2);
Bhagat et al. (2014) [142]	MAHI Exo-II exoskeleton [143]	64 channels (Brain Products GmbH, Morrisville, NC)	EG: 03 healthy subjects and 01 stroke patient CG: N/A (Stroke Severity: Chronic)	i. N/A ii. 04 (modes) iii. 80 (movements per mode)	Upper extremity movements	Classification accuracy of around 75% achieved
Ang et al. (2015) [137]	MIT-Manus	27 channels (Nuamps acquisition by	Randomized Control Trial (RCT) on 25 stroke patients	FOR EG: i. 12 ii. 08 iii. 1040 (per	Shoulder and elbow movement	FMA shows improvement in the patient performance of

		Neuroscan)	EG: 11 stroke patients CG (Only MIT-Manus): 14 stroke patients (Stroke Severity: Chronic of moderate to severe level)	session) FOR CG: i. 12 ii. 04 iii. 160 (per session)		all groups ΔFMA = 4.5 (EG); ΔFMA = 6.3 (CG);
Xu et al. (2015) [139]	WAM robot arm (by Barrett Technology, Inc.)	02 channels	EG: 08 healthy subjects CG: N/A	i. N/A ii. 06 (02 runs for each of the three different cases) iii. 10 (per run)	Vertical flexion/extension for upper limb	Recognition rate for task execution lies between 83.00% and 93.00%.
Frolov et al. (2017) [144]	Robotic hand exoskeleton (Neurobotics, Russia)	30 channels (NVX52, Medical Computer Systems by Zelenograd, Russia)	Randomized Control Trial (RCT) on 74 stroke patients EG: 55 stroke patients CG (Sham feedback): 19 stroke patients (Stroke Severity: Subacute and chronic of severe level)	i. 10 ii. N/A iii. N/A	Affected hand movement	FMA and ARAT shows improvement in upper extremity function ΔFMA (EG) = 5.0, ΔARAT (EG) = 2.0; ΔFMA = 5.0 (CG), ΔARAT = 3.0 (CG)
Jessica et al. (2018) [145]	Customized robotic hand orthosis [146]	11 channels (g.USBamp device by g.tec GmbH, Austria)	EG: 08 healthy subjects and 06 stroke patients CG: N/A (Stroke Severity: Chronic)	i. 02 ii. 03 iii. 20 (per run)	Flexion/extension of fingers	Statistical analysis performed. High system performance and accuracy reported.

FMA = Fugl-Meyer Assessment; **WMFT** = Wolf Motor Function Test; **GAS** = Goal Attainment Score; **FCC** = Functional Connectivity Change; **MRCPs** = Movement Related Cortical Potentials; **ARAT** = Action Research Arm Test

3.3. BCI-VR Hybrid Rehabilitation Systems:

To maximize the rehabilitation therapy outcomes, the stroke patient should be provided with environments that are realistic, exciting and motivating to experience. In this regard, mirror therapy is used which is a patient-oriented and inexpensive treatment method. During this therapy, a patient moves his/her healthy limb and its mirror reflection tricks the brain in believing that the affected limb is moving as well [147]. Research conducted on healthy subjects has revealed that this method of hand movements increases the excitability of the ipsilateral primary motor cortex region of the brain, hence supporting the application of mirror therapy in stroke rehabilitation [148]. However, with time, the patient loses his focus, interest and motivation because of continuous gazing towards the mirror and limited availability of exciting tasks [149]. To overcome these problems, augmented and VR technologies have been introduced within the rehabilitation field, which provides exciting visual feedbacks required for triggering the mirror neurons [150].

VR is a human-computer interface that makes the user feel like a part of the computer-generated 3D environment, allowing to experience and interact with a virtual ambiance in a realistic manner [151]. This technology in stroke rehabilitation is quite new, and studies have shown that VR increases the patient's motivation as well as attention span, which assists in enhancing the speed of stroke recovery [152]. VR based therapy is considered as a useful rehabilitation tool for a number of reasons. Here the subject interacts with a digital environment that is customized for a specific medical condition. The 3D environment can be adjusted according to the patient's improvement and progress to keep the user involved throughout the rehabilitation session [153]. Furthermore, the therapy performed in the dynamic, stimulating environment has proven to be more efficient in performing functional tasks and training problem-solving skills [154]. Another desirable characteristic of VR systems is that they can simulate real-world activities, which are impossible to execute in conventional therapy sessions; for instance, walking in a garden, crossing the road, etc. [155]. Thus, these types of systems could be more enjoyable and interesting, thereby encouraging the patient to perform long periods of therapies [156].

SaeboVR is a VR based rehabilitation system designed to provide virtual assistance to stroke patients for exercising their daily life activities [157]. Mindmaze, the neurotechnology company has introduced a 3D virtual environment therapy named "MindMotion PRO" for neurorehabilitation patients. This system is equipped with real-time multisensory feedback and cognitive exercise games within post-stroke rehabilitation programs, hence empowering the human brain to heal faster [158]. Similarly, TRAVEE (Virtual Therapist with Augmented Feedback for Neuromotor Recovery) rehab system [159] also uses VR which contains a virtual therapist with augmented feedback for neuromotor recovery. Moreover, C.A.R.E.N (Computer Assisted Rehabilitation Environment) [160], nBETTER (Neurostyle Brain Exercise Therapy towards Enhanced Recovery) [161] and Armonia [162] are other commercially available VR based neurorehabilitation systems used to rehabilitate post-stroke patients. Additionally, custom made low-cost VR systems like REINVENT (Rehabilitation Environment using the Integration of Neuromuscular-based Virtual Enhancements for Neural Training) [163] and others [164] have also been designed for stroke upper limb motor recovery.

Nowadays, VR is getting more attention from therapists for implementing in neurological rehabilitation to perform motor disorder treatments [165]. However, regardless of its benefits and innovative strategies, there is no indication that VR based therapy alone can be effectual compared with traditional therapies for patients facing severe stroke conditions, as they possess a very low level of motor control [166]. Therefore, VR must be accompanied by additional technologies like BCI, which allows to control required movements in the virtual environment with the patient's thinking and improves motor recovery. To increase the efficiency of the BCI-VR systems, either haptic feedback (e.g., vibrotactile) or an external assisting unit like FES stimulation or robotic assistance is added to the system, thus creating a "VR based Hybrid BCI System" [167].

3.3.1. BCI-VR Systems for Stroke Rehabilitation

Based on our current search and knowledge, VR was first incorporated with the BCI system by Vourvopoulos et al. in 2016 and until now, most of the research on VR-BCI systems has been accomplished by his group. Firstly, Vourvopoulos et al. compared the performance of 3 different customized VR-BCI systems without any external feedback [168]. Then, they performed power spectral density estimation and statistical analysis, which showed the enhanced impact of the VR-BCI system in neurorehabilitation [169]. Vourvopoulos et al. have also designed NeuRow, a novel BCI-VR environment with vibrotactile (haptic) feedback, and tested its efficacy on healthy subjects [170]. Later, in 2019, another group from Vourvopoulos's research lab designed a new VR-BCI system called "REINVENT" [163], and compared the performance of REINVENT with other BCI systems that provide visual feedback via a computer screen [171]. Preliminary results report that VR may increase embodiment compared to computer screens. Vourvopoulos et al. also conducted several experiments using REINVENT, with [172] and without [173] vibrotactile feedback and achieved a high accuracy in task executions with improvement in sensorimotor brain activities. Moreover, Lupu et al. [174] used a TRAVEE rehabilitation system [159], which comprises of a VR headset, monitoring devices, FES stimulation device, and processing unit. The preliminary result shows that for most of the subjects, the control error rate lies below 20%, with one subject even displaying an error rate under 2%, which is quite promising. These are just preliminary results and therefore the exact accuracy of the designed system is difficult to estimate at the current stage. However, from the patient's feedback, it has been deduced that the VR system has kept them focused and interactive along with providing an exciting environment, which clearly shows an additional benefit for the rehabilitation procedure. Thus, it could be inferred that by incorporating VR with BCI, the overall effectiveness of the rehab system increases when compared to conventional techniques.

Table III. Research studies and their outcomes for BCI-VR neurorehabilitation systems

VR BASED BCI SYSTEMS FOR UPPER LIMB NEUROREHABILITATION (With/Without External Assisting Unit/Feedback)						
Selection Criteria for Included Articles: Only those studies are included in this section which fulfills the following criteria: (1) Manuscript is related to an MI-based BCI controlled system with the VR technology (with/without external controlling unit). (2) Study possesses real-time online testing of the system, i.e., must be tested on either stroke patients or healthy subjects. Article that contains only offline analysis is excluded. (3) Scientific paper is related to BCI application for upper-limb neurorehabilitation.						
	PRE-REHABILITATION		**REHABILITATION TRAINING**			**POST-REHABILITATION**
Study	**Commercialized /Customized Rehabilitation System**	**BCI Methodology/ EEG Acquisition Method**	**Experimental Group (EG) and Control Group (CG)**	**Therapy per Participant (i. Total Sessions, ii. Runs/Session, iii. Trials/Run or Trials/Session)**	**Targeted Areas**	**Outcome Measures/Clinical Scores**
Vourvopoulos et al. (2016) [168]	Customized system with Vuzix iWear VR920 VR headset (Vuzix, NY, USA) and without external assisting unit	Three EEG systems used: i. 8 channels (Open-Source BCI system by Texas Instrument, Dallas, Texas, United States) ii. 8 channels - wireless (Enobio 8 by Neuroelectric, Barcelona, Spain) iii. 8 channels - wireless (g.MOBIlab+ by g.tec, Graz, Austria)	EG: 08 healthy subjects CG: N/A	i. 06 ii. N/A iii. 40 (per session)	Grasping, throwing or waving movements with the corresponding hand	Compared performance of three BCI-VR systems
Vourvopoulos et al. (2016) [169]	Customized system with Oculus Rift DK1 HMD VR headset (Oculus VR, Irvine, California,	8 channels - wireless (g.MOBIlab biosignal amplifier by gtec, Graz,	EG: 09 healthy subjects CG: N/A	i. 03 ii. N/A iii. 40 (per session)	Upper extremity movements	Power spectral density estimation and statistical analysis shows the enhanced impact of VR-BCI system in neurorehabilitation

	United States) and without external assisting unit/feedback	Austria)				
Vourvopoulos et al. (2016) [170]	NeuRow, a novel BCI-VR environment with vibrotactile feedback	8 channels – wireless (g.MOBIlab biosignal amplifier by gtec, Graz, Austria)	EG: 13 healthy subjects CG: N/A	i. N/A ii. N/A iii. 40 (per session)	Boat rowing movement from right/left hands	Design, development, and testing of NeuRow has been described. Moreover, task classification score has been identified
Lupu et al. (2018) [174]	TRAVEE system [159] with Oculus Rift VR headset and FES feedback	16-channels (g.USBamp, g.tec medical engineering GmbH)	EG: 03 healthy subjects and 07 stroke patients CG: N/A	i. 03 ii. 06 iii. 40 (per run)	Flexion/extension of hand and fingers (FES electrodes mounted on extensors muscles of both hands)	High system accuracy obtained with a low error rate
Juliano et al. (2019) [171]	REINVENT, VR-BCI system [163] without external assisting unit/feedback	16-channels (Cyton + Daisy Biosensing OpenBCI Board)	EG: 12 healthy subjects CG: N/A	i. N/A ii. 03 (blocks) iii. 30 (per block)	Arm movements	Compared the performance of VR based REINVENT system with computer screen (for visual feedback) based system.
Vourvopoulos et al. (2019) [172]	REINVENT, VR-BCI system [163] with vibrotactile feedback	8 channels (Starstim 8, Neuroelectric, Barcelona, Spain)	EG: 04 stroke patients CG: N/A	i. 08 ii. 04 (blocks) iii. 20 (per block)	Arm movements	Statistical analysis, diffusion MRI and ERSP maps are reported to analyze the motor function performance
Vourvopoulos et al. (2019) [173]	REINVENT, VR-BCI system [163] without external assisting unit/feedback	8 channels - wireless (Starstim 8 by Neuroelectric, Barcelona, Spain)	EG: 01 stroke patient CG: N/A	i. 16 ii. 04 (blocks) iii. 20 (per block)	Flexion/extension of a hand	95% task execution accuracy and motor improvement is analyzed by FMA and SIS scores Pre-BCI FMA: 13 Post-BCI FMA: 14 Pre-BCI SIS: 45 Post-BCI SIS: 75

ERSP = Event Related Spectral Perturbation; **FMA** = Fugl-Meyer Assessment; **SIS** = Stroke Impact Scale.

4. PART II: Discussion

This review paper presents the designing of MI based BCI controlled neurorehabilitation systems and also illustrates the different kinds of strategies used in such systems to provide motion assistance for post-stroke patients. The adopted strategies include FES stimulation, robotics assistance, and VR based hybrid models. An in-depth stroke application for each method has also been demonstrated. In the following discussion section, an overview of each MI-BCI rehabilitation system has been highlighted along with their comparisons. Finally, some queries regarding the best available system/technology, system reliability, level of comfort, smart design, etc. are reviewed, along with a discussion on the possible future technology in post-stroke rehabilitation.

Among all aforementioned methods, FES is one of the widely used approaches in stroke rehab systems, where motion assistance is obtained via supplying electrical stimulation to the nerves and muscles. As mentioned earlier, the FES stimulation has been used in conventional stroke therapies, where the therapist controls the ON/OFF state of stimulation according to the patient's medical condition [175-180]. Although it helps in inducing movements during rehabilitation therapy, significant improvements are not guaranteed in the patient's motor functions. That being said, FES rehab systems could help in restoring motor activities once it couples with a MI-based BCI system. In the BCI-FES system, the subject uses his/her mind waves for commanding the system to produce desired motion along with improving the neural plasticity process. However, FES based systems have some shortcomings as well. It proves to be helpful for patients with little to moderate motor mobility, i.e., FES systems are not able to assist in regaining the mobility of patients who cannot move their affected limb at all. Additionally, their effectiveness is limited due to the lack of an effectual methodology to control stimulation parameters like current intensity, timing, duration, etc. FES with surface electrodes also show limited performance regarding selective stimulation of deeper muscle groups [181].

Another methodology used is the "Robotics Assisted" method, which is combined with BCI to form "Robotics Assisted BCI neurorehabilitation systems." In such a system, the robotic hardware acts as a motion controlling unit, which is attached to the subject's limb. The robotic unit provides targeted movement assistance based on received inputs by the BCI unit, which corresponds to the subject's thinking regarding performing specific movements. The main advantage of these systems is that they can be used for patients with even "NO" motor function and help them to move their hemiparetic arm according to their desired intention. Many studies illustrated that implementation of the "BCI-Robotics System" in stroke rehabilitation produces promising results, as it makes the direct training of the brain possible along with providing motion assistance (for details refer to table II). However, one of the major concerns in BCI-Robotics systems is to control the precise and accurate movements of robots in a real-time scenario. This motion controlling issue is specifically related to BCI-Robotics systems because it is very challenging to design a highly accurate "Robot Motion Controller" [139]. Due to the processing of large EEG data, it is sometimes challenging to control the precise and accurate movements of robots in a real-time scenario. Moreover, another limitation of BCI-Robotics rehabilitation is its bulky operating system. The patients may feel uncomfortable in performing therapy exercises with the complex and massive robotic setup used in BCI rehabilitation [118-120, 133-135, 139-140]

BCI-FES and BCI-Robotics systems have produced encouraging results in post-stroke rehabilitation, however these methods are lacking an important factor of "MOTIVATION". After a while, it was understood that patients became bored and felt like "BEING A PATIENT" in those clinical surroundings [182]. Hence to overcome this problem, VR has been introduced in the neurorehabilitation therapy of stroke patients. The combination of BCIs with VR allowed providing a virtual environment with entertaining, thrilling and stimulating tasks. It keeps the patients more concentrated and motivated towards the rehab exercises, with the possibility of engaging more neural circuits that can help in restoring their motor functions in a more effective way [150]. VR-BCI systems can be used with or without external assisting units or feedbacks. External feedback mainly includes FES, robotics assistance, and haptic support, which can be integrated with the VR-BCI system to develop VR-BCI hybrid systems. Thus, it can be seen from the presented studies that VR-BCI systems hold an enormous scope in neurorehabilitation (Table III), however many factors still need to be considered and addressed in the future. As VR is a newly adopted method in the BCI rehabilitation procedure, initial research and testing are mostly conducted on healthy subjects of small sample sizes, with minimal implementation on stroke patients (refer to Table III for details). Additionally, the use of low graphics VR can cause simulator sickness in patients and as such, high-quality VR should be designed to replicate an actual environment as realistically as possible. Furthermore, different VR rehabilitation systems like SaeboVR, Mindmaze, and TRAVEE have been mostly used in conventional rehab therapies of stoke patients (without BCI) [44, 183-185]. Hence, more research should be conducted by pairing VR and BCI systems (with/without assisting feedback) to explore the in-depth practical implementation and feasibility of different VR-BCI systems for stroke patients.

In addition to the design, advantages, shortcomings and therapeutic application of various rehabilitation systems, we believe that there are some key questions that need to be addressed for concluding the discussion. These inquiries can provide an overview regarding their current level of implementation, design feasibility, practical credibility and future interpretation.

Are currently available BCI neurorehabilitation systems reliable? Referring to Tables I, II and III, it is evident that most of the research is limited to healthy subjects and small sample sizes. Therefore, it is too early to comment on the system's reliability for stroke patients. However, some well-known commercially available rehabilitation systems like RecoveriX, TRAVEE, etc. are claimed to be reliable and efficient enough. That being said, their performance on stroke patients with large sample sizes is still questionable and therefore, clinical testing on a significant number of patients should be conducted to assert their claim.

Which BCI neurorehabilitation system is the best among all? We believe that there is no so-called "BEST" system, as every system has its pros and cons and their usage depends on the required application. For instance, in general patients having a moderate level of motor functions should use the BCI-FES system and patients having less or no motor functions should use the BCI-Robotics system. However in either case, the VR coupling proves to be a positive add-on and increases the overall efficacy of the rehabilitation system. Therefore based on our research, we can say that VR based BCI rehab systems could be the most optimized and preferred choice for now. In fact, the TRAVEE rehabilitation system has also embedded VR technology in their design and their preliminary results are reasonably satisfactory as well. However, there is still room for improvement in the available rehabilitation devices in terms of factors such as design compactness, comfort, user-friendliness, etc.

Can current systems be implemented at home? Though many research groups have obtained favorable results in the clinical environment, the real challenge remains to transform these complicated protocols into user-friendly, compact and cost-effective systems that are appropriate for frequent use at home. To the best of our knowledge, for now, there is only one research in which BCI controlled powered exoskeleton (named IpsiHand) has been designed for motor recovery in chronic stroke survivors. The system has been tested on ten chronic hemiparetic stroke survivors and results have demonstrated that the BCI based neurorehabilitation system can be effectively delivered in home settings, thus increasing the probability of future clinical translation [186]. As in the research, the BCI tasks were performed at home by the patients and their caretakers, and poor-quality EEG activity was observed on some days. Moreover, they have used commercially available wired EEG systems for data acquisition, which in the future can be improved by being replaced with wireless acquisition systems. Hence, there is still enough room for

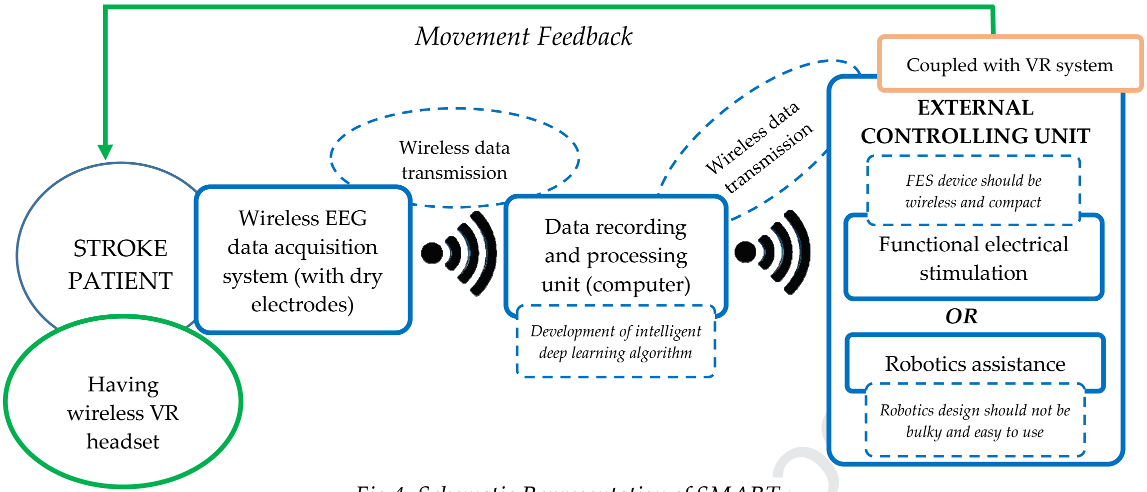

Fig.4. Schematic Representation of SMART Neurorehabilitation System

improvement, which in turn raises an idea of designing a "SMART REHABILITATION SYSTEM" (figure 4) in which every module needs to be wireless, portable and easy to use along with the implementation of intelligent machine/deep learning algorithms. Additionally, dry electrodes could also be used for EEG acquisition, which will speed up the electrode configuration process and will provide ease for using the EEG setup. Hence, such home setting based neurorehabilitation systems would increase the level of ease in stroke patients' lives, as it will allow performing therapy at a low cost without the need for constant practitioner supervision as well as offers flexibility in scheduling the rehabilitation session. However, to implement such systems on a large-scale, several practical aspects will need to be considered. Some of them include designing a cost-effective system, optimizing the wireless EEG headset and controlling unit for improved user experience, and the addition of a sub-system for automatic EEG quality checks and artifacts removal.

What is the future of BCI based neurorehabilitation systems? Is there any technology shift expected in the coming future within this field? As far as the future of BCI neurorehabilitation is concerned, there are high chances that "Flexible Electronics" (FE) would be introduced in this field. It is an advanced technology that provides a flexible hardware platform and can perform signal amplification, enabling closed-loop interaction along with precise sensing features. These days, FE is playing a vital role in revolutionizing neural interfaces and Maiolo et al. (2019) have illustrated the rise of flexible electronics in neuroscience, from materials selection to in-vitro and in-vivo applications (Figure 5) [187]. Moreover, in 2019, research has been published in "Nature Machine Intelligence," in which Mahmood et al. have designed a fully portable, flexible and wireless BCI for EEG data acquisition via FE [188]. Therefore in the future, there is a possibility that FE will establish an

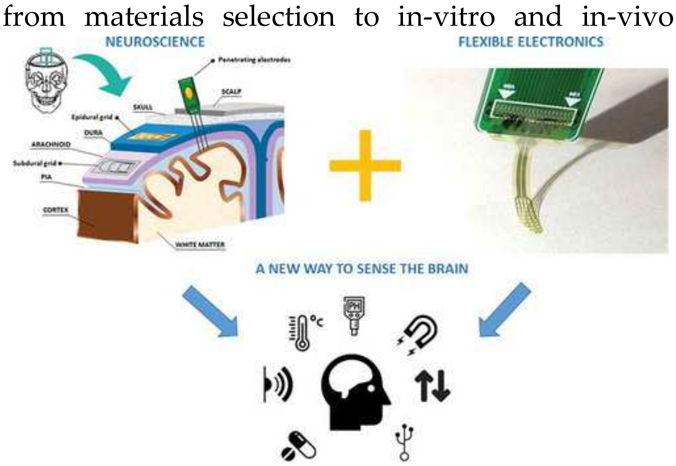

Fig.5. Application of Flexible Electronics in Neuroscience [187]

innovative technological advancement in the field of neurorehabilitation and will be used to design flexible rehabilitation systems for stroke patients.

5. Conclusion

The present systematic review comprehensively describes three types of BCI controlled systems for post-stroke rehabilitation therapy, which include BCI-FES, BCI-Robotics and BCI-VR hybrid (with/without controlling unit or feedback) systems. BCI rehabilitation systems are discussed in terms of their characteristics, advantages, design, and application. Finally, a comparison of all three types of systems has been made based on the sample size, therapy duration (no. of sessions), type of rehabilitation system (commercial or customized), BCI methodology adopted, targeted area, and outcomes. These systems' weaknesses, reliability and practical implementations have been discussed and some recommendations for designing a smart rehab system have also been proposed. Lastly, the possible future of the BCI neurorehabilitation systems has been anticipated with regards to revolutionizing the field by means of the advanced flexible electronics technology.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

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Highlights:

- BCI methods are among the most effective tool for designing rehabilitation systems
- Use of virtual reality (VR) can increase the efficiency of BCI rehab systems
- "FES," "Robotics Assistance," and "Hybrid VR based Models" are main BCI approaches
- In the future, flexible electronics can be used for designing stroke rehab systems

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