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Enhancement of Robot-Assisted Rehabilitation Outcomes of Post-Stroke Patients Using Movement-Related Cortical Potential

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Abstract

Post-stroke rehabilitation is essential for stroke survivors to help them regain independence and to improve their quality of life. Among various rehabilitation strategies, robot-assisted rehabilitation is an efficient method that is utilized more and more in clinical practice for motor recovery of post-stroke patients. However, excessive assistance from robotic devices during rehabilitation sessions can make patients perform motor training passively with minimal outcome. Towards the development of an efficient rehabilitation strategy, it is necessary to ensure the active participation of subjects during training sessions. This thesis uses the Electroencephalography (EEG) signal to extract the Movement-Related Cortical Potential (MRCP) pattern to be used as an indicator of the active engagement of stroke patients during rehabilitation training sessions. The MRCP pattern is also utilized in designing an adaptive rehabilitation training strategy that maximizes patients' engagement.

This project focuses on the hand motor recovery of post-stroke patients using the AMADEO rehabilitation device (Tyromotion GmbH, Austria). AMADEO is specifically developed for patients with fingers and hand motor deficits.

The variations in brain activity are analyzed by extracting the MRCP pattern from the acquired EEG data during training sessions. Whereas, physical improvement in hand motor abilities is determined by two methods. One is clinical tests namely Fugl-Meyer Assessment (FMA) and Motor Assessment Scale (MAS) which include FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements' tests. The other method is the measurement of hand-kinematic parameters using the AMADEO assessment tool which contains hand strength measurements during flexion (force-flexion), and extension (force-extension), and Hand Range of Movement (HROM).

The original contribution of this thesis is the development of an "Adaptive Robot-Assisted Rehabilitation Strategy" which significantly enhances the motor recovery outcomes of post-stroke patients. A series of systematic experiments are designed and tested in this project which leads to the development of the adaptive rehabilitation strategy. Firstly, the changes in the features of the MRCP pattern are understood during different robot-assisted rehabilitation training protocols with both healthy subjects and post-stroke patients. It is found that the negative peak (abbreviated as Npeak in this thesis) of the MRCP pattern in both groups is more prominent during the interactive training protocol (2D games) compared to simple visual-cue protocol. Secondly, the effect of a designed longitudinal rehabilitation training program on the features of the MRCP pattern acquired from post-stroke patients is analyzed. It is observed that the Npeak amplitude significantly decreases as the patients get comfortable with the exercises. Moreover, it is established that the variations in the MRCP features, as well as the training effect on hand motor skills, depend upon the stroke lesion locations. The supratentorial stroke patients show Npeak decrease with a positive association in the improvements of hand motor abilities earlier when compared to infratentorial stroke patients. The infratentorial stroke patients require more training time to show the corresponding Npeak decrease and significant hand motor recovery. Lastly, the practical demonstration of the novel adaptive rehabilitation training strategy is provided in which training modes progress to the next level depending on the individual

patient’s EEG response to the current training mode.

During the adaptive rehabilitation training strategy, the number of days a patient spends on any AMADEO training mode is in accordance with the time he/she needs to master the current training mode. Furthermore, it is found that Npeak amplitude increases at all channels whenever a new training mode is introduced to the subject which is an indication of active engagement while performing the motor task during the new training mode. The efficacy of this rehabilitation strategy is determined by calculating the percentage change in the results of the clinical tests and hand-kinematic parameters for the patients who completed the fixed-training strategy and for those who underwent the adaptive-training strategy. The results revealed that the adaptive-training group achieved 38.98 %, 73.6 %, 39.29 %, and 19.7 % more improvement in FMA-wrist, FMA-hand, MAS-hand, and MAS-advanced hand movements’ test respectively compared to the fixed-training group. While, the force-flexion, force-extension, and HROM parameters improved by an extra 145.37 %, 1.39 %, and 1.89 % for the adaptive-training group compared to the fixed-training group.

EEG is a user-friendly, cost-effective, scalable, and practical method compared to other methods of monitoring brain activities during the rehabilitation process. Therefore, the adaptive rehabilitation training strategy developed in this project could potentially be utilized by therapists as an aid to prescribing individualized exercises that can continuously challenge patients, keeping them engaged. Ultimately, this adaptive-training strategy could promote faster motor and functional recovery for post-stroke patients ensuring the best outcome for patients as well as the rehabilitation centres.

Acknowledgment

It is a great pleasure to express my gratitude to all who provided a great deal of support and assistance throughout my doctoral studies.

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I want to dedicate this work to my dear father (late), my loving mother, and the most amazing parents-in-law for their unconditional love, countless expressions of support, and boundless inspiration. I also thank my siblings and siblings-in-law for their love, encouragement, and support over the years. I am truly blessed to be a part of such a caring and loving family. I am also grateful to all my friends I have made during these four years in Wollongong and their families especially Usman, Zeeshan, and Arbab. You people have made my stay in Wollongong delightful and memorable.

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Certification

I, Maryam Butt, declare that this thesis submitted in fulfillment of the requirements for the conferral of the degree Doctor of Philosophy, from the University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. This document has not been submitted for qualifications at any other academic institution.

Maryam Butt
28th August, 2020

List of Abbreviations

ADL: Activities of Daily Living

AO: Action Observation

ARAT: Action Research Arm Test

AROM: Active Range of Motion for dorsiflexion

AR: Augmented Reality

BP1: Bereitschaftspotential 1

BP2: Bereitschaftspotential 2

BMT: Bimanual Motor Training

BOLD fMRI: Blood Oxygenation Level-Dependent functional Magnetic Resonance Imaging

BCI: Brain-Computer Interface

BEI: Brain Engagement Index

CNS: Central Nervous System

CAR: Common Average Reference

CIMT: Constraint-Induced Movement Therapy

CPM: Continuous Passive Motion

CPMplus: Continuous Passive Motion plus

CLFC: Contralateral FC

CLC: Contralateral C

CLCP: Contralateral CP

CNN: Convolutional Neural Network

DOF: Degree of Freedom

ECG: Electrocardiogram

ECoG: Electrocorticography

EEG: Electroencephalography

EMG: Electromyography

ERD: Event-Related Desynchronization

ERS: Event-Related Synchronization

EOG: Electrooculography

FES: Functional Electrical Stimulation

fMRI: functional Magnetic Resonance Imaging

fNIRS: functional Near-Infrared Spectroscopy

FMA: Fugl-Meyer Assessment

FM-LM: Fugl-Meyer Leg Motor

FMA-wrist test: FMA wrist section test

FMA-hand test: FMA hand section test

Force-flexion: Hand strength measured during flexion

Force-extension: Hand strength measured during extension

GUI: Graphical User Interface

HROM: Hand Range of Movement

HK: Haptic Knob

HE: Horizontal Eye

ICA: Independent Component Analysis

ILFC: Ipsilateral FC

ILC: Ipsilateral C

ILCP: Ipsilateral CP

LDA: Linear Discriminant Analysis

LPP-LDA: Locality Preserving Projection- Linear Discriminant Analysis

LE: Lower-Extremity

MAS: Motor Assessment Scale

MAS-hand movements test: MAS tests for hand movements section

MAS-hand advanced movements test: MAS tests for advanced hand movements section

ME: Motor Execution

MEG: Magnetoencephalography

MF: Matched Filter

MIME: Mirror Image Movement Enabler

MI: Motor Imagery

MP: Motor Potential

MRCP: Movement-Related Cortical Potential

MVC: Maximum Voluntary Contraction

NMES: Neuromuscular Electrical Stimulation

Npeak: Negative Peak

NS: Negative Slope

PET: Positron Emission Tomography

rBSI: revised Brain Symmetry Index

ROM: Range of Movement

RP: Readiness Potential

SD: Standard Deviation

sEEG: Stereotactic EEG

S_m: Strength measure

6MWD: Six-Minute Walk Distance

SL: Short Laplacian

SMRs: Sensorimotor Rhythms

SP: Stroke Patient

SPECT: Single Photon Emission Computed Tomography

SVM: Support Vector Machine

tDCS: transcranial Direct Current Stimulation

TENS: Transcutaneous Electrical Nerve Stimulation

TFSP: Time-Frequency synthesized Spatial Patterns (TFSP)

TMS: Transcranial Magnetic Stimulation

TNR: True Negative Rate

TPR: True Positive Rate

UE: Upper-Extremity

VE: Vertical Eye

VR: Virtual Reality

WAM: Whole-Arm Manipulator

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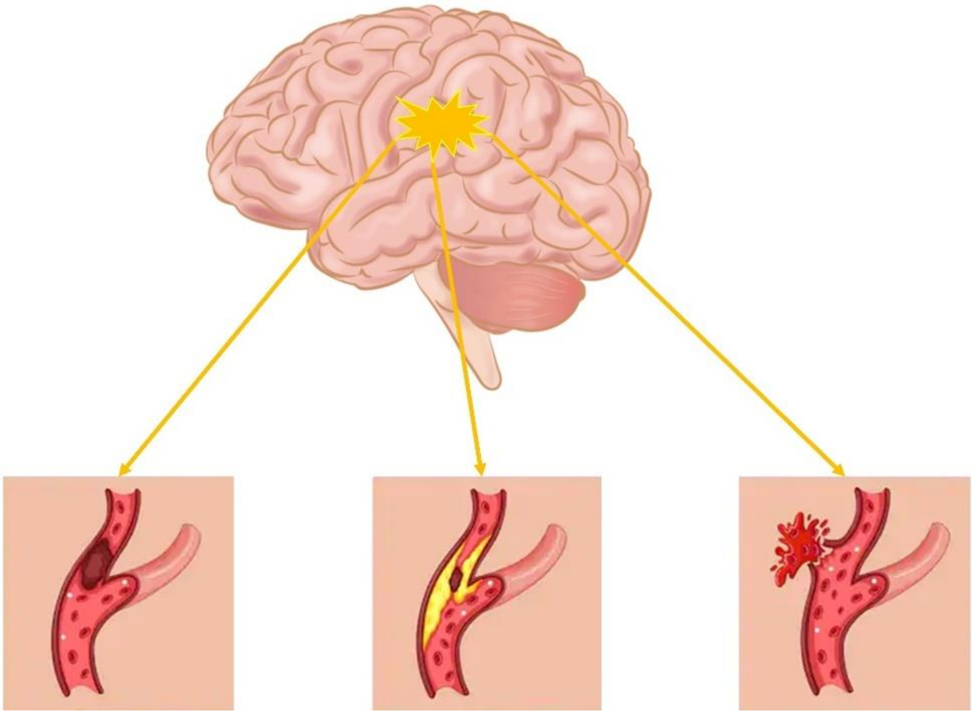
Chapter 1

Introduction

1.1 Stroke and Stroke Therapy

Stroke is considered as one of the leading causes of severe disability in the world today [1]. According to the latest annual report of the World Stroke Organization, approximately 14 million people had their first-time stroke in 2019 and 80 million people live with the impact of stroke globally [2]. Stroke is an acute onset of neurological impairment and abnormality. There are two basic types of stroke; one is known as an ischemic stroke caused by the closure of a blood vessel and the other is known as hemorrhagic stroke due to bleeding from the vessel inside the brain [3]. The ischemic stroke is further divided into two categories which are embolic stroke where a blood clot travels from the heart or a major vessel and lodges in a smaller vessel and thrombotic stroke where fats, cholesterol, or other substances build up inside the blood vessel and blocks it. All these types of strokes are shown in Figure 1.1.



(a) (b) (c)

Figure 1.1: Types of stroke; (a) Embolic (Ischemic), (b) Thrombotic (Ischemic), (c) Hemorrhagic [4]

After stroke onset, the brain cells malfunction due to the lack of oxygen and glucose. Without oxygen, the neurons and the brain cells start to die after 3 to 4 minutes. The effects of stroke vary among patients and it depends on the type of stroke, the brain part that is damaged, and the amount of damage caused by it. Generally, stroke results in changes in the level of consciousness, changes in behavioral styles, and impairment of cognition, perception, language, sensory, and motor skills. The motor skills impairments are reported to be a predominant effect of the stroke where a stroke survivor is unable to move a limb to perform Activities of Daily Living (ADL). The ADLs include bathing, dental hygiene, toileting, eating, dressing as well as transfer and mobility. Specifically, the impairment of the upper extremities can limit the independence of the stroke-affected subjects.

Post-stroke rehabilitation is essential for stroke survivors to help them regain independence and improve their quality of life. The main goal of stroke rehabilitation programs is to teach patients to re-learn their lost skills due to stroke. The re-learning of the lost motor functions for stroke-affected patients is made possible by implementing various motor training strategies which include conventional physical therapy [5, 6], Constraint-Induced Movement Therapy (CIMT) [7, 8], Functional Electrical Stimulation (FES) treatment [9, 10], Mirror-Box therapy [11, 12], Motor Imagery (MI) therapy [13], Virtual Reality (VR) therapy [14, 15] and Robotic Rehabilitation therapy [16, 17] - a new method of therapy that has emerged over the last decade with the advancement in robotic technology. The description of the aforementioned motor training strategies is given in Table 1.1.

Table 1.1: Motor training strategies for post-stroke rehabilitation

Sr. No.	Types of Motor Training Strategies	Description
1.	Conventional Physical Therapy	Re-learning of daily life motor activities such as walking, standing, sitting, lying down, and switching process from one type of movement to another. It relies initially on repeatedly performing exercises to improve strength, balance, and coordination followed by graduated task practice. It may also involve developing compensatory learning when sufficient motor recovery of the affected limb is thought not to be possible.
2.	Constraint-Induced Movement Therapy	CIMT involves the restriction of the non-affected limb over an extended period, in combination with a large number of task-specific repetitive training of the affected limb. This form of therapy forces patients to use their affected limb by preventing them from developing compensatory skills with their unaffected limb.
3.	Functional Electrical Stimulation Treatment	In FES treatment, electrical shocks are delivered to the affected peripheral nerve which activates the muscle to move. It is primarily used to reduce pain and prevent muscles from permanently contracting.
4.	Mirror-Box Therapy	A rehabilitation therapy in which a mirror is placed between the arms or legs so that the image of a moving non-affected limb gives the illusion of normal movement in the affected limb. It is believed to activate neural cells in the affected side of the brain.
5.	Motor Imagery Therapy	In MI therapy, a mental rehearsal of the movement of the affected body parts is performed, without actually attempting to perform the movement. This may also activate neural cells on the affected side of the brain.
6.	Virtual Reality Therapy	By simulating real-life activities using VR technology, stroke patients can practice motor skills in a setting that is usually impossible to create in a hospital environment.

7.	Robotic Rehabilitation Therapy	Robotic rehabilitation therapy involves the use of intelligent devices that uses sensors to monitor movement and positioning of a limb, then use this feedback to interact with the environment. This type of therapy can deliver high-intensity and task-specific training, making it useful for stroke patients with motor disorders.

All the above-stated types of motor training strategies promote the mechanism of neuroplasticity in stroke patients that reinforces the neural pathways controlling the movement [18]. In this way, these training strategies help post-stroke patients to achieve their motor and functional recovery. Motor recovery refers to the ability of patients to perform voluntary movements with the affected limb in the same way as before the stroke onset, while functional recovery refers to improvements in the ability to perform ADLs independently [19].

1.2 Neuroplasticity and Motor Skill Re-learning in Stroke Patients

The ability of the brain to adapt, even in adulthood, is called "Neuroplasticity" or "Brain Plasticity" [20]. Neuroplasticity can take place at both microscopic and macroscopic levels inside the brain. At the cellular level, neuroplasticity is depicted as new or strengthened synaptic connections made by surviving neurons [21] while at the structural level, cortical re-mapping occurs whereby other parts of the brain, usually adjacent to the damaged brain tissues, take over the functions previously performed by the damaged brain part(s) [22, 23]. It can occur if the brain receives an external stimulus such as what might be provided by task-oriented motor training [23].

Skill is the ability to perform a task with consistency, efficiency, and flexibility [24]. In clinical practice, two types of rehabilitation strategies are employed depending on stroke severity and stage of recovery. The first approach primarily focuses on compensatory training of patients to regain their motor skills (e.g., performing a task with the unaffected limb(s), using a wheelchair instead of walking). The second approach is task-oriented training focusing on practicing parts of a task and consolidate these parts into the completion of a whole task with the affected limb(s). Some centres are also incorporating new technology including robotic devices and computer-based training strategies. This transition in rehabilitation methods is happening because neuroscientific research has shown that neuroplasticity changes in the cerebral cortex and other parts of the Central Nervous System (CNS) are the primary reasons for the underlying mechanisms of motor skill re-learning after stroke [25-27]. More specifically, task-oriented training that focuses on the practice of skilled motor performance is the critical link to facilitating neural reorganization and rewiring in the CNS following stroke [28-31]. Therefore, whenever possible, task-oriented training at an intense level should be incorporated into the rehabilitation program for any patient with stroke-related motor deficits.

The neurological recovery of stroke patients has two distinct phases; one is an acute phase and the other is a post-acute phase [32, 33]. The acute stroke phase lasts for about 2 weeks after the onset of the lesion while the post-acute stroke phase usually lasts up to 6 months after the onset [33]. In the acute phase, a rapid and natural recovery usually occurs where surrounding cells, that are still alive, return to function. The recovery in the acute phase is possible because of the restoration of viable blood supply to the affected region as well as the resolution of perilesional edema and inflammation [34]. Another important factor of recovery in the acute phase is the phenomena of "diaschisis" in which neuronal networks in the undamaged brain regions remote from the original damaged site but functionally connected assume some of the roles of the damaged part of the brain. Neuroimaging techniques have confirmed that diaschisis may arise from subcortical regions on the affected side of the brain or the contralateral motor cortex [35]. These mechanisms are less important in the post-acute stages of stroke whereas the neuroplasticity mechanism described above becomes more important [32]. Therefore, a better understanding of the pathophysiology of functional deficits at various phases after stroke onset is important to optimize the outcomes of rehabilitation interventions [32].

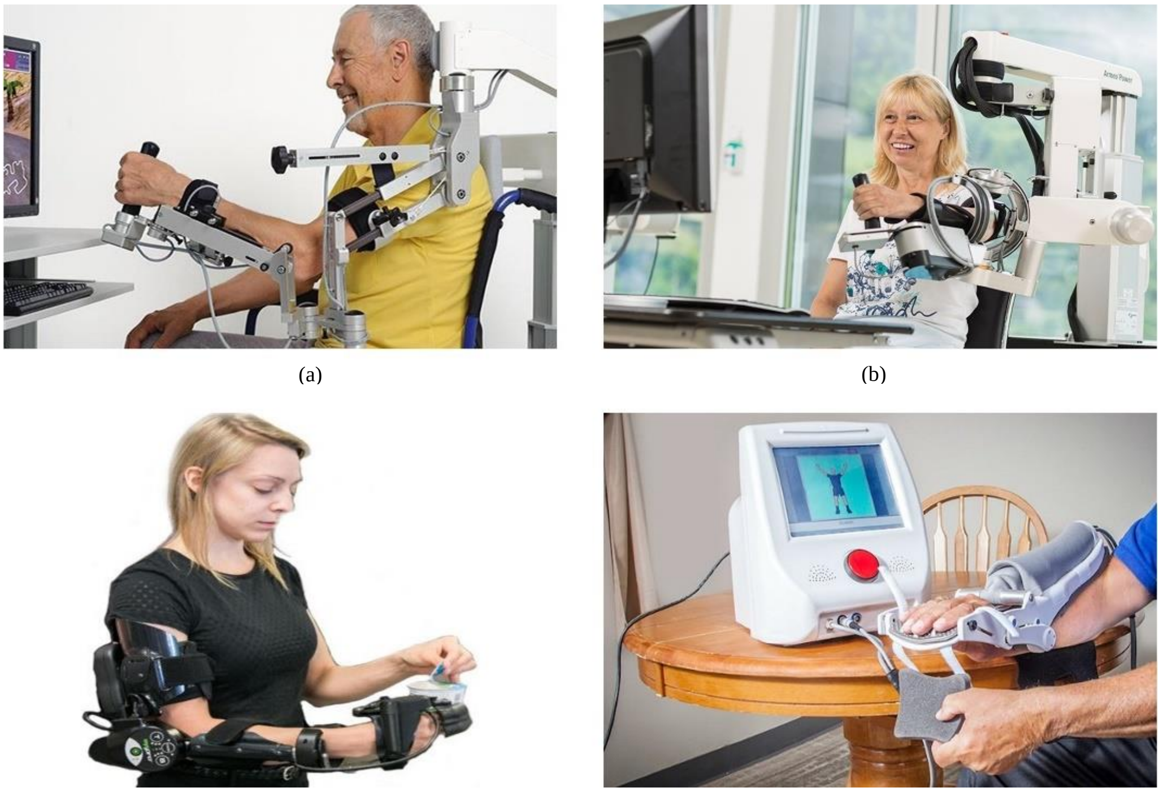
1.3 Post-Stroke Robot-Assisted Rehabilitation

As stated in Section 1.2, the intensive dosage of task-oriented training may facilitate significant improvement in motor skills following a stroke due to neuroplasticity phenomena. Conventional rehabilitation therapy usually consists of a one-to-one session between therapists and patients. Such types of therapies are subject to labor and cost limitations that, in turn, prevent the execution of high-frequency and high-intensity rehabilitation interventions [36, 37]. Moreover, manual rehabilitation therapies are associated with significant intra and inter-individual variations in delivery and therefore, rehabilitation outcomes may not be consistent [36]. Due to the advancement in robotic technology, robot-assisted therapy is being investigated and coming into clinical practice [17, 38, 39]. Robot-assisted therapies can provide more consistent and frequent rehabilitation training to patients with motor deficits [40]. They also provide a more accurate and reliable measure for changes in motor performance compared to measurements in conventional therapy for stroke rehabilitation [40]. According to literature, robot-based rehabilitation training is superior in improving motor impairments of stroke patients as compared to conventional therapy [38, 41], and further meta-analysis studies suggest that using robot-assisted therapy in conjunction with conventional therapy is more effective than deploying either alone [36, 38, 41, 42].

Robot-assisted therapies utilize intelligent devices with sensors to monitor limb's movement and positioning to adapt to the requirements of the patient under treatment [16, 17]. The rehabilitation robots use various techniques which include but are not limited to passive exercise, active-assisted exercise, active-constrained exercise, active-resistive exercise as well as adaptive exercise [43, 44]. Passive exercises require no or little involvement of the patient. In active-assisted exercises, the patient moves his or her limb in a predetermined pathway without any force pushing against it. The active-constrained exercise involves the movement of the patient's limb with an opposing force if the movement is outside the defined pathway. The active-resistive exercise is the movement with an opposing force. Lastly, an adaptive exercise involves the adaptation of a robot to a new unknown pathway.

In literature, robot-based therapy is being applied for the recovery of both Upper-Extremity (UE) and Lower-Extremity (LE) functions. It has been established as a safe and effective method for UE restoration, while the role of robotic devices in the rehabilitation of LE remains to be determined [17]. It is proposed that for task-oriented rehabilitation of the UE, the robotic devices should possess the following characteristics: skill acquisition of functional motor tasks, active participation of the patient in the training process, and individualized adaptive-training [37]. This project is based on the recovery of fine hand motor skills by using robot-assisted therapy.

There are two basic categories of robotic devices used in the field of neurorehabilitation: exoskeleton and end-effector robots. Exoskeleton robotic devices are connected to the patients at multiple points and allow accurate determination of the kinematic configuration of human joints. Some examples of commercially available exoskeleton robots for upper limb recovery include Armeo Spring, Armeo Power, MyoPro Motion-G, and Hand Mentor devices as shown in Figure 1.2 [45-48]. Whereas, the end-effector robotic devices are connected to the limb at only one point and exert forces at the interface (some distal part of the affected limb). Examples of end-effector robots available commercially for recovery of the UE are the InMotion, Mirror Image Movement Enabler (MIME), Burt, Kinarm, REAplan, and AMADEO as shown in Figure 1.3 [49-53]. Both categories of robotic devices enable the implementation of intensive training for patients with upper limb motor deficits. There are, also, many other devices in different stages of development or commercialization [54, 55].



(a) (b)

(c) (d)

Figure 1.2: Exoskeleton robotic devices; (a) Armeo Spring [45], (b) Armeo Power [46], (c) MyoPro Motion-G [47], (d) Hand Mentor [48]

(a)

(b)

(c)

(d)

(e)

(f)

Figure 1.3: End-effector devices; (a) InMotion [49], (b) MIME [50], (c) Burt [51], (d) Kinarm [52], (e) REAplan [53], (f) AMADEO

1.4 Methods for Brain Activity Measurement

There are various modalities developed to date to capture neural activities over different parts of the brain [56]. These modalities include Electroencephalography (EEG), Electrocorticography (ECoG), Stereotactic EEG (sEEG), Magnetoencephalography (MEG), Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), functional Magnetic Resonance Imaging (fMRI), and functional Near-Infrared Spectroscopy (fNIRS). All these modalities help to understand the complex brain structure and its associated functions. The brain activity measurement methods are divided into two major categories which include invasive and non-invasive techniques. The non-invasive techniques measure brain activities over the scalp surface without breaking the skin, whereas invasive techniques require surgery to open the skull and cutting the membranes that cover the brain to place the electrodes directly on the surface of the cortex or inside it as shown in Figure 1.4 [57, 58]. Out of these modalities, EEG, MEG, PET, SPET, fMRI, and fNIRS are non-invasive techniques, while ECoG and sEEG are invasive techniques. All these techniques characterize different aspects of neural activities and they possess different temporal and spatial resolutions as shown in Figure 1.5 [59].

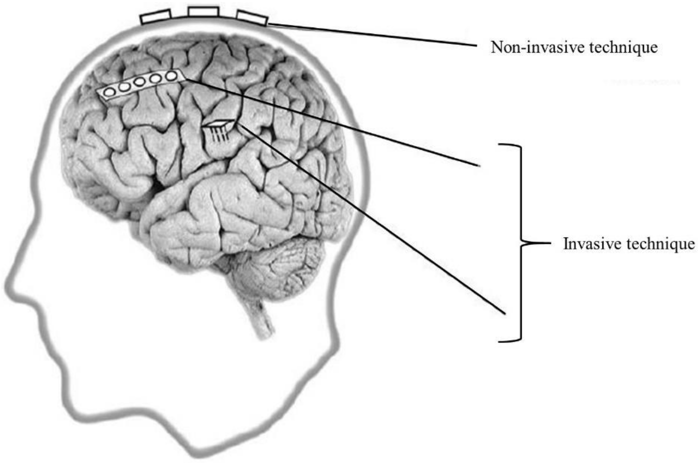


Figure 1.4: Categories of brain measuring techniques [57]

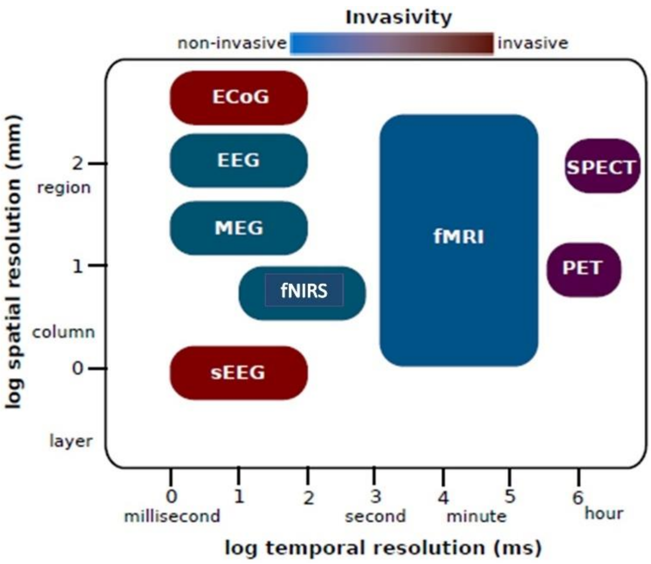


Figure 1.5: Comparison of spatiotemporal resolution for brain activity measurement methods [59]

1.4.1 Non-Invasive Techniques

This section describes the basic characteristics and applications of all aforementioned non-invasive techniques commonly employed to capture brain activities.

EEG measures, over the scalp, the electrical activities that are generated in various cortical layers of the brain. It represents a direct measurement of neural activities. It always measures the cortical potential with respect to a specific location on the body (usually a mastoid point behind one of the ears). It has a good temporal resolution, typically in the order of milliseconds. However, its spatial resolution is poor as indicated in Figure 1.5. The reason for poor spatial resolution is the distortion and attenuation of the electrical signals by intervening tissues such as cerebrospinal fluid, skull, and the scalp [59].

MEG records the magnetic field induced by the electrical activity of the neurons whilst the patient lays or sits in a motionless state. Although EEG and MEG are produced by the same physiological process, MEG has better spatial resolution because the magnetic field gets less distorted by intervening tissues. It possesses both high temporal and spatial resolutions (see Figure 1.5), however, it is sensitive to movement, is costly, and requires extensive training to operate the equipment. It mainly finds its application in neurosciences research to understand the structure of the skull and the brain activities precisely [60].

PET is an imaging modality that works by detecting changes in sugar glucose levels. During PET scan, radioactive tracers (gamma rays) induce in a subject that reaches the parts of the brain through blood flow and activates those parts for that time. This creates visible spots of neural activity, which are picked up by detectors and projected onto the screen as a video image of the brain performing a certain task [61]. SPECT is a similar scanning modality to PET because it also uses tracer material and the detection of gamma rays. However, the tracers used in SPECT emit gamma radiation that is measured directly, whereas PET tracers emit positrons which, in turn, emit two gamma photons in opposite directions due to their annihilation with electrons.

fMRI is a non-invasive neuroimaging technique that measures small changes in the blood flow associated with neural activities. It uses a strong magnetic field to measure neural activities indirectly. It has a trade-off between spatial and temporal resolution (see Figure 1.5), yet it possesses low temporal resolution compared to EEG and MEG because the blood flow is slower than the transmission of electrical activity. On the other hand, it has full-brain coverage, and it is not limited to the activity measurement from the cerebral cortex like in EEG and MEG. Having good spatial resolution, fMRI can be used to reconstruct the individual skull shape as well as the cortical layers of the subjects. Although fMRI is one of the commonly employed modalities for the acquisition of brain activities, yet its use is still limited compared to EEG due to expensive equipment, the requirement of stationary laboratory set-up, and intensive operator training [62].

fNIRS is an optical technique that determines variation in blood flow due to brain activities. In particular, the fNIRS relies on the absorption spectrum of hemoglobin varying with its oxygenation status in the infrared spectrum range as a result of changes in the level of neural activity in specific brain regions [63, 64]. It is an indirect way of measuring brain activity similar to fMRI, however, it is a comparatively affordable technique with portable equipment.

1.4.2 Invasive Techniques

ECoG and sEEG are the invasive versions of EEG developed to improve the spatial resolution of EEG. They directly record the spontaneous or evoked neural activities using electrodes placed on subdural and/or depth electrodes. The ECoG records the integrated high-frequency activities of a large number of neurons using the electrodes placed on the surface of the cortex. While sEEG uses depth electrodes that penetrate the brain tissue to record localized brain activities [59].

The advantages of invasive methods include excellent quality of brain signal, good spatial resolution, less interface from artifacts as well as a higher frequency range. However, due to the requirement of surgical procedures, invasive methods are not very popular in research communities for the measurement of brain activities. Such techniques are only suitable when the patient is already scheduled for a medical procedure that involves opening the scalp.

1.5 EEG and its Movement-Related Patterns

Among all the aforementioned non-invasive modalities, EEG is the most well-established method to measure brain activities in both clinical and research settings [65, 66]. Having high temporal resolution and being a safe, cost-effective, and easy method to administrate, makes EEG suitable for clinical and research purposes [67]. Moreover, it can be used to record brain activities during a motor task which best suits the requirements for this research project. Although, it is more sensitive to different artifacts such as eye and muscle movements, there are well-established signal processing techniques in the literature to remove such artifacts. Therefore, EEG is selected to measure brain activities during motor tasks performed by both healthy subjects and post-stroke patients during the experimental work in this project.

The brain activity changes when a person moves a limb or even just contracts a single muscle. It can also be changed even when one imagines a limb movement. The motor intention is a conscious willingness of moving a limb before its actual execution [68]. This can be considered as a part of a motor action planning stage. When there is an intention or imagination about limb movement, brain oscillations measured over sensorimotor or motor cortices change. These brain oscillations, also termed Sensorimotor Rhythms (SMRs), are divided into specific frequency bands and termed as delta band (< 4 Hz), theta band (4-7 Hz), alpha band (8-12 Hz), beta band (12-30 Hz) and gamma band (> 30 Hz). The alpha band activity recorded over sensorimotor areas is termed as mu activity [57]. The reduction in the amplitude of SMRs, usually in the alpha and beta band frequency range, is known as Event-Related Desynchronization (ERD) [69]. On the other hand, after the execution of movement, the amplitude of the EEG signal gradually increases. This is called Event-Related Synchronization (ERS). The waveform for ERD/ERS pattern is shown in Figure 1.6.

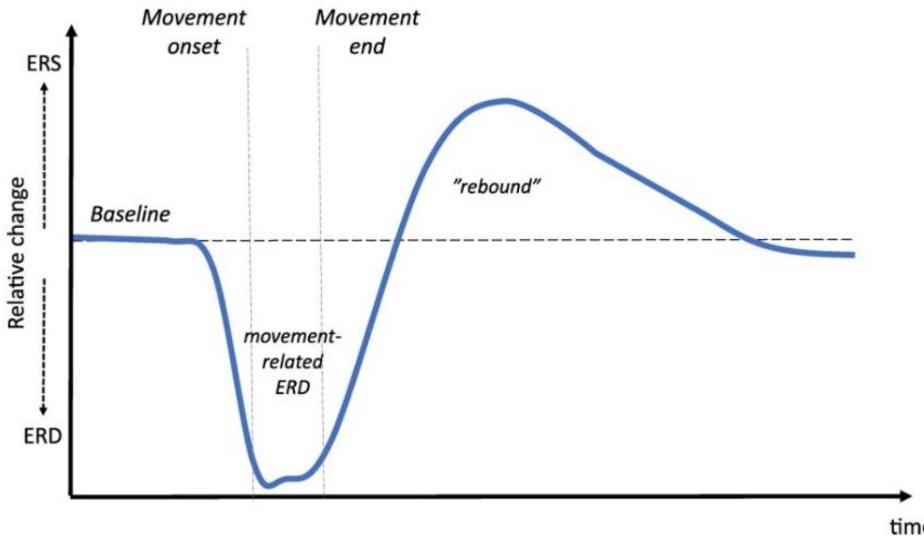


Figure 1.6: ERD/ERS EEG-derived pattern [70]

Another EEG-derived movement-related pattern is known as Movement-Related Cortical Potential (MRCP). MRCP is a slow, time-domain event-related potential that appears in the delta frequency band of the EEG signal. It appears as a direct-current shifts up to 2 s prior to cue-based as well as self-initiated movements [71]. The waveform of the MRCP pattern is shown in Figure 1.7. The MRCP pattern can be divided into three components that convey movement-related information. The first pre-movement component is a slow decrease in the cortical potential that starts around 2 s before movement onset and it is termed as Bereitschaftspotential 1 (BP1) [71]. The second pre-movement component is a steeper decrease in cortical potential compared to BP1 and starts at about 0.5 s before movement onset, which is named Bereitschaftspotential 2 (BP2) [71]. Finally, the lowest potential near the movement onset is the third pre-movement component of MRCP, termed as Negative Peak (Npeak) [71]. In literature, these MRCP components are also termed with various names such as BP1 is termed as Readiness Potential (RP) [71], BP2 as Negative Slope (NS) [72], and Npeak as Motor Potential (MP) [73]. These pre-movement MRCP components i.e., BP1 or RP, BP2 or NS, and Npeak or MP reflect the cortical activity involved in planning and preparing to perform a voluntary movement [71]. They also occur when there is an intention to move or while imagining movements [71]. In this thesis, these three pre-movement MRCP components will be referred as BP1, BP2 and Npeak.

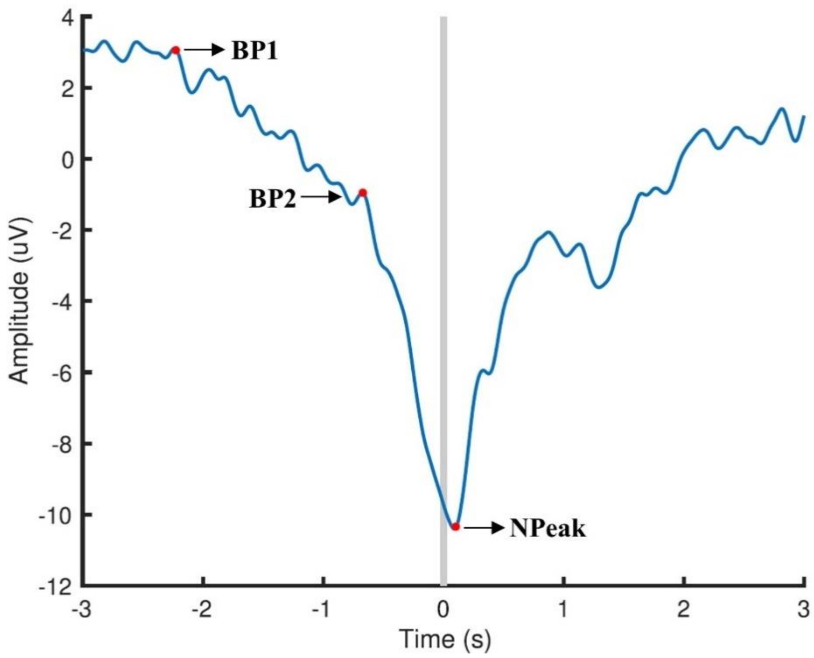


Figure 1.7: MRCP EEG-derived pattern [74]. Here 0 s is the movement onset point.

Both ERD/ERS and MRCP patterns are also termed as motor intention signals in the literature [75-80] because they appear when the subject intends to perform a motor task and disappear when he/she completes that motor task. Therefore, both ERD/ERS and MRCP patterns are called intention signals in this thesis.

1.6 Research Hypothesis, Objectives, and Approach

Robot-assisted rehabilitation is an efficient method to recover the motor impairments of post-stroke patients. However, excessive assistance from a robotic device can have a negative effect on the recovery of stroke patients [81]. That is, unnecessary assistance from robots can make patients perform the therapeutic training sessions passively. Therefore, monitoring of active participation of subjects during robot-based motor training is essential. This research project hypothesizes that it is possible to measure the engagement and active participation of post-stroke patients towards the development of an efficient rehabilitation strategy to maximize their motor recovery outcomes. Section 1.6.1 describes the research gaps identified after performing a comprehensive literature review. Whereas research aims and objectives developed under the light of research gaps are presented in Section 1.6.2. Lastly, the research approach adopted to address the designed objectives is described in Section 1.6.3.

1.6.1 Research Gaps

The literature review is performed to determine various applications of EEG for the recovery of post-stroke motor impairments. The literature confirms that the active participation of stroke patients can be ensured by detecting the intention signal (EEG-derived movement-related patterns) during motor training tasks [82-84]. Moreover, it confirms the patients' active participation during training sessions can enhance the outcomes of their motor recovery [85-88]. Although intention detection or classification during motor tasks is addressed in the literature, there is still a gap to understand the variations of intention signals during different robot-assisted training protocols.

Of the commercially available robotic devices mentioned in Section 1.3, the AMADEO rehabilitation device (Tyromotion GmbH, Austria) is developed for patients with fingers and hand motor deficits [89]. The studies in the literature demonstrate the usefulness of the AMADEO device for the improvement of fine motor skills of different patients [90-94]. However, none of these studies detect the intention signal to estimate the engagement level or active participation of subjects during motor tasks. An attempt to ensure the active participation of subjects during rehabilitation training using the AMADEO device was made by Xianwei et al. [93, 94]. The authors developed a novel algorithm "Assist-As-Needed" and evaluated the algorithm's performance with post-stroke patients. While working along the same path, there is a research gap to estimate the active participation of stroke patients with the help of the EEG signal using the AMADEO device.

Generally, a stroke patient requires multiple sessions of rehabilitation training to recover the lost motor activities in the affected limb(s). In literature, the outcomes of such training are usually determined with the help of clinical tests or measuring the improvement in the performance of the practiced task [85, 86, 93-97]. There is a need to find the effect of multi-session robot-assisted training on the EEG signal which could lead to the estimation of the neuroplasticity induction that occurs in the repairing brains of the stroke patients. Previous researchers have mainly focused on determining the effect of single-session and multi-session training on EEG signals with healthy subjects. There is a requirement to establish the changes in the EEG signal acquired from post-stroke patients after they complete a multi-session training strategy.

Another limitation in post-stroke rehabilitation is the use of fixed rehabilitation training strategy for a couple of weeks until patients show recovery in their motor skills. It is challenging for the patient to maintain concentration during training sessions that are fixed on each training day. Therefore, it is beneficial to design an adaptive and dynamic rehabilitation program that varies according to the patients' participation level. EEG-derived patterns vary with the engagement level of both healthy subjects and stroke patients during the motor tasks [84, 98-102]. In particular, the amplitude of these patterns has been reported to increase or decrease with the engagement level of subjects while performing motor tasks. These variations in the features of EEG-derived patterns can be utilized to design adaptive rehabilitation training.

1.6.2 Research Aims and Objectives

The research aim of this project is to improve the outcomes of robot-assisted stroke rehabilitation programs based on the identified research gaps and limitations during the literature review. More specifically, an effort is made in this project to develop an efficient rehabilitation technique that increases the engagement of the stroke subjects during motor training sessions and, in turn, enhances the outcome of the developed rehabilitation program for post-stroke patients. The following objectives are set to fulfill the research aims:

a. To identify which EEG-derived pattern can be used to measure the level of the subject's engagement in hand motor tasks.

b. To understand the changes in the selected EEG pattern during different robot-assisted rehabilitation training protocols.

c. To develop and validate a longitudinal motor training design for hand motor recovery of post-stroke patients.

d. To determine the effect of the designed longitudinal training strategy for hand motor recovery of stroke patients on the EEG signal.

e. To correlate the changes in the EEG signal with the results obtained from commonly employed clinical tests and robot-based assessment methods.

f. To design and implement an adaptive robot-assisted motor training technique for post-stroke patients to enhance their rehabilitation outcomes.

1.6.3 General Research Approach

A series of experiments are designed to address the aforementioned research objectives. An ethics application for all the experiments performed during this research project was approved by the University of Wollongong (UOW) Ethics Committee and the New South Wales (NSW) Health Authority. The Ethics application number was 2014/400 which was granted for a year and with the possibility of renewing the application for the following years. Furthermore, before the study commencement on both healthy participants and stroke patients, written informed consent was read and duly signed by every participant. The approvals of the UOW Ethics application and consent form used for all experiments of this project are also presented in Appendix 1.

At Port Kembla Hospital located at Warrawong NSW Australia, a rehabilitation specialist was actively engaged in identifying potential subjects for the experiments. The AMADEO robotic device and EEG acquisition system were moved to Port Kembla Hospital Physiotherapy Rehabilitation Department. An honorary appointment has also been received to conduct experimental work at the physiotherapy rehabilitation department. The appointment of an honorary research application is also given in Appendix 1.

The general research approach for this project is presented in Figure 1.8. In this study, the post-stroke patients are recruited according to well-defined inclusion criteria. The AMADEO hand rehabilitation device is selected for fine hand motor skill training of the recruited patients. Before the start of the training, two assessment procedures are performed to determine the current impairment level in the hand motor skills of the patients. Firstly, clinical tests of the UE are conducted that are normally used at rehabilitation centres. Secondly, hand-kinematic parameters using the AMADEO assessment tool are measured.

Stroke patients participate in a multi-session robot-assisted training of their affected hand on the AMADEO device. The EEG measurement is performed during training sessions to monitor the active participation level of the participants. After the literature review, the MRCP pattern is selected as an indicator of active participation in this project. If the engagement level of the subjects is high or moderate (indicated by the variations in the MRCP pattern) then the same training continues. However, if their level of engagement is low then the training session is made more challenging. In this way, the patients can maintain the level of active participation throughout the designed rehabilitation program. At the end of the training, both clinical tests and hand-kinematic parameters measurements were performed again to compare with the corresponding pre-training measurements.

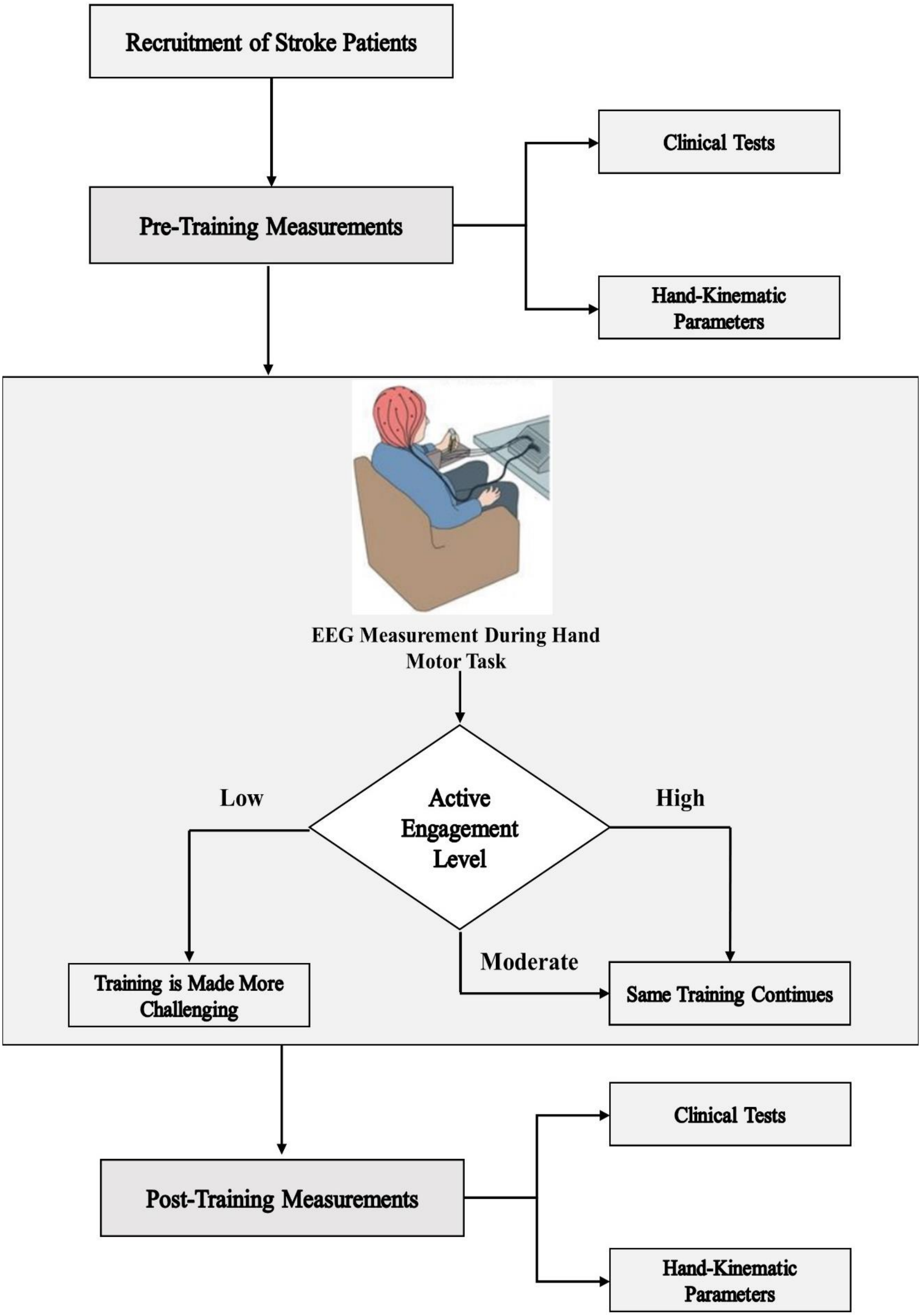


Figure 1.8: The overview of the general research approach of this project

With this approach of post-stroke motor training, the rehabilitation outcomes will be enhanced which will improve the quality of life for stroke patients. The overall rehabilitation period of stroke patients will also be reduced that is in the best interest of both patients and rehabilitation centres. Furthermore, the outcomes of this research project can be a guideline for rehabilitation centres to implement the developed rehabilitation strategies on a large scale.

1.7 Research Contributions and Outcomes

1.7.1 Contribution of the Thesis

Towards fulfilling the research aims and objectives of this project, the following major contributions were made by this study:

(i) A comprehensive review of the literature was conducted on the various applications of the EEG signal for post-stroke rehabilitation. The literature review provided an overview of the major works and trends in this area of research, as well as, identifying the research gaps in this field.

(ii) The difference in intention signal produced during hand motor tasks for two distinct training protocols was established with both healthy subjects and stroke patients. Visual-cue protocol was based on simple pictures of hand movements while another protocol was one of the interactive 2D games available in the AMADEO rehabilitation device. It was found that the intention signal during the interactive 2D game was greater in amplitude compared to that during the visual-cue protocol. These results helped in designing further experiments of this project.

(iii) A multi-session robot-based rehabilitation training was designed and conducted for recovery in hand motor skills of post-acute stroke patients using the AMADEO device. The effect of the designed rehabilitation program on the EEG signal was measured by analyzing the changes in the features of the MRCP patterns. Moreover, the improvements in hand motor skills were determined with the help of clinical tests and hand-kinematic parameters' measurements. These improvements were correlated with the variations in the MRCP pattern. The experimental results confirmed that the amplitude of the MRCP pattern decreased when the stroke patients achieved competency in performing the required motor tasks. Furthermore, the decrease in the MRCP pattern showed a positive relationship with the physical improvements in hand motor skills.

(iv) The multi-session robot-based training was tested on stroke patients with different lesion locations. It was found that the variations in the MRCP pattern, length of rehabilitation training as well as corresponding improvements in hand motor skills depended on the lesion location.

(v) A novel "Adaptive Robot-Assisted Rehabilitation Training" program was devised for post-stroke rehabilitation using AMADEO robotic device. This training strategy was progressively advanced after a stroke patient achieved competency in the current training protocol. In this way, every stroke patient underwent specific training on the AMADEO device in accordance with their needs. It was also found that the improvements in the hand motor skills were more pronounced in post-stroke patients who underwent this adaptive-training strategy compared to those patients who underwent the fixed-training strategy implemented earlier in this project.

1.7.2 Dissemination of Research

The outcomes of the research were systematically disseminated through various publications listed below:

Published

(1) M. Butt, G. Naghdy, F. Naghdy, G. Murray, and H. Du, "Investigating Electrode Sites for Intention Detection During Robot Based Hand Movement Using EEG-BCI System," *in Proceedings of IEEE 18th International Conference on Bioinformatics and Bioengineering (BIBE)*, Taichung, Taiwan, 2018, pp. 177-180.

(2) M. Butt, G. Naghdy, F. Naghdy, G. Murray, and H. Du, "Investigating The Detection of Intention Signal During Different Exercise Protocols in Robot-Assisted Hand Movement of Stroke Patients and Healthy Subjects Using EEG-BCI System", *Advances in Science, Technology and Engineering Systems Journal*, vol. 4, no. 4, pp. 300-307, 2019.

(3) M. Butt, G. Naghdy, F. Naghdy, G. Murray, and H. Du, "Patient-Specific Robot-Assisted Stroke Rehabilitation Guided by EEG – A Feasibility Study," *in Proceedings of IEEE 42nd Annual International Conferences of the IEEE Engineering in Medicine and Biology Society (EMBS),* Montreal, Canada, 2020.

(4) M. Butt, G. Naghdy, F. Naghdy, G. Murray, and H. Du, "Assessment of Neuroplasticity Using EEG Signal in Rehabilitation of Brain Stem Stroke Patients," *in Proceedings of the Annual IEEE Canadian Conference of Electrical and Computer Engineering (CCECE),* London, Canada, 2020.

Under Review

(5) M. Butt, G. Naghdy, F. Naghdy, G. Murray, and H. Du, "Effect of Robot-Assisted Training on EEG-Derived Movement-Related Cortical Potentials for Post-Stroke Rehabilitation," submitted to IEEE Access on February 01, 2021.

1.8 Thesis Outlines

According to the work conducted in this project and the outcomes produced, this thesis is structured as follows:

Chapter 1 – Introduction: As highlighted so far, this chapter provides a brief introduction to the research background and the rationale behind the study. It also states research gaps, research aims, and objectives as well as the research approach based on the highlighted research gaps. The research contributions and achieved outcomes, and the thesis structure are presented at the end of the chapter.

Chapter 2 – Literature Review: In this chapter, a comprehensive literature review on the various applications of EEG signals in the field of post-stroke motor rehabilitation has been presented. This review discusses studies on eight distinct applications of EEG signals involving motor tasks for post-stroke rehabilitation. It also identifies research gaps and future research fields in the selected topic.

Chapter 3 – Experimental Set-Up and Data Processing Details: Chapter 3 describes the complete EEG acquisition system, data processing software, AMADEO rehabilitation device, its training programs, and its assessment procedures. Lastly, the details on signal processing steps involved in extracting the MRCP pattern from the acquired EEG signals for the data analysis of all experiments are explained.

Chapter 4 – Movement-Related Cortical Potential during Different Exercise Protocols for Single-Session Hand Motor Training: In this chapter, the intention detection for hand motor tasks during two distinct training protocols is performed and validated using healthy and stroke subjects. This chapter establishes the concept of EEG signal variations during different training protocols which act as a foundational concept for the subsequent experiments.

Chapter 5 − Quantification of Movement-Related Cortical Potential Associated with Motor Training after Post-Stroke Rehabilitation: This chapter explains the experimental protocol to determine the effect of multi-session robot-assisted rehabilitation training on the recovery of hand motor skills. The designed protocol is validated with post-stroke patients in clinical settings by analyzing MRCP pattern variations. These variations in the MRCP pattern are correlated with the results obtained from the clinical tests and the measurements of hand-kinematic parameters.

Chapter 6 – Adaptive Robot-Assisted Stroke Rehabilitation Guided by EEG – Two Case Studies: A novel adaptive and dynamic rehabilitation strategy for the motor recovery of post-stroke patients is proposed in this chapter. The proposed training strategy is tested on two post-stroke patients. Also, the clinical results (clinical tests and hand-kinematic parameters) obtained from the fixed training protocol used in Chapter 5 are compared with those obtained during the adaptive-training protocol to evaluate the overall benefits of using the adaptive-training protocol for post-stroke rehabilitation.

Chapter 7− Conclusion and Future Work: This chapter provides a critical review of the outcomes produced in this research project, draws some conclusions, and provides some recommendations for future works in this field.

Chapter 2

Literature Review

2.1 Introduction

Stroke is considered to be one of the main causes of prolonged disability among adults [1]. The most common impairment occurs when a stroke survivor has a motor loss of limb(s) on one side of the body causing difficulty with walking and affects the ability to perform ADLs. There are many types of post-stroke rehabilitation therapies currently being practiced, and others being investigated. One of the therapy types being investigated and coming into clinical practice is robot-assisted therapy. During this therapy, the active participation of stroke patients while performing motor tasks needs to be monitored. One way to determine the active participation of subjects during motor tasks is to acquire their brain activities. Among many modalities available to capture brain activities during motor tasks, this project has selected EEG modality to acquire brain activities during post-stroke rehabilitation motor tasks.

A comprehensive literature search was performed to explore how EEG is being deployed in stroke rehabilitation research to recover their lost motor functions. This literature search also helps to identify research gaps, discover the latest developments in the field, and to explore future trends. The search was performed on several databases including Scopus, Web of Science, and IEEEXplore. The keywords or phrases used in these database search engines are listed in Table 2.1.

Table 2.1: Keywords used for literature search

	Keywords / Phrases
1.	"EEG" OR "Electroencephalography"
2.	"Stroke"
3.	"Rehabilitation"
4.	intention OR motivation OR anticipation OR cognition OR engagement OR participation OR "motor training" OR "motor learning" OR "motor task" OR "motor practice"

As a result of the search, 834 research articles were identified, which were rigorously and thoroughly processed, and the duplicate articles were removed. Initially, the title and abstract of each paper were examined to identify the aim and hypothesis of the study. This resulted in 415 papers with sound and relevant hypotheses. Furthermore, the following selection criteria were applied to the remaining papers:

a) The aim, hypothesis, and objectives of the paper were clearly described.
b) The experimental design in the papers involved some motor tasks imagined or performed by the subjects.
c) Articles involved human subjects.

d) The intervention and methodology deployed in the paper were comprehensively explained.

e) Papers were using EEG as a major diagnostic tool.

f) Papers discussed ERD/ERS and MRCP as movement-related EEG patterns.

g) Review papers were excluded.

The outcome was 171 papers that were selected for in-depth review. The selected papers were subsequently structured according to their contents as illustrated in Figure 2.1.

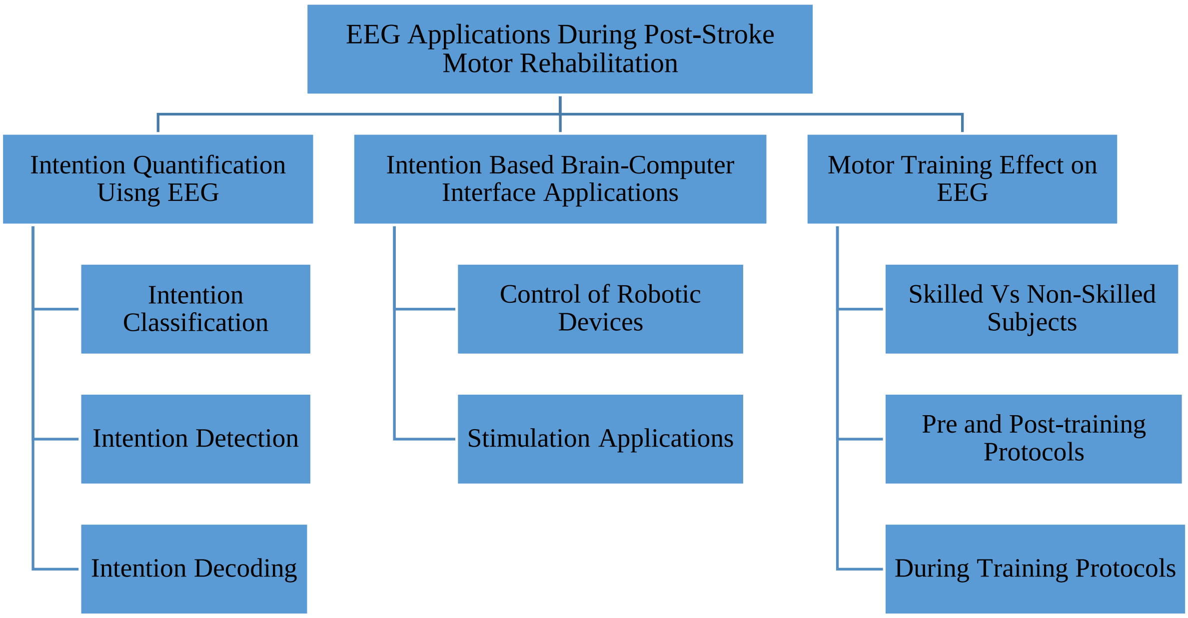


Figure 2.1: Structure of review chapter according to the applications of EEG in post-stroke motor rehabilitation

The rest of this chapter is organized as follows. Section 2.2 covers studies that use EEG as a motor intention signal for classifying various movement types, detecting a particular motor intention, and decoding the intention signal. Section 2.3 reviews papers illustrating those applications of the EEG-based Brain-Computer Interface (BCI) systems that deploy motor intention signal to either control the movement of robotic devices or to apply various stimulations. In Section 2.4, different studies demonstrate the effect of various motor training protocols on the EEG signal. Finally, a summary of the chapter is provided in Section 2.5, research gaps in this discipline are discussed, and future trends are identified.

2.2 Intention Quantification using EEG Signal Analysis

As mentioned in Section 1.5 of Chapter 1, the EEG movement-related patterns change when a person imagines or executes a movement of a limb and therefore, they are termed as an intention signal in the literature. MI is the most popular protocol used in experiments involving motor activities [103]. There are various techniques developed to classify or detect the intention signal or decode it into various kinematics properties. The intention signal classification of various movement types is described in Section 2.2.1. The detection and decoding of intention signals are discussed in Sections 2.2.2 and 2.2.3, respectively.

2.2.1 Classification of Intention Signal

In most studies, the classification of intention signals is performed by using machine learning algorithms. These intention signals can be associated with the movement of single as well as multiple limbs. In a single limb motor task, the classification is performed by studying the kinematics properties within a limb, whereas, in the latter case, classification is based on intention signals extracted by different limbs. Table 2.2 summarizes various techniques proposed for the classification of the intention signal during different types of motor tasks.

Table 2.2: A comparison of studies on the classification of intention signal

Sr. No.	Author(s) (years) / Ref.	Movement Types	Classifier Type / Classification Method	Average Classification Results
1.	Deng et al. (2005) / [104]	shoulder-abduction versus elbow-flexion torques	Time-Frequency synthesized Spatial Patterns (TFSP) algorithm	89 % accuracy for healthy subjects, 76 % accuracy for stroke subjects.
2.	Zhou et al. (2006) / [105]	shoulder-abduction versus elbow-flexion torques	Support Vector Machine (SVM) classifier	92.9 % accuracy for healthy subjects, 84.1 % accuracy for stroke subjects.
3.	Zhou et al. (2009) / [106]	isometric shoulder-abduction versus elbow-flexion torques	classifier-enhanced TFSP	92 % accuracy for healthy subjects, 75 % accuracy for stroke subjects.
4.	Rodrigo et al. (2011) / [107]	rest, motor preparation and Motor Execution (ME) of right arm	multi-class Linear Discriminant Analysis (LDA) classifier	65 % accuracy for 2-class classification, 55 % accuracy for 3-class classification.
5.	Antelis et al. (2012) / [108]	unaffected versus affected arm movement	SVM classifier	71 % average accuracy for stroke subjects.
6.	Ortner et al. (2012) / [109]	MI of the left hand versus right hand	LDA classifier	90.4 % accuracy for 3D virtual feedback, 89 % accuracy for static bar feedback with healthy subjects.

7.	Lou et al. (2013) / [110]	finger-extension versus thumb-adduction, finger-flexion, and rest	LDA classifier	78.96 %, 81 %, and 78.03 % accuracies respectively, to distinguish finger-extension from thumb-adduction, finger-flexion, and rest with healthy subjects.
8.	Xie et al. (2013) / [111]	knee-extension versus knee-flexion	An extreme learning machine algorithm based on EEG-Electromyography (EMG) fusion features	98.9 % accuracy for healthy subjects, 84.4 % accuracy for stroke subjects.
9.	Lechner et al. (2014) / [112]	MI of the left hand versus right hand	LDA classifier	81.16 % accuracy for VR feedback, 77.84 % accuracy for static bar feedback with healthy subjects.
10.	Mohanchandra et al. (2014) / [113]	MI of the right hand versus right foot	SVM classifier	94.2 % accuracy for healthy subjects.
11.	Taylor et al. (2014) / [114]	MI versus ME of wrist movements	NeuCube algorithm	76 % accuracy for healthy subjects.
12.	Garcia-Cossio et al. (2015) / [115]	active and passive walking versus baseline	Logistic regression classifier	Healthy subjects: 94 % accuracy for active walking versus baseline, 93.1 % accuracy for passive walking versus baseline, and 83.4 % accuracy for active versus passive walking. Stroke subjects: 89.9 % accuracy for active walking versus baseline.
13.	Jochumsen et al. (2015) / [116]	one foot varying in movement kinematics	SVM classifier	70 % accuracy for ME task, 66 % accuracy for MI task, and 63 % accuracy for attempted movements of stroke patients.
14.	Choi et al. (2016) / [117]	gait versus standing conditions	LDA classifier	73.2 % accuracy for chronic stroke patients.

15.	Gunay et al. (2016) / [118]	two different speeds of the right arm (nail and cotton scenarios) versus rest. (Note: nail condition has higher speed than cotton condition)	LDA classifier	64 % accuracy for nail versus rest, 59 % accuracy for cotton versus nail, 67 % accuracy for cotton versus rest, and 56 % accuracy for cotton versus nail versus rest conditions with healthy subjects.
16.	Jochumsen et al. (2016) / [119]	palmar, lateral, and pinch grasp versus idle hand state	LDA classifier	75 % accuracy for 2-class problem and 63 % accuracy for the 3-class problem with healthy subjects.
17.	Tang et al. (2016) / [120]	MI and ME for left versus right hand and left hand versus both feet	SVM classifier	Wearing exoskeleton scenario: 84.29 % accuracy for MI sessions, and 87.37 % for ME sessions.
18.	Qiu et al. (2017) / [121]	MI of paretic hand versus non-paretic hand	SVM classifier	Not stated.
19.	Wang et al. (2017) / [122]	MI of 30 % of Maximum Voluntary Contraction (MVC) versus 10 % of MVC versus rest	SVM classifier	70.9 % accuracy for the 3-class problem.
20.	Paul et al. (2018) / [123]	MI of thumb versus middle finger versus index finger versus wrist-extension versus wrist-flexion versus rest	SVM classifier	91.5 % accuracy for healthy subjects.
21.	Suwannarat et al. (2018) / [124]	MI of hand opening versus closing (M1), forearm pronation versus supination (M2), wrist-flexion versus its extension	LDA and SVM classifiers	84.71 % accuracy of M1 versus M2 task with left hand and 84.64 % accuracy with the right hand, 88.38 % accuracy of M1 versus M3 task with left hand and 87.59 % accuracy with the

		(M3)		right hand, 77.59 % accuracy of M2 versus M3 task with left hand and 80.98 % accuracy with the right hand.
22.	Karacsony et al. (2019) / [125]	MI of the left hand versus right hand (2-class), MI of the left hand versus right hand versus rest (3-class), MI of the left hand versus right hand versus both feet (4-class)	Deep learning and Convolutional Neural Network (CNN) architecture	87 % accuracy for the 3-class problem, 70 % accuracy with the 4-class problem with healthy subjects.
23.	Park et al. (2019) / [126]	gait versus stand condition and gait ready versus stand ready conditions	CNN algorithm using spatial-spectral model	83.4 % accuracy for gait versus stand, 77.3 % accuracy for stand versus gait ready, 77.7 % accuracy for gait versus stand ready.

From Table 2.2, it is noted that LDA and SVM classifiers are the two most commonly employed classifiers for the intention signal classification. Recently, an adaptive SVM classifier with Common Average Reference (CAR) has been used to classify hand opening and closing tasks by acquiring beta EEG activity from both hemispheres [127]. However, the TFSP algorithm, regression classifiers, classification tree, NeuCube algorithm, deep learning algorithms as well as convolutional neural network algorithms are also deployed in classification problems (see Table 2.2). A unique idea of using a combination of classifier algorithms consisting of a deep neural network with a convolutional neural network and recurrent neural network is explored in [128] to classify grasp and pour tasks with a robotic arm. MI-based protocols are commonly used in the classification problems as shown in Table 2.2. In addition, upper-limb movements' intention classification is more addressed compared to that for lower-limb movements.

The EEG signal processing for the classification of the intention signal occurs in three stages; pre-processing, feature extraction, and classification or detection. The pre-processing step usually consists of artifact removal, channel selection, and filtering of EEG data to extract a specific-frequency band. While the feature extraction stage consists of extracting various features from EEG-derived pattern(s) and selection of appropriate features which will then be used by the classifier. Therefore, many studies have discussed the effect of pre-processing and feature extraction strategies to enhance the performance of their designed classification strategies. For instance, after acquiring an EEG signal from 163 electrodes, Zhou et al. [129] devised a method of optimal channel selection used for feature extraction and proved that similar or even better classification results could be obtained using an optimal number of channels. One of the commonly used filters for spatial filtering, before the intention classification step, is the Common Spatial Pattern [130, 131]. However, this filter requires prior knowledge of the appropriate frequency band and suitable channels' selection [132]. This problem can be solved by applying linear dynamic system modeling for the characterization of EEG dynamics as described in [133].

The training of the classifier model for a particular motor task requires time and effort. The idea of developing a generalized classification model, which is trained for one motor task and then can be used for the classification of various similar tasks, is attractive. Zhang et al. [134] provided a practical demonstration of this idea for the upper limb movement classification problem. The EEG-based classification model was trained for the elbow joint MI task and then the trained classifier model was tested on eight other MI tasks of the upper limb. The authors concluded that a single-joint motor task could be utilized as a training model to classify other MI tasks with reasonable classification accuracy. Furthermore, Kaiser et al. [135] used active and passive hand motor tasks to train the LDA classifier and then tested it using the MI hand motor task to reduce the training time of classifiers for stroke patients.

2.2.2 Detection of Intention Signal

The detection of motor intention signals involves distinguishing a particular limb movement from the rest of the brain activities. The motor intention signal indicates the active participation of the subjects undergoing the rehabilitation process. The active participation of post-stroke patients is considered to be a core reason for neuroplasticity induction inside the brain [18]. The early detection of intention signals is also important in robot-assisted motor tasks. Therefore, the detection of motor intention signals has been addressed extensively in the literature.

Niazi et al. [75] detected the intention of self-paced ankle dorsiflexion using features extracted from the MRCP pattern and obtained an average True Positive Rate (TPR) of 82.5 % for ME protocol with healthy subjects, 64.5 % for MI protocol with healthy subjects as well as 55.01 % for attempted movement by stroke patients. Muralidharan et al. [136] extracted the attempted movement of finger-extension versus resting state by post-stroke patients using ERD/ERS features. Similarly, Planelles et al. [76, 77] compared the performance of various classifiers to detect the intention signal during gait and arm movements using ERD/ERS features. Lew et al. [78] detected the intention of a self-paced reaching arm movement with an average TPR of 81 % for left hand movement and 79 % for right hand movement. Hortal et al. [137] obtained a TPR of 56.1 % in a real-time test for gait movement. Recently, Mahmoodi et al. [138] demonstrated the use of a robust beam-forming algorithm for intention detection of hand movement with temporal EEG features and obtained a TPR of 77.1 %.

A combination of spectral and temporal features, extracted from ERD/ERS and MRCP patterns respectively, have also been explored for intention detection during motor tasks. For instance, the intention signal during voluntary arm reaching movement was detected using features obtained from both ERD/ERS and MRCP patterns in [139]. The results of the experiment showed that TPR for healthy participants was 74.5 % while for stroke patients, it was 82.2 %. The TPR of the patient group was reported slightly higher than that in the healthy group, however, more delayed intention detection was obtained in the former group compared to the latter. Similarly, Sburlea et al. [140] demonstrated the detection of intention to walk in stroke patients by using both ERD and MRCP patterns. Nine chronic stroke patients performed a self-initiated walk with the help of auditory cues. The authors used a sparse LDA classifier and obtained an average accuracy of 64 % to detect the walking intention. Similarly, the researchers in [79] developed a protocol that continuously detected the intention of the walking movement of 10 healthy subjects using features from the MRCP and ERD patterns. They concluded that their designed protocol was able to continuously detect the intention signal with up to 70 % accuracy for intra-session and up to 66 % accuracy for inter-session without recalibration of their designed system. Hadsund et al. [141] obtained average detection accuracy between 82 % to 87 % and 74 % to 80 % for foot and hand motor intention detection respectively. They concluded that temporal features contributed more to the foot motor intention detection whereas, spectral features were more dominant in the detection of hand motor intention. On the other hand, Kamavuako et al. [142] showed that spectral features outperformed temporal features while detecting intention signals for lower limb movements with both healthy and stroke subjects.

A combination of EEG and EMG signals for detection of the intention signal is also being explored to increase the reliability of the results. Lopez-Larraz et al. [143] showed that the highest accuracy was achieved when features extracted from both EEG and EMG signals were used in detecting the hand motor intention signal of stroke patients. An exoskeleton device was triggered after detecting the intention signal of finger movement using the EEG signal and by developing coherence between EEG and EMG signals in [144]. It is shown in [145] that the appropriate choice of the input signal (EEG or EMG) for detecting the intention signal could improve the adaptability of assistive devices with respect to individual user's needs.

Multiple efforts have been made to understand the effect of various factors on the intention detector's performance. For example, a comprehensive study was conducted by Xu et al. [146] to determine the effect of types of a motor task, selection of EEG patterns as well as the choice of signal processing technique on intention detector's performance. They found that ballistic motor task intention detection using time-series analysis of the MRCP pattern was the best option to obtain the highest detection accuracy. Lopez-Larraz et al. [147] demonstrated that the detector's performance could also be influenced by the choice of recalibration methods during a multi-session protocol. They observed that the selection of appropriate recalibration schemes depends on the selected features (ERD/ERS or MRCP features) used to detect the motor intention signal. Moreover, they suggested that the correct recalibration scheme could enhance the performance of the detector.

A personalized rehabilitation device for intention detection could be an important step in providing a home-based rehabilitation system for post-stroke patients. Therefore, the novel idea of a personalized rehabilitation system used to detect the intention of the pedaling movement was proposed in [80]. The designed protocol was tested on five healthy subjects in which epoch window size, algorithms for features extraction, and EEG electrode configurations were subjective. The EEG data were acquired with the help of a wireless EEG acquisition system and ERD/ERS signals were assessed from mu and beta EEG bands to detect the motor intention signal. An average TPR of 76.7 % and detection accuracy of above 55 % were achieved by the authors.

A self-paced motor training system normally requires detection of the motor intention signal for which the classifier model should be trained with subject-dependent data at the beginning of the experiment. This could be time-consuming and sometimes frustrating for the participants, especially patients. To solve this problem, researchers have explored various techniques by either training the classifier with the ME foot task, then testing it for MI task [148, 149], or by implementing a template matching technique [150].

Due to stroke, the brain area (e.g. contralateral sensorimotor cortex) generating motor intention signal could be damaged in some stroke patients. Therefore, the right choice of the brain area and EEG channels used for intention detection of the required limb is important. Antelis et al. [151] investigated the possibility of using an unaffected brain motor cortex to continuously detect the intention for movements or attempted movements of the unaffected and affected hand. The authors recruited six severe chronic stroke patients to perform the simple reaching task. EEG signals were continuously acquired over the unaffected brain area to extract the ERD features. They concluded that their proposed protocol could detect the intention of the affected arm movement continuously using brain signals from the unaffected brain area with significantly higher detecting accuracy. Li et al. [152] observed that selecting channels showing prominent ERD instead of using channels over the contralateral sensorimotor cortex could significantly enhance the accuracy in detecting the movement of paretic hand performed by stroke patients. Whereas, the authors in [153] demonstrated that stroke lesion locations could influence the detection accuracy of unaffected and affected hand movements. The intention detection accuracy can also be affected by different physiological artifacts contaminating the EEG signal. By analyzing the effect of various artifacts removal on the intention detector's performance, Lopez-Larraz et al. [154] showed that rejecting trials containing artifacts could help to capture more accurate brain activities which eventually improved the performance of the intention detector.

Many researchers also explored novel techniques and novel EEG features for intention detection. A novel technique using Locality Preserving Projection together with LDA classifier (LPP-LDA) for intention detection of dorsiflexion with the right ankle was investigated in [155] using MRCP features. The authors compared the performance of their proposed algorithm with that of the Matched Filter (MF) algorithm. The experimental results showed that MRCP was detected with approximately 11 % better TPR and 145 ms earlier using the LPP-LDA algorithm compared to the MF algorithm. Sburlea et al. [156] tested a novel feature i.e. the instantaneous phase of MRCP to evaluate its effect on the classifier's performance used for gait motor intention detection. They concluded that the use of this feature demonstrated the best results for the session-specific condition.

2.2.3 Decoding of Intention Signal

Kinematic and kinetic factors of a motor task can change the features of movement-related EEG patterns during both MI and ME motor tasks. Therefore, along with the classification and detection of motor intention signals, many researchers have explored the possibility to decode the intention signal into various physical parameters including task directions, force, speed, or other kinematics properties.

Lew et al. [157] decoded the direction of a hand reaching task for self-paced reaching arm movement with the help of a haptic device. The movement directions were decoded using MRCP pattern with up to 76 % accuracy for healthy subjects, and up to 47 % accuracy for stroke patients performing the task with their impaired arm as well as on average 312.5 ms before the actual movement onset. Whereas, Jochumsen et al.

[158] used only one EEG channel for detecting the motor intention for palmar grasp performed with a handgrip dynamometer. Moreover, the detected signal was decoded into the motion force and speed. The experimental results demonstrated that about 75 % of all movements were detected 100 ms before the onset and about 60 % of the movements were accurately decoded into the force and speed level in accordance with the movement tasks. Kim et al. [159] decoded the three-dimensional trajectories of the MI task of arm movement when the subjects imagined the movement or observed the movement demonstrated by the volunteer's arm and the robotic arm using both linear and non-linear decoders. They suggested that their experimental results were an important step forward towards the development of an accurate decoder for BCI applications.

The concept of decoding the intention signal is also being investigated on the lower limb kinematics properties. The intra and inter-limb kinematics during feed-forward and feedback walking tasks on the treadmill were decoded in [160]. Six healthy subjects were asked to walk on a treadmill as guided by real-time visual feedback. The ankle, knee, and hip joints kinematics of the participants were recorded through an infrared optical motion capture system while their brain activities were recorded by a 12 electrode EEG system. The authors calculated the Pearson correlation coefficient between the known measured signal and the predicted output of the decoder to represent the decoding accuracy. They obtained the Pearson correlation coefficient of 0.68 with their designed protocol. Luu et al. [161] designed a real-time closed-loop VR-based multi-session protocol to decode the joint angles of the lower limb during a treadmill walking task. They tested their designed experiment on four healthy subjects. The state-space non-linear adaptive filter called the unscented Kalman filter was employed for decoding the walking patterns. The amplitude variations in the MRCP pattern were analyzed for decoding purposes. After eight days of training, significant improvements in the decoding accuracy of knee, ankle, and hip joints were measured. It is noted that the protocols used for decoding of intention signal for lower limb movement were mostly based on treadmill walking.

2.3 Brain-Computer Interface System

A brain-computer interface is a computer-based system that acquires brain signals, analyzes them, and translates them into commands to an output device to carry out the desired actions [162]. Thus, BCIs do not use the brain's normal output pathways of peripheral nerves and muscles. For many years, BCI systems have been used to assist people with impairments. After the stroke, the patient is unable to perform ADLs efficiently. For stroke rehabilitation, BCI systems can be employed as a communication device or can allow patients to control devices like robotic arms, wheelchairs, or orthoses and prostheses, which in turn assist them while performing ADLs [163]. Moreover, current robotic devices along with BCI systems allow patients to participate in rehabilitation exercises, which require their own mental inputs. Neurophysiological input signals can avoid slacking and provide robotic support only when the brain is particularly responsive to peripheral input. Such active rehabilitation exercises can induce neuroplasticity and help in the recovery of post-stroke patients [164]. Researchers have explored various input modalities for BCI systems used for stroke rehabilitation, with EEG-based BCI systems proven to be the most popular.

The general framework of the BCI system is illustrated in Figure 2.2. For invasive BCI approaches (left side of Figure 2.2), ECoG or sEEG signals are used as input into the BCI system. However, this approach is not widely applicable due to the need for surgical procedures. On the other hand, non-invasive BCI approaches (right side of Figure 2.2) include EEG, Blood Oxygenation Level-Dependent (BOLD) fMRI, as well as fNIRS as an input modality. After the acquisition, brain signals are processed to extract specific features according to the aim of the BCI system (such as communication or control) and then classification is performed to translate the signal into a control signal that drives the BCI system. There are two main categories of BCI system applications; one category is the assistive BCI that is used to help patients with communication or performing the movement and the other category is rehabilitation BCI systems used to help patients restoring their lost motor functions. The studies discussed in this section are mainly focused on rehabilitation-based EEG-BCI systems that utilize one of the movement-related EEG patterns namely ERD/ERS and MRCP.

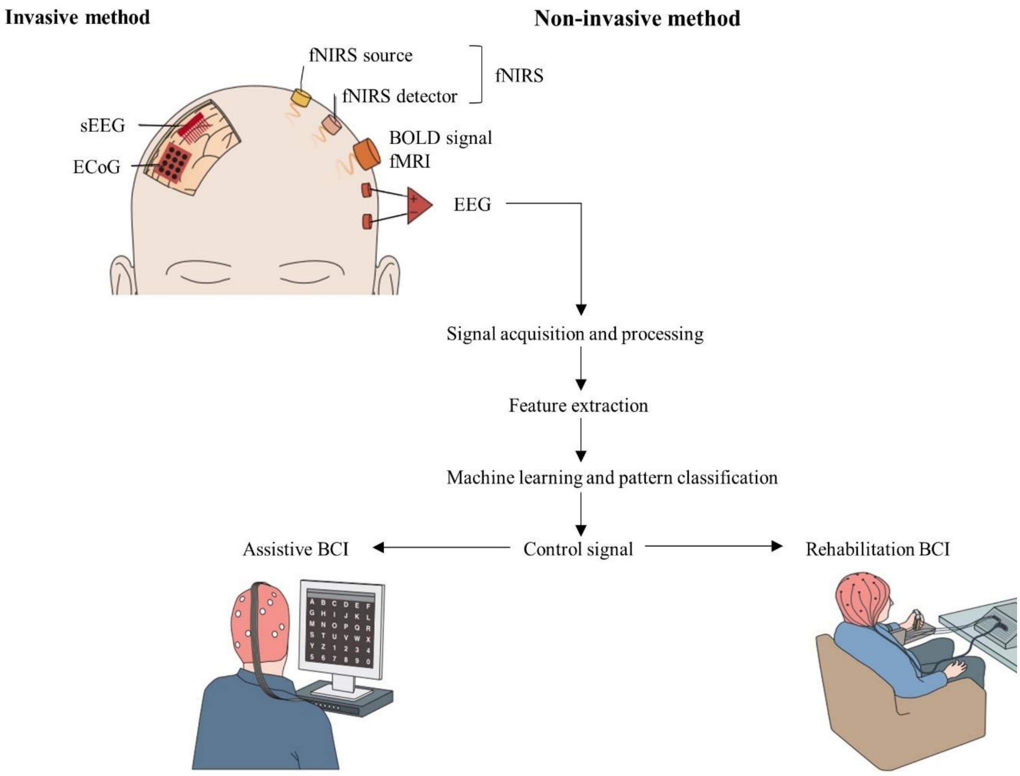


Figure 2.2: General framework of BCI systems [163]

In rehabilitation, EEG-BCI systems are extensively applied to trigger various robotic devices using the intention signal of the participants. Such studies are discussed in Section 2.3.1. Another use of the EEG-BCI system in stroke rehabilitation is the application of various electrical stimulations to modulate the brain activities of stroke patients to induce neuroplasticity in their brains. The studies describing the application of stimulation using EEG-BCI systems are described in Section 2.3.2.

2.3.1 Robotic Device Control with Intention Signal

To control the movement of the robotic devices, the motor intention signal is either classified or detected using the EEG-BCI system. Some researchers have also explored the decoding of intention signals according to the kinematic properties of the selected limb. The decoded intention signal is then used to control the movement of a robotic device.

Wang et al. [165] detected MI of arm movement to control the movement of the Manus robot and achieved 76.05 % average online accuracy for their designed system. A custom-made upper-limb rehabilitation robotic device was used by Xu et al. [166] for MI classification of left and right arm of healthy subjects and achieved an averaged online classification accuracy of 86 %. Another custom-made mechanical hand robot that was operated by MI detection using the EEG-BCI system is proposed in [167]. In this work, the hand's force and angle were fed back to the robotic device to adapt its movement accordingly. The authors state that their designed system achieved an accuracy of 89.7 % with an information transfer rate of 0.5099 bits per second. Nakatani et al. [168] tested the feasibility of their designed pedal-driven wheelchair-based rehabilitation system which was operated by detecting the intention signal of leg pedaling movement. They achieved approximately 79.8 % accuracy in moving the wheelchair in a forward direction. Luu et al. [169] designed a closed-loop EEG-BCI system to control the walking of the virtual avatar by decoding the intention signal into lower limb kinematics. Recently, Kotov et al. [97] tested the working of hand exoskeleton triggered by the MI classification using the EEG-BCI system for hand motor recovery. The authors observed improvements not only in the participants' clinical tests but also in performing ADL by post-stroke patients within the first year of their stroke.

An EEG driven motorized ankle-foot orthosis-based BCI system was developed by Xu et al. [170] that triggered the orthosis on detecting ankle dorsiflexion movement using the MRCP pattern. They achieved a TPR of 73 % and stated that neuroplasticity was induced in the subjects after using their designed system for only 15 minutes. Another study on triggering robotic devices through the subject's intention signal was performed by Bhagat et al. [171] for elbow joint movement using an asynchronous EEG-BCI robot-assisted system. The motor intention signals of four chronic stroke patients were detected by using the MRCP pattern which then triggered an exoskeleton device called MAHI-EXO-II. Norman et al. [172] developed an EEG-BCI paradigm that provided only partial assistance to unimpaired volunteers when they tried to move the FINGER robotic exoskeleton device using their index and middle fingers. The partial assistance motivated subjects to apply adequate force to complete the task. The study also considered the effect of audio-visual stimuli on ERD signals. The authors observed that audio-visual stimuli resulted in better detection of ERD patterns when the subject performed voluntary movement or robot-assisted movement. Marghi et al. [173] demonstrated the working of a unique EEG-BCI-based control robotic mirror-box therapy for the recovery of foot and ankle movements. The designed system was tested for both offline and online sessions and an accuracy of 94.5 % and 75 % were achieved, respectively. Most recently, Kapsalyamov et al. [174] implemented a novel assist-as-needed technique for elbow-flexion and extension movement using the exoskeleton and EEG-BCI system. The authors achieved an accuracy of 78 % and stated that their designed protocol kept the subjects involved in the training by providing assistance when required.

Brauchle et al. [175] tested the feasibility of a system in which the movement of a 3D multi-joint exoskeleton device was controlled by MI during reaching arm movements on three healthy subjects. Another feasibility test was performed by Nagai et al. [176] where the movement of a 1-Degree of Freedom (DOF) robotic device was controlled by the intention signal during flexion of upper limb movement. The authors claimed to achieve an accuracy of 79 % for their designed protocol. These feasibility studies are still in their developmental stage and need more investigation using actual stroke patients.

The concept of using the unaffected hemisphere to control EEG-BCI system-based movements has also been explored in the literature. Four chronic hemispheric stroke patients were recruited to control the 1D cursor movement using brain signals from their unaffected hemisphere in [177]. Each subject demonstrated cortical activations in the unaffected hemisphere associated with the intended movement of the affected hand and achieved accuracies were between 68 % and 91 %. Similarly, ten stroke patients were trained to use their unaffected hemisphere for controlling the movement of exoskeleton robotic device with a home-based EEG-BCI system in [96]. The authors stated the subjects controlled the movement of the exoskeleton device that opened and closed their affected hand using brain signals from their unaffected side. After 12 weeks of the training, there was an increase of about 6.2 points in the clinical test namely, the Action Research Arm Test (ARAT).

The effect of various feedbacks including haptic and kinematic feedbacks on EEG-BCI performance has also been a topic of interest. Gomez-Rodriguez et al. [178] demonstrated that by modulating SMR activity using haptic feedback, the online decoding performance of the BCI-operated Whole-Arm Manipulator (WAM) robotic arm could be enhanced. Another attempt on studying the effect of haptic feedback on the performance of the EEG-BCI system was performed in [179, 180] by controlling the triggering of a haptic device (Barrett WAM). In these studies, the mu and beta rhythms of EEG were used by a fuzzy proportional derivative position controller to control the movement of the haptic device that was triggered only on correct detection of the motor intention signal through the EEG-BCI system. Ivanova et al. [181] demonstrated that the motor functions of the arm could be improved by providing kinematics feedback during EEG-BCI system robot-based rehabilitation training.

Researchers have also explored different multimodal set-up in operating EEG-BCI systems. A state-of-the-art multimodal system consisting of the EEG-BCI system, the eye-tracking system as well as Kinect system was developed by Frisoli et al. [182] to decode the intention signal of the arm reaching action into each joint movement of Light Exoskeleton device. They tested their developed system on three healthy subjects and four chronic stroke patients and achieved an average accuracy of 89.4 %. Another hybrid rehabilitation system was designed and tested by Hortal et al. [183] which consisted of the Armeo Spring exoskeleton device and FES system. In this system, the motor execution was performed after the EEG-BCI system detected the intention signal. The authors achieved an average accuracy of 76.7 % for healthy subjects and 71.6 % for stroke patients in the experimental results.

The EEG-EMG based BCI systems were also explored for robot-assisted motor rehabilitation of post-stroke patients. For example, Sarasola-Sanz et al. [184] controlled the movement of the 7-DOF exoskeleton device after decoding the elbow joint angle using the EEG-EMG hybrid BCI system. In another study, a knee exoskeleton device was driven by using both EEG and EMG signals based BCI system [185]. Furthermore, Chowdhury et al. [186] developed a BCI system to trigger an orthosis during the upper-limb movement using both EEG and EMG signals. The authors achieved an accuracy of 92.81 % for healthy participants and 84.53 % for stroke patients.

The efficient control of the robotic device using the EEG-BCI system depends on the reliable detection of the intention signal. Therefore, many attempts were made to increase the detection accuracy for EEG-BCI system-based robotic control applications. Shimizu et al. [187] devised a new method for intention detection using the EEG signal which could decrease noise interference as well as it could adapt to the needs of the individual user. The authors implemented their designed technique on the control of a 1-DOF robotic device for arm and elbow movements. A novel control strategy that integrated a VR environment and a low-cost motion sensor was developed to detect intention with EEG-BCI system for the movement of the HIT-ULR^2 rehabilitation robot in [188]. In addition, Sarac et al. [98] controlled the movement of the AssistOn Mobile device by detecting the intention signal for arm movement using the EEG-BCI system. The authors first trained the designed system using offline sessions and then tested it for self-paced asynchronous online sessions. Through their designed system, they ensured the active engagement of the subjects during their rehabilitation training. A fuzzy template matching technique was proposed in [189] to enhance the intention detector's performance of the EEG-BCI system for ankle dorsiflexion. The authors claimed that their designed system could detect the intention signal within several tens of minutes. However, this study design needs to be evaluated further with actual stroke patients.

In order to facilitate the access of robot-based rehabilitation training for the stroke-affected subjects, many researchers developed a user-friendly and mobile rehabilitation unit. In this regard, Xiao et al. [190] developed an EEG-driven robotic rehabilitation system, consisting of a wireless EEG headset and 4-DOF exoskeleton, triggered using the intention signal of the subjects performing UE movements including the forearm, elbow, and wrist. Bi et al. [191] tested another robot-assisted EEG-BCI system containing a hand exoskeleton device and mobile wireless headset. The movement of the hand exoskeleton was controlled by MI detected through the BCI system. The authors reported an estimated time delay range of 1.8 to 2.9 s in operating their designed system.

The effect of robot-based motor training using the EEG-BCI system on the physical outcomes of post-stroke patients has been studied extensively by clinicians and researchers. The post-stroke patients received an exoskeleton-based MI-EEG-BCI system training for hand motor recovery in [85]. An improvement in ball grasp, finger pinch grip, and gross arm movements was found for the BCI-exoskeleton group compared to the control group. The effect of BCI-driven exoskeleton training compared to the passive movement of exoskeleton with fingers was investigated in [86]. The first participants' group controlled the movement of the robotic device with their brain signal while the second group performed the passive movement using the same device. At the end of the training, the first group showed a 21.8 % improvement in ARAT and 36.4 % in Fugl-Meyer Assessment (FMA) score while there was only a 5.1 % improvement in ARAT and 15.8 % in FMA score for the second group. Twenty-six stroke patients were recruited to take part in randomized-controlled robotic training in [95]. In the Manus group, the subjects performed a robot-aided movement of their shoulder and elbow whereas, in the BCI-Manus group, the same robotic movement was triggered by intention detection through an EEG-BCI system. The clinical test FMA was performed at multiple intervals during the training. Moreover, the revised Brain Symmetry Index (rBSI) was measured to find its correlation with FMA improvement. The experimental results showed that the BCI-Manus group outperformed the Manus group in regard to motor recovery and rBSI was negatively correlated with the improvement in the FMA score. The negative correlation of rBSI with the increase in FMA score suggests that the rBSI can be used as a diagnostic predictor for BCI-based stroke rehabilitation.

The robot-based motor training using EEG-BCI system in combination with physiotherapy for post-stroke rehabilitation has also been investigated. Ramos-Murguialday et al. [87] presented a clinical-based study in which 32 chronic stroke patients participated in EEG-BCI robot-assisted rehabilitation training followed by physiotherapy. The experimental group controlled the movement of orthoses with modulation in the EEG SMRs while in the control group, the robotic orthoses movement occurred randomly and did not depend on EEG SMRs. Different clinical tests were measured at the start and the end of training including motor function scores for upper limb, effects of placebo–expectancy, EMG of hand and arm, FMA, and fMRI BOLD tests. A significant improvement in all the clinical tests was measured after the BCI training for the experimental group compared to the control group. Ang et al. [88] proposed an MI-based EEG-BCI system that included a haptic robotic device namely Haptic Knob (HK) for recovery of wrist and hand movements. The experimental set-up was tested on three randomly assigned groups. Group 1 underwent EEG-BCI controlled movement with the help of HK followed by 30 minutes of physiotherapy. Group 2 received only HK movement-based trials along with the same duration of physiotherapy as for group 1. Lastly, group 3 received only one and a half-hour of physiotherapy. At equal intervals during and after training, the FMA score was calculated to assess the efficacy of the designed rehabilitation program. The results confirmed that group 1 showed better motor recovery of UE compared to group 3 while there was no difference measured between groups 2 and 3 in regard to gain in the motor ability.

2.3.2 Stimulation Applications of EEG-BCI System

In literature, the EEG-BCI system has been used extensively to apply different electrical stimulation over the affected limb(s) or the damaged brain area(s). FES is the most commonly employed stimulation for such applications, however, some other stimulation types have also been explored.

Meng et al. [192] used the EEG-BCI system to detect motor intention signals for wrist and hand movement tasks which, in turn, triggered the FES electrode placed over the arm muscles. The authors showed that their designed multi-session protocol had less than 20 % online error rate and improved the clinical tests of the stroke patients. An FES-based EEG-BCI intervention was developed in [193] for upper-limb recovery of post-stroke patients. The authors recruited four chronic post-stroke patients to complete eight training sessions of arm reaching actions. The motor intention signal was detected using the EEG-BCI system which then triggered the application of FES for further assistance to perform the task. They stated that their protocol correctly classified about 66 % of the movements and 112±278 ms before the actual movement onset. Furthermore, Irimia et al. [194] detected the intention of arm movement which then triggered the FES system using an MI-based BCI system. The authors reported an average accuracy of 87.4 % in operating their designed system by all subjects.

The application of stimulation can also enhance the performance of the EEG-BCI systems. For instance, Bhattacharyya et al. [195] showed that the classification accuracy of the EEG-BCI system for MI tasks could be improved if visual feedback and the electrical stimulation were fed back to the system. Cheng et al. [196] obtained improved classification results for distinguishing left and right arm movements using the EEG-BCI-based FES system.

The idea of modulation of the EEG-derived patterns using FES has also been explored. For example, Takahashi et al. [197] showed that if the extracted ERD pattern using the EEG-BCI system was modulated with FES during ankle dorsiflexion, the range of movement of ankle joint as well as EMG signal amplitude of the affected muscle could be significantly enhanced. Hommelsen et al. [198] modulated the mu rhythm using FES and then fed back to the EEG-BCI system to improve the classification accuracy of the system for upper-limb movements. Recently, Remsik et al. [199] performed a study on the modulation of ERD pattern with FES for UE rehabilitation of post-stroke patients. The authors observed an increased ERD pattern over the ipsilesional brain area as well as improvement in the clinical tests.

Along with FES, many other stimulation techniques have been investigated for BCI applications. For instance, Tan et al. [200] demonstrated that post-stroke patients were able to trigger Neuromuscular Electrical Stimulation (NMES) with the help of an MI-based EEG-BCI system used for wrist-extension and finger-extension tasks. Similarly, Mukaino et al. [201] showed that if NMES were triggered by observing significant MRCP patterns for finger opening tasks, then improvement in muscle tones, as well as clinical tests, could be achieved. Most recently, a portable NMES triggered BCI system was designed for subacute stroke patients in [202] and the authors observed a significant change in ERD pattern over the damaged hemisphere. In addition to NMES, transcranial Direct Current Stimulation (tDCS), Transcutaneous Electrical Nerve Stimulation (TENS), and tactile stimulation were also tested for EEG-BCI system-based applications. A tDCS based BCI system was used for a randomized control multi-session study for improvement of the affected hand in [203]. The authors observed an increase in ERD patterns as well as in FMA test scores after the training. Niazi et al. [204] showed that triggering peripheral electrical stimulation on correct detection of the intention signal during ankle dorsiflexion using an asynchronous EEG-BCI system could induce corticospinal neuroplasticity. Jacob et al. [205] controlled the application of TENS on the arm after the detection of motor intention signal through a BCI system. The authors achieved an average accuracy of 87 % for their designed system. Finally, Shu et al. [206] showed that by controlling the attempted movement of the wrist with tactile stimulation assisted by the EEG-BCI system, the brain activation could be enhanced and detection accuracy of 85.1 % could be achieved.

The control of the robotic device movement and application of stimulation with the help of the EEG-BCI system are also jointly investigated in some research articles. Resquin et al. [207] controlled the movement of the exoskeleton device by intention detection of reaching arm movement using the EEG-BCI system and the intensity control of FES. In addition, Ushiba et al. [208] tested the feasibility of their designed user-friendly and cost-effective EEG-BCI system that enabled chronic stroke patients to control the movement of an exoskeleton device as well as FES stimulation application during finger-extension movement. However, these studies are still in their developmental stage and further investigations are required.

2.4 Motor Training Effect Quantified with EEG

Motor skill acquisition is essential throughout the lifespan including learning new motor skills or re-learning of movements that are lost after a brain injury such as stroke. Depending on the motor skill, a different amount of motor training is required for motor learning. Post-stroke patients re-learn their lost motor skills as a result of different rehabilitation training strategies. The assessment of motor training during these training strategies is an important step in evaluating the overall benefit of any designed rehabilitation program. Commonly used clinical assessment tools to evaluate the motor recovery of stroke patients are the FMA scale and Motor Assessment Scale (MAS) [209]. These clinical tests provide information on post-stroke recovery only at the physical level. However, at the neuronal level, neuroplasticity occurs where new neural pathways are established, existing pathways are reinforced and adjacent surviving neuronal tissues assume the role of the damaged neuronal tissues [18]. Therefore, there is a requirement to understand the effect of motor training on the cortical activities of the brain.

Researchers have explored different technologies to determine the effect of various motor training on brain activities. Examples include EEG [210-220], MEG [221], fMRI [222-225], fNIRS [226, 227], Transcranial Magnetic Stimulation (TMS) [228-231], tDCS [232]. Among these technologies, EEG is a low-cost, safe, and user-friendly method to record brain activities. Different parameters derived from the EEG signal could potentially be used as a quantification tool to determine the effect of motor training in post-stroke patients during their rehabilitation period.

Various EEG-derived measurements have been explored in the literature to determine the effect of motor training. These measurements include EEG coherence analysis [233-237], EEG source localization [238], as well as analyzing changes in EEG-derived movement-related patterns (ERD/ERS and MRCP). The sections given below will discuss studies that analyzed the changes in ERD/ERS or MRCP patterns due to motor training. Many studies discuss the motor training effect using EEG-derived patterns between skilled and non-skilled subjects and such studies are described in Section 2.4.1. Moreover, studies in which the effectiveness of motor training protocols are determined by performing assessment procedures at pre and post-training periods are reviewed in Section 2.4.2. Lastly, numerous studies that measure the effect of motor training on the EEG signal during the actual training protocol are discussed in Section 2.4.3.

2.4.1 EEG Analysis of Skilled Vs Non-Skilled Subjects

In this section, the effect of motor skills learned by playing athletic games, gun-shooting training, or playing musical instruments has been discussed. For this purpose, various features extracted from both ERD/ERS and MRCP patterns have been analyzed.

In [239], the karate and fencing athletes, as well as non-athletes, participated in simple bipodalic and more engaging monopodalic movements while EEG was continuously recorded. A decrease in alpha power during the monopodalic condition showed that the athlete group had achieved neural efficiency, which means neural activity is reduced in the athlete group, compared to the non-athletes group. Baumeister et al. [240] performed the EEG analysis during goal-directed games like golf by dividing the EEG data into different frequencies i.e., theta (4.75–6.75 Hz), alpha-1 (7–9.5 Hz), alpha-2 (9.75–12.5 Hz), and beta-1 (12.75–18.5 Hz) and calculating their performance-related power values. The authors observed higher values of frontal-midline theta power and higher parietal alpha-2 power in the golfer group compared to the non-golfer group. The authors concluded that these higher values of power measured by EEG were associated with the level of skill during golf putting task in their study.

During a self-paced wrist-extension task, a significantly reduced Bereitschaftspotential (BP) amplitude, shorter latency, and contralateral localization of MRCP pattern in the motor cortex have been observed in the athlete group compared to the non-athlete group in [241]. In a single session study, the brain activities of the kendo players and the control group were compared while they performed brisk handgrip self-paced movement with their dominant and non-dominant hands in [73]. This study found the shorter BP onset and the larger MP amplitude of MRCP for non-dominant hand movements only. These studies indicate the neural circuit of athletes alters through training compared to non-athletes and therefore, the MRCP features showed modulation.

The MRCP features also show variations for professional shooters compared to the control group. For instance, ten professional rifle shooters and 12 non-shooters participated in the self-paced movement task with their right and left index fingers in [72]. The amplitude of BP and NS decreased, and their latencies increased for the only right finger tasks in the shooters group compared to the non-shooters group. In addition, the authors in [242] observed a decrease in BP and an increase in skilled performance positivity when the shooters and non-shooters groups learned a new motor skill using their index finger of both hands. These studies prove that when an expert group learns a new motor skill, the amplitude of MRCP components decreases.

The variation in brain activities for the experienced musicians versus non-musicians during a motor task is also investigated in the literature. Such studies show that experienced musicians exhibit significant variations in the amplitude of MRCP components due to their level of skills achieved over years. For example, in [243], ten experienced guitarists and ten non-musicians healthy subjects performed the G major scale on the guitar while their EEG activity was recorded The results indicated that the BP component of MRCP showed no significant change. However, the NS and MP showed a significant decrease in their amplitudes and NS had a lag for the experienced guitarists compared to the control group. In [244], six piano players and six non-musician subjects participated in a series of force production tasks using their index and ring fingers. The MRCP amplitude increased at most electrode sites for ring finger movement only in the musician group while no common trend in MRCP features was observed in the non-musician group.

2.4.2 EEG Acquisition during Pre and Post-Training Periods

The effect of the designed motor training determined by comparing EEG signal variations before and after the motor training is discussed in this section.

Wright et al. [219] recruited healthy non-musicians subjects who received training in playing guitar for five weeks. In weeks 1 and 5, the EEG activity was recorded while the participants were playing the G Major Scale on the guitar. The authors observed a reduced amplitude and later onset of MRCP pattern in the post-training EEG measurements compared to that measured in the pre-training period. Jochumsen et al. [220] performed a comprehensive study to determine the effect of their designed training based on laparoscopic surgery simulation with a non-dominant hand on the features of both MRCP and ERD/ERS patterns. An increase in the amplitude of BP, NS, and MP features of the MRCP pattern, as well as an increase in beta band ERD magnitude after single-session training, were observed. NS and MP amplitudes decreased and no change was observed in ERD/ERS patterns after the multi-session motor training.

The effect of Bimanual Motor Training (BMT) on brain signals is also explored in the literature. Smith et al. [218] recruited subjects to undergo short-term bimanual training of the wrist. By comparing the earlier and later trials of BMT, the authors found a significant increase in the amplitude of the early component of the MRCP pattern while its later component significantly decreased. In the same experiment, the EEG was recorded at the pre and post-training periods during unimanual wrist movements. For unimanual tasks, the authors found a decrease in the MRCP early component and a decrease in reaction time to the task. Hence, the authors concluded that the effect of bimanual motor training could be transferred to unimanual motor tasks, and change in MRCP components and task reaction time could be measured. Smith et al. [245] recruited ten healthy subjects for in-phase BMT, antiphase BMT and repetitive unimanual training of right wrist-extension. After completion of training, the results indicated that there was a significant increase in MRCP amplitude during the preparation period of in-phase BMT with enhancement in motor performance.

In the aforementioned studies, the authors used different motor tasks to analyze brain changes induced by the designed motor training protocol. For instance, the subjects in [219] learned different notes playing on guitar, however, its effect on EEG was determined when they played G Major Scale. Similarly, Jochumsen et al. [220] trained participants in a bead formation task with laparoscopic surgery simulator, but a simple palmar grasp task was used to assess the training effect on brain patterns. Moreover, the authors in [218, 245] recruited subjects for bimanual motor task training. However, their brain activity was recorded during a unimanual motor task. The authors stated that during the motor task of the designed training protocol, it was difficult to control various factors such as force level, speed level, and cortical activation during actual motor training tasks, therefore, the motor tasks used for training and assessment periods were different [220]. However, to measure the actual effect of the designed training on the EEG-derived pattern, the motor training and the tasks used during pre and post-training assessment periods should be similar.

The effect on electrophysiological changes due to shooting task training after single-session and multi-session training designs has also been observed. After a single-session shooting task training, there was a significant decrease in alpha power in the motor execution block when compared to baseline and learning control blocks in [212]. Whereas, an increase in the mean value of event-related alpha-2 power (11–13 Hz) was observed in the temporal region after a multi-session pistol shooter training of about 12-14 weeks in [211].

The effect of neurofeedback training on cortical activation using the EEG signal was studied in a randomized control trial experiment in [246]. The authors found a decrease in the desynchronization of the beta EEG band at the training completion in the group who received neurofeedback during each session of the training. In [247], the effect of Action Observation (AO) and MI protocol with neurofeedback on the modulation of brain activity was also studied. The healthy subjects participated in four training sessions in which three were AO+MI+neurofeedback training sessions and the fourth one was only MI session. After the training, the experimental group showed increased bilateral cortical activation compared to the control group. Another study to understand the effect of neurofeedback on brain activities after the dual-motor task was conducted by Lee et al. [248]. The authors found that the group who received neurofeedback during motor training not only improved in regulating their SMR activities but also improved in their dual-task performance compared to the control group after completion of the training strategy.

There are many studies in which EEG is being recorded continuously during motor training tasks. However, the EEG data are analyzed in pre-training and post-training fashion. For instance, 61 healthy subjects were recruited to study the learning effect of mirror star trace task in a randomized control trial experiment in [210]. The authors stated that after the first 10 acquisition trials, the experimental group not only showed better results in task performance than the control group, but they also showed higher alpha activity compared to the control group. Similarly, the authors in [217] investigated the effect of learning the control of the cursor over the screen with the joystick on the EEG signal. The subjects were more accurate in task performance in post-training trials compared to pre-training trials. Moreover, the authors observed the MRCP associated with movement onset had a larger amplitude and earlier onset in post-training trials compared to that in pre-training trials at the centro-parietal electrode sites. Whereas the amplitude of MRCP related to cue to move increased initially and then decreased with practice at fronto-central electrode sites. The authors concluded that the initial increase in MRCP amplitude might be associated with an early phase of learning and the MRCP decreased when the participants achieved competency in the task.

EEG-BCI systems also find their applications in motor training protocols where they are extensively used to understand the effect of various robot-assisted or non-robot-assisted training effects on EEG signals. For instance, Shindo et al. [249] conducted an experiment on eight chronic stroke patients suffering from hand paralysis in which they were instructed to perform MI tasks with their impaired hands. Only successful MI attempts detected using the EEG-BCI system were used to trigger the orthosis device for partial assistance to fingers. After a training period of four to seven months, the authors also measured variations in ERD/ERS patterns in both parts of the brain as well as enhanced EMG activities in the impaired fingers.

The effect of EEG-BCI system motor training in conjunction with conventional physiotherapy has also been determined. Yilmaz et al. [250] designed an EEG-BCI robot-assisted multi-session training protocol for stroke patients where they controlled the movement of the hand exoskeleton using their brain signals. The patients also went through physiotherapy sessions following each BCI training session for their paretic and non-paretic hands. The authors observed a decrease in MRCP amplitude and its later-onset for paretic hand movement compared to the baseline measurement. Hence, they concluded that the patients who underwent their designed intervention required less mental effort and shorter motor preparation time before motor execution.

The effect of real-time cortical feedback for MI-based EEG-BCI system enabled training protocol on brain activation has been studied in [251]. The experimental group received ERD modulated feedback while the control group did not receive such feedback during the training session. The cortical activation using ERD/ERS patterns was measured for the wrist-extension task during pre and post-training periods. A significant decrease in ERD patterns was observed after the training for only the experimental group. Therefore, the authors stated that the cortical activation could be influenced by providing real-time cortical feedback during MI-based EEG-BCI training paradigms. Chowdhury et al. [252] developed a multi-session robot-assisted EEG-BCI training protocol which incorporated an active physical practice session using the

BCI system followed by a mental practice session with feedback. The authors observed an enhanced ERD pattern and calculated a 6.38 kg increase in handgrip strength as well as a 5.66 increase in ARAT clinical test in four hemispheric stroke patients after completing their rehabilitation training.

The feasibility of the EEG-BCI-based FES system to quantify the motor training effect for foot dorsiflexion was investigated in [253]. The designed EEG-BCI-FES system detected motor intention of affected foot performed by nine stroke patients and once that intention was detected, electrical stimulation pulses were sent to their respective deep peroneal nerve. At equal intervals, during a 12 session training period, the authors measured different parameters of the subjects including speed of gait, Active Range of Motion for dorsiflexion (AROM), six-Minute Walk Distance (6MWD), and Fugl-Meyer Leg Motor (FM-LM) score. A large number of patients showed an increase in their gait speed and AROM scores while a small number of patients displayed improvement in 6MWD and FM-LM scores during their post-therapy assessment. The subjects who showed improvement in gait speed or 6MWD also displayed a noticeable increase in ERD/ERS patterns.

A multimodal multi-session training protocol was designed by Sale et al. [254] in which MIT-Manus robotic movement was controlled using EEG-EMG-EOG (EOG stands for Electrooculography) based BCI system and tested on one subacute and one chronic stroke patients. The authors observed improvement not only in clinical measurements and robotic control but also observed a decrease in alpha band desynchronization in both subjects after the training completion. Another multimodal multi-session training for stroke rehabilitation is described in [255]. Five chronic stroke patients underwent robot-assisted rehabilitation training for upper-limb using EEG-EMG based BCI system. The variations in EEG signal, kinematic variables as well as clinical tests were observed during pre and post-training intervals. The participants showed a decrease in the ERD pattern of the beta band, improvement in clinical scores, and performed the motor task smoother compared to pre-training measurements.

2.4.3 EEG Acquisition during Motor Training Protocols

This section describes the studies in which variations in either ERD/ERS or MRCP patterns are observed during the motor training protocol.

Taylor [214] investigated the effect of skilled motor learning during the training of pressing buttons using the index finger of the right hand. EEG signals at Fz, C3, C4, and Cz electrodes were recorded to extract MRCP patterns. With the improvement in response time, the BP increased steadily at all selected electrodes. However, when the response time reached asymptote, the BP at Fz and C4 decreased and BP at Cz and C3 remained almost constant. Similarly, the effect of learning of complex motor skills of fingers (to and fro movement of match-stick) compared to that during a simple task (pressing the button) on the EEG signal is described in [216]. EEG was recorded at five electrodes which include Fz, C1, C2, Cz, and Pz. The authors observed a significant decrease in MRCP features at Cz, C1, C2, and Pz but not in Fz during the complex task. However, there was a slight inconstant decrease in MRCP features at all electrodes during the simple task.

Variations in EEG patterns during different training protocols such as MI, passive, active, and robot-assisted hand training protocols were studied in [82]. It was found that during the subject's active movement, significant ERDs started earlier whereas, in the case of robot-aided movement, longer ERDs were achieved that extended towards the end of the movement. Similarly, the brain activities during MI, passive, active, and BCI-controlled hand movements were analyzed in [83]. The better ERD patterns were observed in the motor cortex of both hemispheres during all the training protocols. However, for BCI-controlled tasks different neural activities were observed, suggesting that the unique brain processes occur during BCI aided control tasks compared to MI, passive, and active motor tasks. The active engagement of the participants during hand-grasping and supination robot-assisted tasks was assessed in [84] using the EEG-BCI system. The results showed that during active hand movement, more distinctive ERD patterns were observed in beta and mu rhythms as well as BCI system classification accuracy has also improved after the training. These studies demonstrate that active robot-assisted training for post-stroke patients is a promising training protocol for their rehabilitation.

There are some studies in the literature in which the effect of multiple parameters of any training protocol is explored. For example, the effect of visual tasks on the cortical potential during a task of tracking a stimulus on the TV screen was demonstrated in [215]. The authors found an increase in the MRCP pattern negativity at F3, Fz, and F4 electrode sites as well as a significant correlation in MRCP features' changes with the learning of visuomotor tasks. In [256], the authors explored the effects of goal-directedness on the MRCP by training healthy subjects to perform simple reach and touch tasks with their right hand. They observed that MRCP patterns differ during goal-directed and no-goal-directed tasks and the detection accuracy of the BCI system improved with goal-directedness in mind. Moreover, it was found that different motor areas of the brain were involved in the goal and no-goal tasks.

Nakano et al. [213] assessed the motor training performance of healthy subjects by dividing them into two equal groups of high-motor-learning and low-motor-learning, based on their performance of a clockwise rotation of two balls task. For the high-motor-learning group, it was found that the EEG activity in alpha-2 (10.5–12.0 Hz) and beta-2 (18.5–21.0 Hz) rhythms were significantly decreased at left sensorimotor and parietal areas of the brain when compared to the low-motor-learning group. Li et al. [257] used a combination of ERD, MRCP, and time-frequency mapping to determine the difference in brain activities during the motor intention, preparation, and execution of the unilateral wrist-extension task. The authors found that the motor intention phase mainly relied on contralateral activation from sensorimotor cortices whereas the motor execution phase activated bilateral cortices.

Robot-assisted training protocols are a popular choice to understand brain variations during training. By analyzing EEG signals during robot-assisted treadmill walking task, Wagner et al. [99] showed that SMRs in central midline areas of the brain were suppressed in mu and beta band as well as at C3 site for mu, beta and gamma band during active robot-assisted walking task compared to passive condition. Most recently, Liu et al. [258] demonstrated the feasibility of robot-assisted gait training using a split-belt treadmill with synchronized EEG recording. The author observed that the contralateral brain activities were different during affected and non-affected limb movement for their designed protocol.

The effect of various modes of robot-assisted hand movement on brain activity has been investigated in [100]. The authors recruited eight healthy subjects to perform eleven unilateral and bilateral tasks during active, passive robot-assisted, and MI training modes. They observed a contralateral ERD activation during unilateral tasks and the bilateral ERD activation during the bimanual task. Moreover, for active-to-passive tasks, the contralateral side was activated when the right hand drove the left hand and bilateral activations occurred when the left hand drove the right one. Lastly, no common trend was found during the MI task among all subjects.

There are also some studies on the effect of adaptive robot-assisted motor training on stroke recovery. Norman et al. [259] developed a three-phase adaptive robot-assisted protocol for finger-extension motor training. During the first phase, features of SMRs related to finger-extension tasks were identified for each subject, while in the second phase, the subjects were trained to modulate brain activity during an MI task with visual feedback. In the final phase, the subjects performed the cue-based MI task to increase or decrease the amplitude of SMR which then triggered the FINGER robotic exoskeleton device. The authors found that those subjects who completed all three phases of motor training showed the highest improvement in their clinical tests. Zhang et al. [260] tested the feasibility of their linearly progressing multi-session robot-assisted rehabilitation program for upper limb motor recovery of one chronic stroke patient. The protocol consisted of both mental and physical training of hand and elbow movements for six weeks. By the end of the training, the stroke patient was able to control the movement of orthosis by using EEG signals and force sensor signals at a higher accuracy. Moreover, the clinical test scores of the patients were improved after the training.

AO-based training protocols have been widely investigated in the literature where EEG acquisition was performed during the training. For instance, Ono et al. [261] developed an AO-based MI protocol to determine the effect of appropriate neurofeedback on ERD patterns. After performing multi-session training on healthy subjects, the authors found a significant increase in ERD power in the neurofeedback group compared to the control group. Tani et al. [262] compared the effect of MI and AO protocols on the brain activity of post-stroke patients during hand motor tasks. The authors found that the ERD power during the AO-based protocol was significantly higher compared to the MI-based protocol. Therefore, the authors suggested that AO could be used as an alternative method for the modulation of brain activities. Furthermore, Nagai et al. [263] showed that the ERD pattern in the alpha band was the strongest when the subjects performed the hand motor task by observing one own’s hand during MI+AO EEG-BCI protocol compared to that when the subjects performed AO protocol by observing AO of non-participant’s hand or during only MI protocol.

The VR-based motor training strategy is widely being employed in stroke rehabilitation. Through the VR rehabilitation gaming system for left and right arm movements, Bermudez i Badia et al. [101] concluded that large brain areas were actively involved if ME and MI protocols were employed simultaneously during VR-based EEG-BCI training. In [264], the cortical activation difference was determined between the rest state and bimanual motor tasks using a VR-based EEG-BCI system. The authors found significantly higher delta band activations and simultaneous activation of somatosensory and primary motor cortices during bimanual tasks compared to the resting state. In another study, the brain activations involved during VR-based EEG-BCI system training to that during the Augmented Reality (AR)-based EEG-BCI training were investigated in [265]. The smaller alpha activities were found in frontal and temporal regions during both VR and AR modes whereas, higher beta activities were measured in frontal and temporal brain areas in AR compared to VR mode.

The EEG analysis of stroke patients can be influenced by the stroke lesion location. For instance, Park et al. [266] used ERD/ERS analysis of the EEG signal to show that beta band power decreased significantly among stroke patients groups with different lesion locations. Similarly, Ray et al. [267] showed that the amplitude of ERD decreased for stroke patients having lesion locations involving the motor cortex. Furthermore, by implementing an MI-based EEG-BCI protocol for hand motor recovery, it was shown in [102] that ERD amplitude was reduced in the affected hemisphere and when the motor task was performed with the affected hand, ERD was lateralized to the ipsilateral (unaffected) hemisphere.

The difference in EEG-derived patterns can also be influenced by variable motor impairments caused by the stroke. Kaiser et al. [268] found that for stronger ERD signals, there was higher impairment in the unaffected hemisphere and again stronger ERD signals were observed when higher spasticity was observed in the affected hemisphere. Higher impairment and higher spasticity were found to be associated with stronger ERS in the affected hemisphere only. In [269], the differences in cortical activation in chronic stroke patients having variable sensory-motor impairments and in the healthy control group were observed using a robotic wrist manipulator and the EEG-BCI system. The brain activation occurred in contralateral brain areas of healthy subjects and chronic stroke patients with no or mild sensory impairments during passive motor tasks, while a significant reduction in cortical activation was observed in chronic stroke patients with severe sensory impairments. During the active motor task, only chronic stroke patients with mild sensory impairment displayed reduced cortical responses.

Tangwiriyasakul et al. [270] observed brain activity during hand motor tasks four times over four months. A modulation strength (S_m) parameter was calculated using the ERD amplitude and its area. The S_m parameter was used to quantify the motor training effect. A significant increase in S_m over ipsilesional brain area as well as a decrease in S_m of the contralesional side was observed. The increase in ipsilesional brain activity could be due to neuroplasticity occurring throughout stroke recovery while the decrease in contralesional brain activity showed less dependency on that side to support the affected hand movements. A longitudinal study was performed to understand the cortical variations across sessions as well as their relationship with stroke onset time and upper-limb motor recovery in [271]. The authors observed that beta band activities had a higher association with stroke onset time as well as motor recovery of upper-limb compared to alpha band activities. Whereas, alpha band cortical variation was found to be more related to a motor learning effect, an indication of neuroplasticity.

The assessment of the subject's engagement level during learning of a motor task for stroke rehabilitation applications has become a topic of interest in recent years. Bartur et al. [272] tested their developed Brain Engagement Index (BEI) to monitor the level of engagement of post-stroke patients during rehabilitation training. BEI monitor displayed real-time value every 10 s by exploring the sampled EEG data for the occurrences of an attention-related template. The authors found that there was a clear association between BEI and the improvement in functional parameters. Koyanagi et al. [273] used the EEG power spectrum ratio of alpha and beta band i.e. beta/alpha to evaluate the subject's concentration during passive robot-assisted upper-limb movement tasks. The authors observed that the concentration of the subjects affected by the scoring system during the training using their developed method.

A combination of EEG and EMG signal analysis has also be used to determine the level of participation of subjects during the motor training protocol. Gandolla et al. [274] monitored the level of engagement during the training with EMG-triggering of the muscle and EEG-based biofeedback system. The authors stated that the subjects had more attention and participation in operating their designed system compared to other standard systems. Whereas, Li et al. [275] investigated the effect of increasing game task difficulty on a person's engagement level during the training. They measured EEG and EMG signals to determine the cognitive and motor engagement during the task respectively. It was found that by increasing the game difficulty level, both cognitive and motor engagement of the subjects could be increased.

2.5 Summary, Research Gaps, and Future Trends

EEG is an easy to administrate and cost-effective way to determine brain dynamics as well as to measure cortical activations during post-stroke motor rehabilitation exercises. Therefore, EEG has been used in the literature in a variety of ways for motor recovery of post-stroke patients. Out of eight research categories of EEG applications in stroke rehabilitation discussed in this chapter, robotic device control using intention signal has the highest rate as illustrated in Figure 2.3. The second topmost categories include intention signal classification, intention signal detection as well as measuring brain activities during training protocols. The application of stimulation assisted by the EEG-BCI system and measuring EEG with pre and post-training protocols are the third most active research areas. However, intention signal decoding and comparison between the brain activities of skilled versus non-skilled subjects have received the lowest attention in the literature.

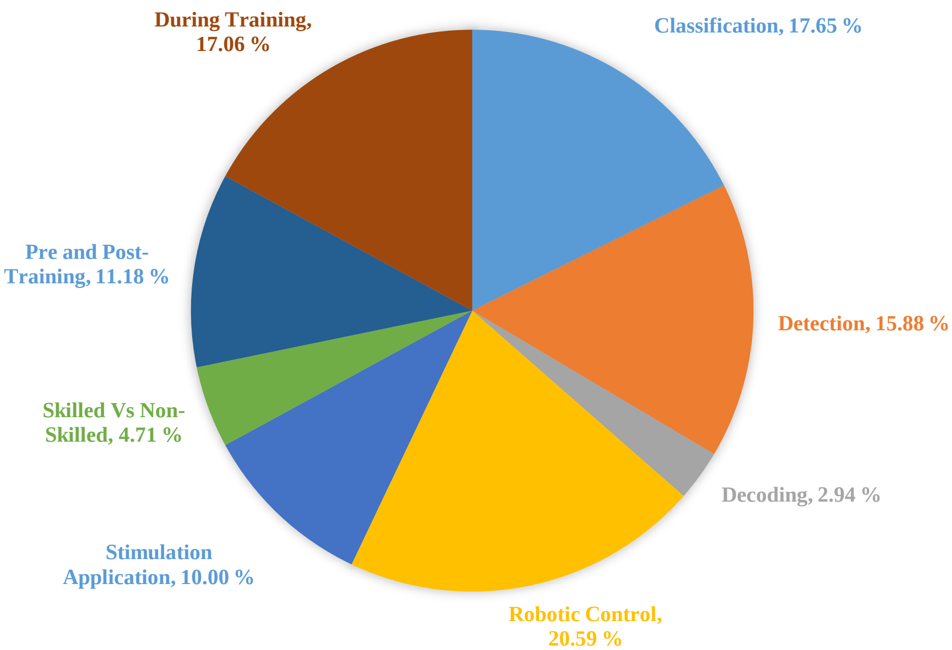


Figure 2.3: Applications of EEG in post-stroke motor rehabilitation

Post-stroke motor rehabilitation includes recovery of both upper-limb and lower-limb. The UE motor recovery of stroke patients involves the recovery of arm, shoulder, elbow, wrist, hand, and fingers, whereas, LE motor recovery involves foot, ankle, knee, and gait. During any of the upper-limb or lower-limb motor imaginations or actual movement execution, specific EEG-derived patterns (ERD/ERS and MRCP patterns) emerged in motor and sensorimotor cortices which could be measured and analyzed. The studies included discussed more of UE motor recovery compared to LE because of its importance in performing ADLs as well as more DOF involved. However, even in UE stroke recovery, more research focus lied on the coarse movement of the upper-limb.

Robot-assisted rehabilitation programs are efficient as well as they can be used for active participation of stroke patients during the training which is essential for neuroplasticity induction. Various kinds of robotic systems have been developed and tested for both upper-limb and lower-limb motor recovery of post-stroke patients. However, very little research is conducted on the development and deployment of user-friendly, and commercially available rehabilitation robotic systems for post-stroke patients giving benefit to a large cohort of stroke patients. In addition, more research work is required to monitor brain activity especially during robot-assisted training which is important to prevent the passive reaction of patients during the training.

Future research on the topic of EEG applications in post-stroke rehabilitation should focus on the following areas: (1) Detecting, classifying, or decoding the intention signal of fine motor skills. (2) Developing an EEG activity monitoring system during robot-assisted rehabilitation to avoid passive training. (3) Including actual stroke physiotherapy exercises in motor training protocols to ensure EEG dynamics are well understood during the training protocols. (4) As stroke affects the brain in various ways depending on the location and intensity of stroke, therefore, there is still a research gap to understand the cortical activities of stroke patients having different lesion locations. (5) In current literature, EEG analysis is performed during rehabilitation training which is pre-defined before the experiment commencement, however, there should be a mechanism of changing the rehabilitation training depending on the variations in EEG-derived movement-related patterns for a particular stroke patient.

Chapter 3

Experimental Set-Up and Data Processing Details

3.1 Introduction

The primary purpose of this project is to understand brain activities when post-stroke patients undergo hand motor rehabilitation. Therefore, the experimental work of this project is conducted using a state-of-the-art EEG acquisition system and AMADEO hand rehabilitation device. The EEG acquisition system consists of a Grael 4K EEG amplifier, Quick-Cap, and an acquisition software called CURRY 8X developed by Compumedics Neuroscan Company. The EEG acquisition system is used to acquire brain activities during different experiments. The AMADEO hand rehabilitation device by Tyromotion GmbH Company was deployed for fine finger motor skills training of post-stroke patients. The complete experimental set-up used in all experiments for this project is shown in Figure 3.1.

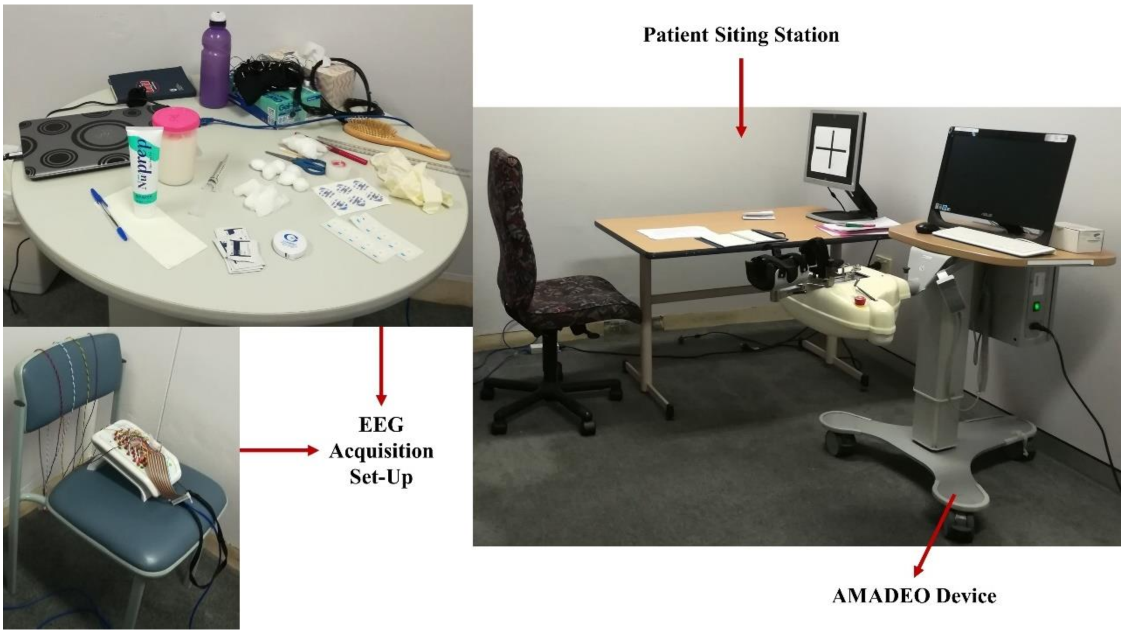


Figure 3.1: Complete experimental set-up

The remaining chapter is organized as follows. The details of the EEG acquisition system and its application in this project are discussed in Section 3.2. Section 3.3 describes various training modes and the assessment tools available in the AMADEO hand rehabilitation device used in this project. The main EEG signal processing steps involved in the data analysis of this project are explained in Section 3.4.

3.2 EEG Acquisition System

3.2.1 Grael 4K EEG Amplifier

In this series of studies, a 40-channel Grael 4K EEG amplifier (Version 1) is utilized for the EEG signal acquisition for both healthy and post-stroke subjects. It is a standalone unit that can record EEG, EOG, ECG (Electrocardiogram), and respiratory signals received from the electrodes and sensors connected to the human subjects [276]. However, in this study, this amplifier is used to record EEG and EOG signals only. All the electrodes and sensors are connected to the Grael 4K amplifier which is powered by a network cable. The connection set-up of the amplifier to the host PC is shown in Figure 3.2.

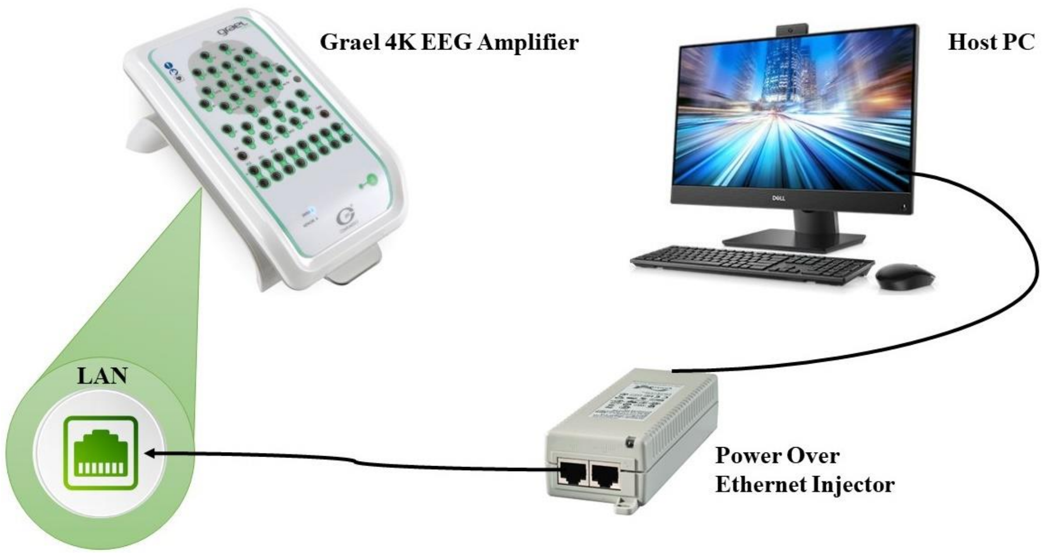


Figure 3.2: Connection of Grael 4K EEG amplifier to host PC

A single IP connection to the Grael 4K amplifier is provided for both power and data transmission purposes. Due to the IP connection option, the IP address of the host PC and Grael 4K amplifier needs to be set. The IP addresses for the host PC and the amplifier are given in Appendix 2. The IP address for the host PC can be set using the Network and Sharing Centre item of the Control Panel in the Windows Operating System. While the IP address for the Grael 4K amplifier can be set using the Network Amplifier Tools present in the Acquisition tab of the CURRY 8X software.

The Grael 4K EEG amplifier is well-suited for EEG-based studies in both clinical and research applications. The main specifications of the Grael 4K EEG amplifier (Version 1) are stated in Table 3.1.

Table 3.1: Specifications of Grael 4K EEG amplifier (Version 1) [277]

Name of Specification	**Details**
EEG channels	32
Bipolar channels	8
Extra inputs	Event button, and oximeter with pleth waveform
AC/DC	DC
Sampling rate options (Hz)	256, 512, 1024, 2048

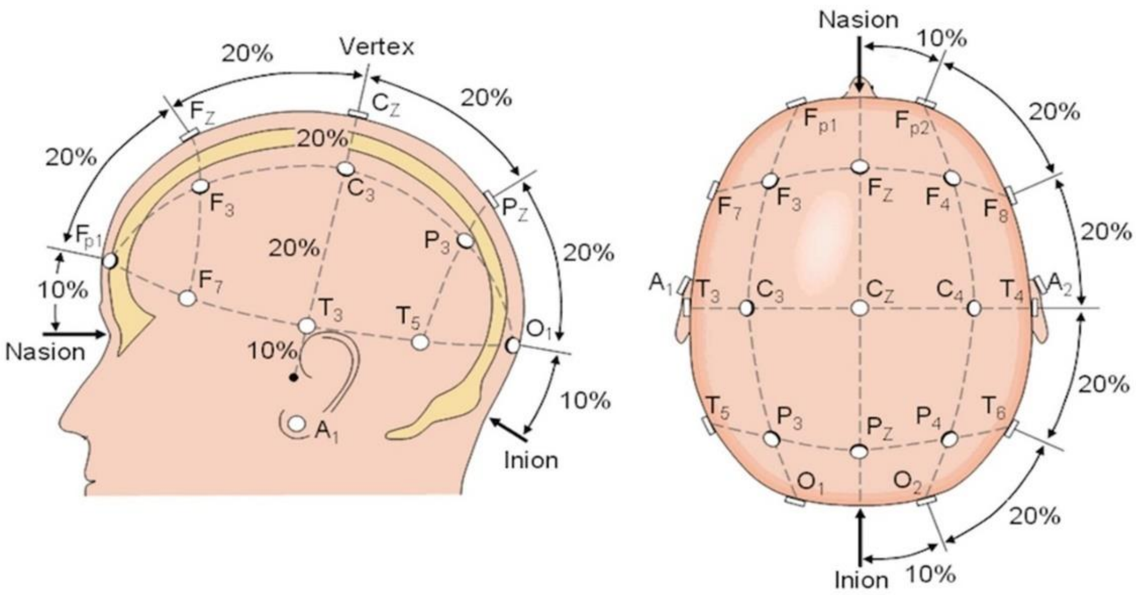
Bandwidth (Hz)	DC to 580
Resolution	24-bit
Input range (mV)	300 to 3000 (4 modes)
Sensitivity (nV)	18
Trigger	8-bit TTL
Impedance check option	available

3.2.2 EEG Quick-Cap

In all the studies conducted in this project, a 32-channel Quick-Cap with two integrated bipolar leads for vertical and horizontal EOG is used as shown in Figure 3.3. The Quick-Cap provides a consistent and speedy application of electrodes for data acquisition. It is manufactured using highly elastic breathable Lycra material with soft neoprene electrode gel reservoirs to enhance the comfort of the patient. It comes in a variety of sizes such as infants, small, medium, and large. Small, medium and large caps are used in different experiments of this project. The small Quick-Cap is suitable for participants having head circumference between 48 – 54 cm. While, for medium and large Quick-Caps, the suitable head circumferences are between 55 – 59 cm and 60 – 65 cm, respectively.

Figure 3.3: The 32-channel Quick-Cap [278]

All the electrodes in the Quick-Cap are placed according to the International 10-20 electrode placement standard [279]. The 10-20 system is an internationally recognized system for placing the EEG electrodes over the scalp. It ensures equal inert-electrode spacing. The electrode placement is proportional to skull size and shape. This system is based on the relationship between the location of an EEG electrode and the underlying area of the cerebral cortex. Figure 3.4 (a) shows the left side-view and Figure 3.4 (b) shows the top view of the possible positions of the electrodes in the 10-20 system. The position of each electrode has a letter that indicates the lobe and a number or another letter that indicates the location of the hemisphere. The letters Fp, F, C, P, O and T stand for pre-Frontal, Frontal, Central, Parietal, Occipital, and Temporal, respectively. Although there is no central lobe in the brain, the defined notation of the central lobe is used here for identification purposes. The odd numbers refer to the left hemisphere and even numbers refer to the right hemisphere. The letter z refers to an electrode that is positioned over the midline. Moreover, the smaller the number of an electrode, the closer is the electrode to the midline and vice versa.



(a) *(b)*

Figure 3.4: International 10-20 system for EEG electrode placement [279, 280]

The position of electrodes according to the 10-20 system for 32-channel Quick-Cap is shown in Figure 3.5 and the wiring diagram of the 32-channel Quick-Cap by Compumedics Neuroscan is given in Appendix 3. By default, the ground electrode is set at the Fpz electrode position whereas, CPz is set as the reference electrode. However, the position of the reference electrode can be changed using the configuration setting available in the acquisition software. The A1 and A2 electrodes (referred to as M1 and M2 in the wiring diagram of the 32-channel Quick-Cap) can be used over the mastoid point or ear lobe depending upon the requirements of the experimental design. Also, the two electrodes are placed below the left eye and on the supraorbital ridge to record Vertical Eye (VE) movements as well as eye-blinks. Moreover, two other electrodes placed over the outer canthus of both eyes are used to monitor Horizontal Eye (HE) movements as shown in Figure 3.6. These vertical and horizontal electrodes are connected to the positions of the bipolar channels available in the Grael 4K amplifier during the data acquisition.

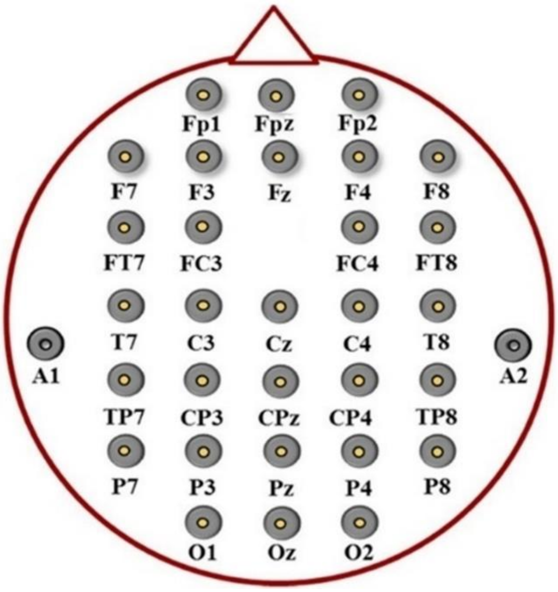


Figure 3.5: The 32-channel Quick-Cap electrodes' position diagram [281]

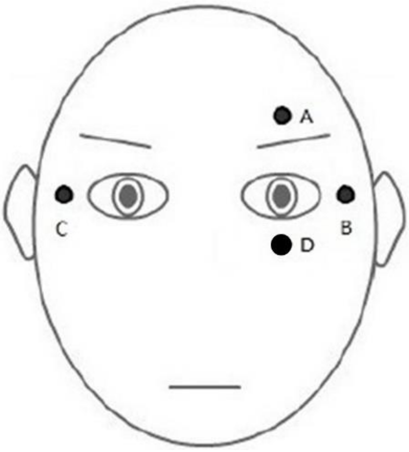


Figure 3.6: Placement of EOG electrode; A-D records VE movements,
B-C records HE movements

3.2.3 EEG Acquisition Software

The data acquisition software namely CURRY 8X from Compumedics Neuroscan is used in this project which supports the acquisition of EEG data with the Grael 4K amplifier. It is a reliable and easy-to-use tool for EEG data acquisition and online/offline data processing. It supports all the features required for data acquisition including amplifier configuration setting, impedance checking, online filtering, real-time event averaging, online artifact reduction, as well as montage setting. The montage is the way of connecting EEG electrode pairs to the amplifier.

The impedance check before data acquisition is an important step to ensure the high quality of the acquired signals. The CURRY 8X allows impedance check in a simple visual display with impedance values showing for each electrode. The impedance check can also be performed during the experiments without interrupting data acquisition. Figure 3.7 shows an impedance checking screen in CURRY 8X software for a 32-channel Quick-Cap having a reference electrode at CPz and a ground electrode at Fpz. All impedance values are measured with respect to the set reference electrode. The threshold value of the electrodes' impedance is set at 5 kΩ. The impedance of each electrode is set to less than 5 kΩ before the start of data acquisition for all of the experiments.

In this project, CURRY 8X software is employed to set the amplifier configuration before the data acquisition step. It is also used for impedance checks and for sending procedure of digital event marker during every data acquisition session. Moreover, some initial signal processing steps are performed in CURRY 8X software before importing data into EEGLAB.

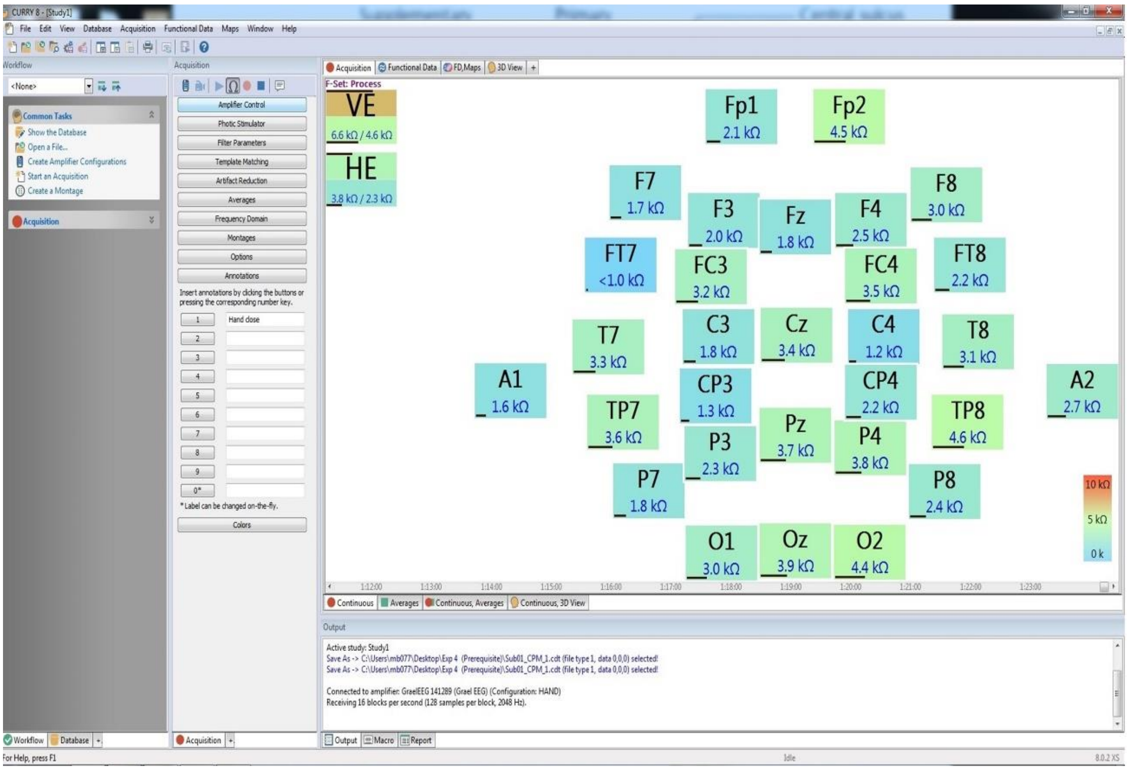


Figure 3.7: Impedance-check in CURRY 8X software for a 32-channel Quick-Cap

3.2.4 EEGLAB

The EEGLAB is an interactive MATLAB toolbox with Graphical User Interface (GUI) display allowing visualization of single-trial or averaged data, time or frequency analysis, artifacts rejection, event-related statistics as well as Independent Component Analysis (ICA) algorithm. It can be used to process continuous event-related EEG, MEG, or other physiological data.

In this project, all offline EEG data processing is performed primarily in EEGLAB. The acquired data files from CURRY 8X software are not compatible with EEGLAB. They need to be converted into other formats, such as *.edf* or *.cnt*, within CURRY 8X software. Moreover, a freely available loadcurry 2.0 plug-in extension needs to be downloaded before importing data files into the EEGLAB. Figure 3.8 shows the EEGLAB GUI and epoched EEG data windows where numbered red lines represent event marker triggers manually sent to the CURRY 8X software.

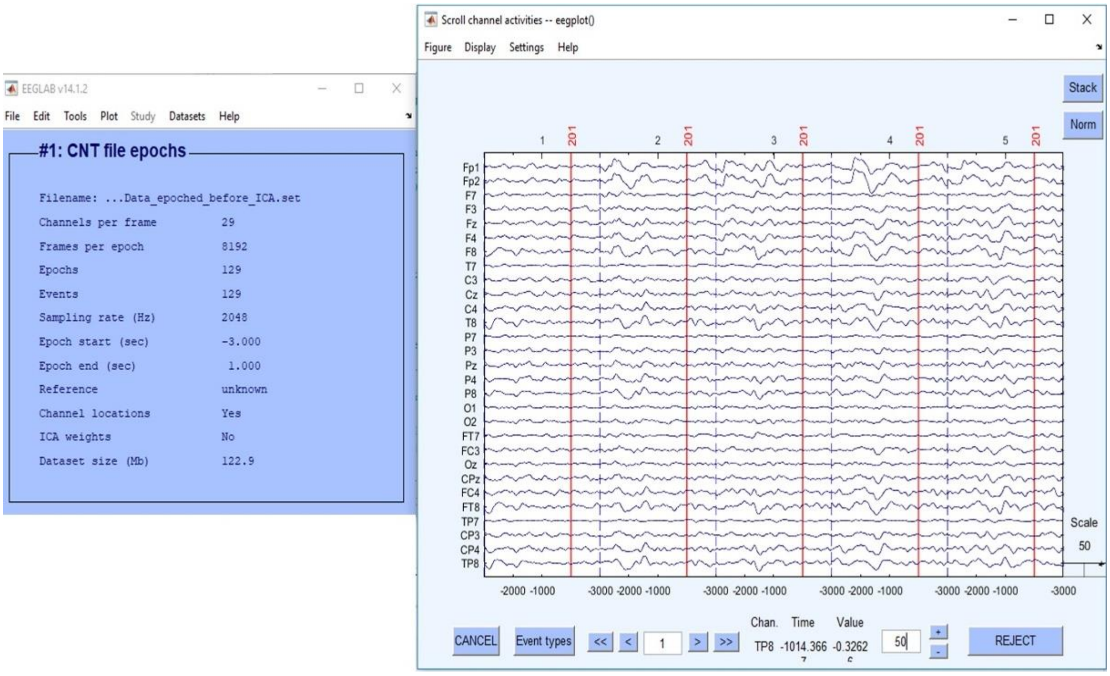


Figure 3.8: EEGLAB GUI and data scroll window

3.3 AMADEO Hand Rehabilitation Device

AMADEO hand rehabilitation device is a 5-DOF distal UE robot used for fine hand motor skill training of patients having motor deficits. It provides position-based passive, assistive, and active training modes that are based on extension and flexion training of fingers and thumb. The AMADEO finger slides are attached to each finger and thumb with the help of a small magnetic disc and cohesive tape. The moving slides can then transfer extension and flexion movements to the fingers and the thumb. During the training, the patient is positioned directly in front of the AMADEO device in a comfortable and upright posture. The hand-arm holding assembly in the AMADEO device can be adjusted to an appropriate position to support the weight of the arm and hand during the training as shown in Figure 3.9.

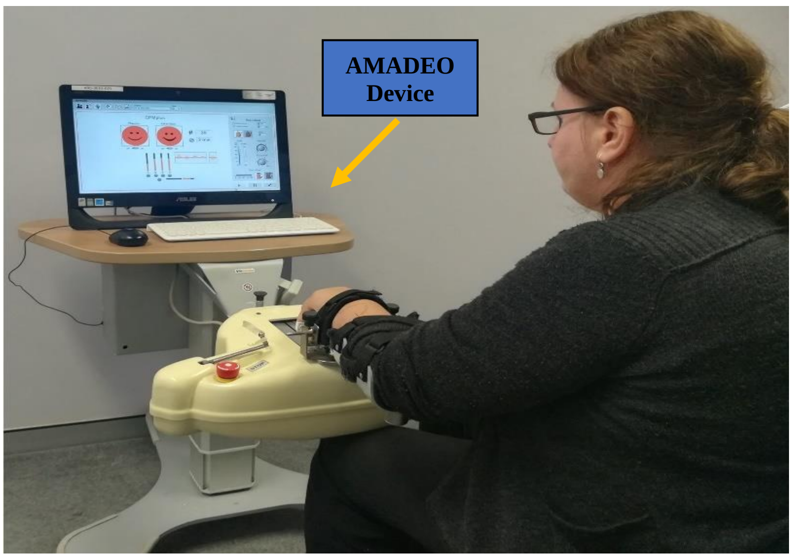


Figure 3.9: Patient while receiving AMADEO training

3.3.1 AMADEO Standard Training Modes

The software used to perform AMADEO's operation is known as GRIPS and it can only be operated in combination with the AMADEO device. After entering the patient's details into the system, the Range of Movement (ROM) of the fingers and thumb is set manually by the operator. In order to set the ROM, the patient's hand needs to be attached to the device using a magnetic disc and tape. AMADEO allows four basic training modes, as shown in Figure 3.10, which include Continuous Passive Motion (CPM), CPMplus, assistive, and active training modes. All these training modes in AMADEO aim to train the affected hand of the patient according to the pre-set ROM, thus ensuring safe rehabilitation training for the patient.

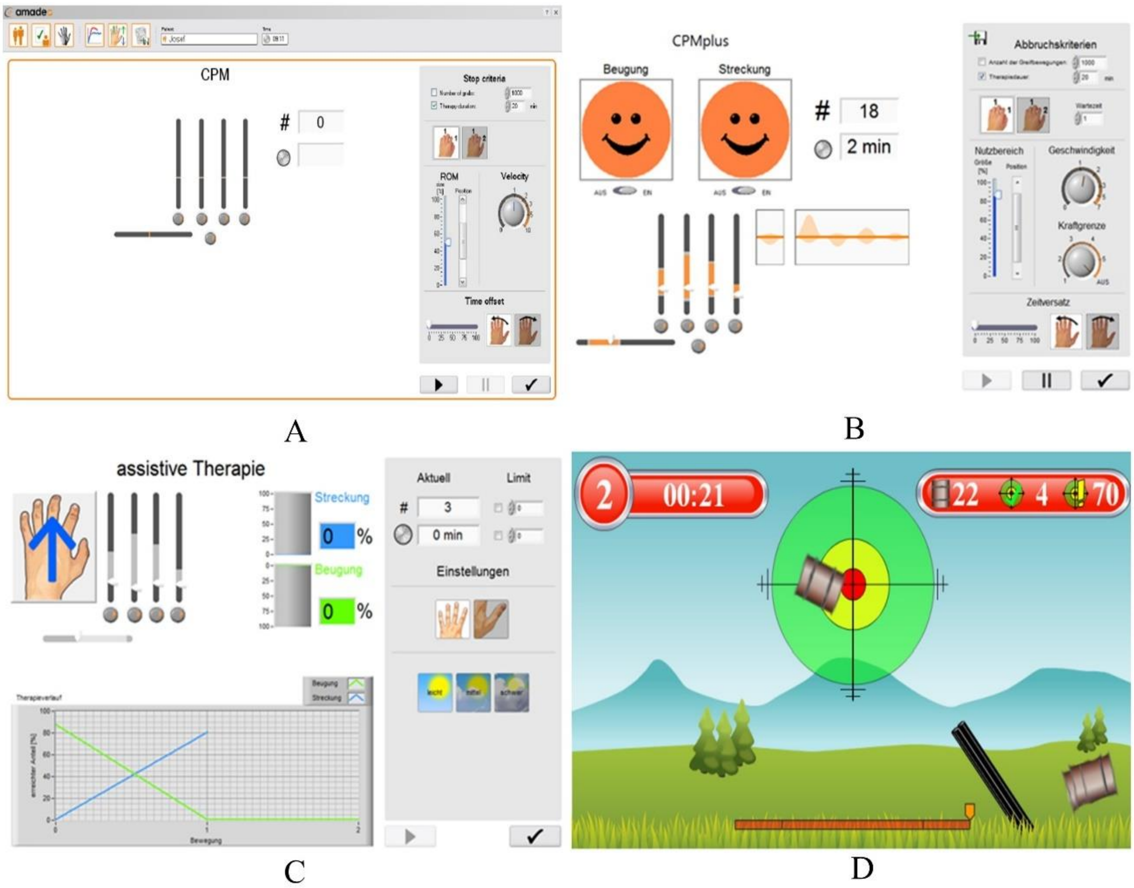


Figure 3.10: AMADEO training modes; (A) CPM, (B) CPMplus, (C) Assistive training, (D) Active training (Shootout 2D game)

(1) CPM training mode – The hand is trained in continuous passive motion. It allows settings for speed, ROM, and time offset.

(2) CPMplus training mode – During CPMplus, the subject is encouraged to apply force during extension and flexion actions of hand through biofeedback display. The biofeedback display encourages patients to apply force at the end of each flexion and extension motion. It offers additional delay and forces limit options compared to CPM.

(3) Assistive training mode – The hand movement is assisted by the AMADEO control algorithm, depending on individual fingers' functional limitations and abilities. In this training mode, the patients carry out the hand movement actively as far as possible using the fingers' force. However, when the fingers stop moving actively, the system takes over and completes the rest of the hand movement path.

(4) Active training mode – This mode utilizes 2D interactive games in which the patient actively controls the position of virtual objects in various simulated environments. AMADEO contains five 2D games namely Shootout, Recycle, Balloon, Firefighters, and Applehunter. A screenshot of the Shootout game is shown in Figure 3.10 (D) while the rest of the games are shown in Figure 3.11. At the end of each game, the patient receives the score indicating the performance of the hand movement during the game. The achieved score in these games indicates the force and the position applied by each finger. This scoring procedure motivates patients to perform their best during the training.

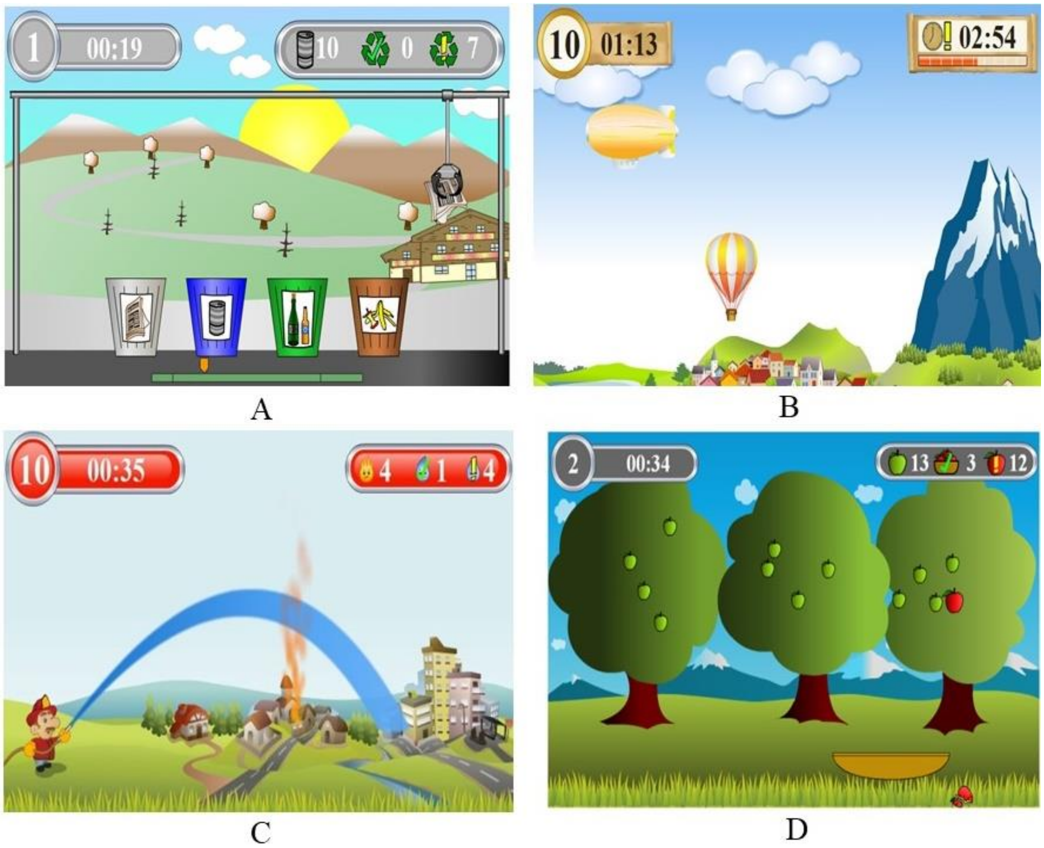


Figure 3.11: AMADEO Active training Programs; (A) Recycle, (B) Balloon, (C) Firefighters, (D) Applehunter

3.3.2 AMADEO Assessment Tool

In order to evaluate the effect of AMADEO training on patients' fine hand motor skills, AMADEO allows two types of assessment tools i.e. force assessment and ROM assessment. The force assessment tool measures the finger force as well as grip force by calculating active force output applied during flexion and extension tasks by the patient as shown in Figure 3.12 (A). Whereas the ROM assessment tool measures the active range of movement of fingers and thumb in both extension and flexion directions with respect to pre-set ROM of the patient as shown in Figure 3.12 (B). Hence, both of these assessment parameters in AMADEO enable easy and timely assessment of motor skill improvement as a result of the training.

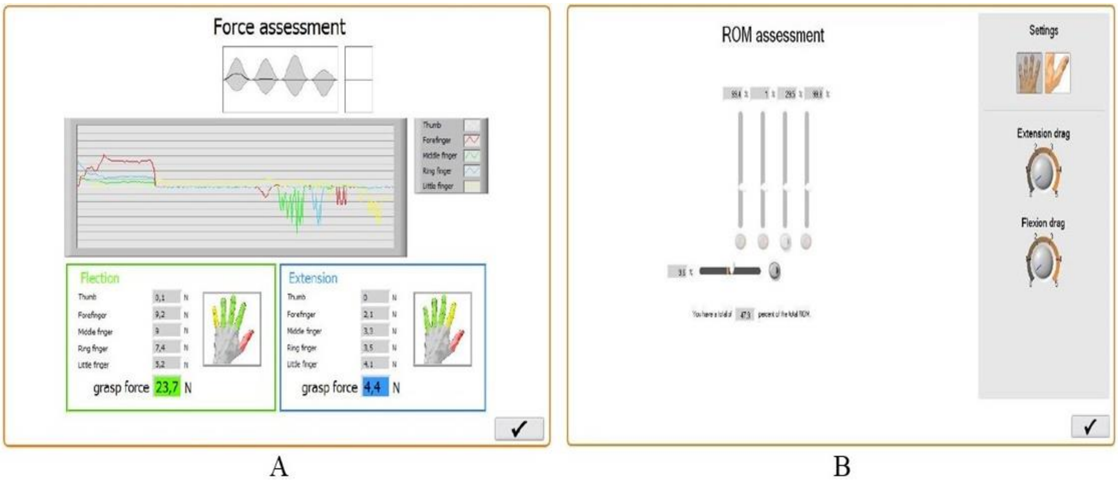


Figure 3.12: AMADEO assessment tool; (A) Force assessment, (B) ROM assessment

To ensure the validity and consistency of the data, both force and ROM assessments are repeated three times before and after the designed multi-session training strategies and their average values are chosen as the measured score in the further analysis.

3.4 EEG Signal Processing Steps

This research project is based on the analysis of the MRCP pattern extracted from the acquired EEG data during different motor training protocols for post-stroke rehabilitation. Different signal processing steps are involved to extract MRCP patterns from the raw EEG data acquired during experimental work. These steps generally include data filtering, the formation of the epoch, channel selection as well as extraction of the MRCP features as shown in Figure 3.13.

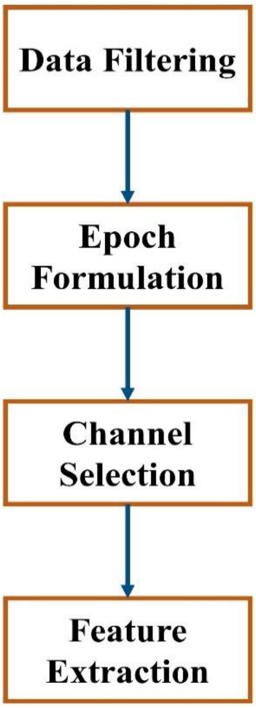


Figure 3.13: Sequence of steps for EEG signal processing

The experimental works conducted in the research project can be divided into two groups. The experiments in the first group are designed to detect the motor intention signal using the MRCP pattern during robot-assisted hand tasks. Whereas, the second sets of experiments determine the effect of the robot-assisted motor training on the MRCP patterns. Sections 3.4.1 to 3.4.4 describes the general EEG signal processing steps for extracting the MRCP pattern and how these steps are used in both groups of experiments.

3.4.1 Data Filtering

The first signal processing step is to filter the acquired EEG data for the frequency band in which the MRCP pattern exists. As mentioned in Chapter 1, the MRCP pattern appears in the delta frequency band (0-5 Hz) [71]. Different ranges of frequency, within this band, can be used depending upon the type of experiment to filter the EEG data.

For intention detection of motor tasks, the EEG signals are passed through a band-pass filter within the narrow range of 0.1-1 Hz [171] as this frequency range best captures the anticipatory based MRCP pattern [282] compared to the complete delta band. The exact data filtering step, used for intention detection for the hand motor task in this project, is applied in three stages; stage 1: a high-pass filter (4^{th} order Butterworth, causal) with cut-off frequency (f_c) of 0.1 Hz, stage 2: a CAR filter for re-referencing, and stage 3: a low-pass filter (4^{th} order Butterworth, causal) with f_c of 1 Hz. The filtered signals are then down-sampled from 2048 Hz to 20 Hz to increase computational efficiency [171].

To determine the effect of the designed motor training on the MRCP pattern, the acquired EEG data are first passed through a notch filter (49–51 Hz) to remove any power line noise. It is then low-pass filtered (2nd order Butterworth, causal) with f_c of 5 Hz. The signal is finally high-pass filtered (2nd order Butterworth, causal) with the f_c of 0.5 Hz [220, 283].

3.4.2 Epoch Formation

An important step in EEG signal processing is to create epochs by dividing the continuous EEG data into small portions with the help of event markers because the MRCP pattern appears only within 2 s before actual movement onset. These event markers represent the onset points for the actual movement execution performed by the subjects. The epochs help to identify the vicinity in which the MRCP pattern can be found.

The intention detection is performed by dividing continuous EEG signals into two types of epochs. The Move epochs, containing the MRCP pattern, are extracted between -2 s to 0 s with 0 s indicating the instance of actual motor execution. While, the No-Move epochs, which do not have an MRCP pattern, are extracted from 0.5 s to 2.5 s. The epoch length for both Move and No-Move epochs is fixed at 2 s. After epoch formation, all Move epochs are inspected visually for artifacts, for instance, eye-blinks, head movement, and other movement-related artifacts, and the epochs containing these artifacts are removed from the data.

For motor training experiments, epoch formation consists of four steps. First, the filtered EEG data are divided into epochs using movement onsets obtained from event markers. The duration of these epochs is set from -5 s to 5 s, where 0 s is the movement onset obtained using event marker triggers. These epochs are termed long epochs. Second, the ICA algorithm is applied to the long epochs to remove eye-related artifacts. ICA algorithm is usually employed to remove eye-related artifacts from EEG data [284]. It is based on the assumption that brain activities and artifacts are separate physiological processes, and this separation is reflected in the statistical independence between the signals generated by these processes [285]. Third, an automatic voltage threshold detection is also applied to the epochs to remove any remaining eye-blink artifacts having a threshold level of 100 µVpp (pp stands for peak-to-peak) in either of the pre-Frontal electrodes (Fp1, Fp2). If a peak-to-peak value in either of Fp1or Fp2 electrodes is greater than 100 µVpp in any epoch, then that epoch is removed from the final data. Finally, to overcome the human error involved in placing the event markers, movement onset correction is performed. MRCP has the lowest potential around the movement onset point. Therefore, the minimum point in each cleaned long epoch signal is found and that point is considered as the actual movement onset. Short epochs are then be formed starting from -3 s to 1 s where 0 s represents the actual movement onset

3.4.3 Channel Selection

The selection of appropriate channels for data analysis is an important step. The motor intention detection experiment is associated with either right or left hand. Therefore, the channel selection depends on the hand in use during the experiment. The selected electrodes for both hand movements are given in Table 3.2.

Table 3.2: Choice of electrodes for intention detection experiment

Hand Movement Type	**Selected Channels**
For right hand motor intention detection	C3, FC3, Cz, CP3, T7, and Short Laplacian (SL) channel calculated using the formula given as C3-(FC3+Cz+CP3+T7)/4 [286]
For left hand motor intention detection	C4, FC4, Cz, CP4, T8, and SL channel calculated using the following formula C4-(FC4+Cz+CP4+T8)/4 [286]

The above-mentioned channels are selected for both Move and No-Move epochs. The C3 and C4 channels are selected as suggested by Jochumsen et al. [287] to be the most appropriate electrode site for the right hand and left hand motor intention detection respectively using the MRCP pattern. Along-with C3 and C4 channels, their four neighboring electrodes, and their linear combination are also explored to find the best electrode choice for the designed protocol.

On the other hand, eight single EEG electrodes are considered for the analysis during motor training experiments. These channels include FC3, FC4, C3, C4, CP3, CP4, Cz, and CPz. The selected electrodes are located over the motor and sensory cortices of both hemispheres to determine which part of these cortices showed the effect of the designed rehabilitation training.

3.4.4 Feature Extraction

MRCP pattern exhibits various features that can convey movement-related information. The main MRCP time-domain features include BP1, BP2, and Npeak as explained in Chapter 1. For both groups of experiments of this research, the features extracted from the processed global MRCP patterns at the selected electrodes are explained as follows. For group analysis in this thesis, global MRCP refers to the averaged MRCP signal with respect to the number of participants in the group at a selected electrode site.

The Npeak and slope features of the MRCP pattern are used for intention detection of hand movement. The Npeak of the MRCP pattern is its lowest amplitude that exists near the movement onset and is always negative in amplitude, while the slope is calculated by using the two-point slope equation between BP1 onset and Npeak onset. The Npeak and slope features of the MRCP pattern are indicated in Figure 3.14 (a). Both these features are extracted for each trial of the motor task from both Move and No-Move epochs.

For motor training experiments, five different time-domain pre-movement features using global MRCP patterns namely; BP1 onset, BP1 amplitude, BP2 onset, BP2 amplitude, and the Npeak of MRCP are extracted at all the selected electrodes as indicated in Figure 3.14 (b). These features' extraction is performed using a newly developed MATLAB toolbox called 'visualEEG' which is specifically designed to extract the pre-movement features from the MRCP pattern [74].

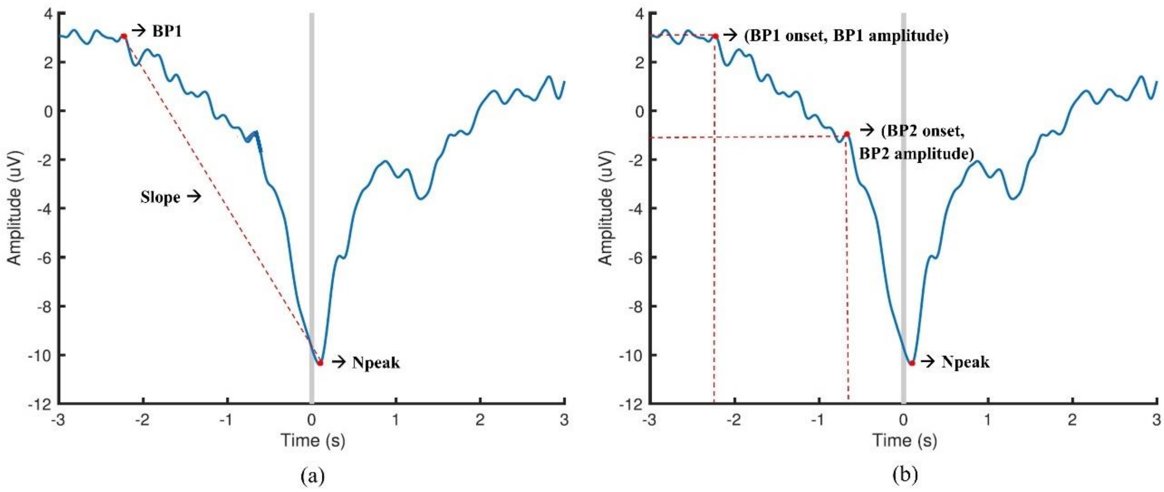


Figure 3.14: Extracted features from global MRCP pattern; (a) For intention detection protocol, (b) For motor training protocol

3.5 Summary

This chapter provides detailed information about the two types of equipment used for the experimental work of this project. The first equipment is the EEG acquisition system which is used to acquire brain activities during hand motor tasks while the second equipment is an AMADEO rehabilitation device which is used to improve the hand motor skills of post-stroke patients. This chapter also explains the signal processing steps which are applied to extract MRCP pattern from the raw EEG data. Moreover, the details of the software used for data analysis are also mentioned in this chapter.

Chapter 4

Movement-Related Cortical Potential during Different Exercise Protocols for Single-Session Hand Motor Training

4.1 Introduction

The main aim of this research project is to use EEG brain signals to enhance the effectiveness of the rehabilitation processes in post-stroke patients with fine finger motor impairments. This chapter studies how the engagement of a subject in the rehabilitation process affects the EEG signals. It is shown that, as attested by the previous studies using the AMADEO rehabilitation device [93, 94, 288], the efficacy of the rehabilitation process is enhanced when the stroke patients are actively engaged during hand motor training. In future chapters of this thesis, the finding of this study is used to design a novel adaptive rehabilitation training strategy.

During the experimental work conducted in this chapter, the MRCP patterns that appear during motor tasks are studied. In the experimental work, participants complete a single-session training of their hand movements through two distinct protocols. Protocol A is based on a simple visual-cue that guides participants to start and stop their hand movements. While protocol B is based on a 2D interactive game that provides the subjects with attention-grabbing tasks to move their hands. There are two-fold objectives of this experiment. First, the MRCP pattern variations are determined in both healthy and stroke subjects during two different training scenarios. Second, the intention signal during a motor task performed for both training scenarios using MRCP pattern are detected through an SVM classifier and the classification rates are compared for healthy and stroke subjects. The classification process aims at testing the hypothesis that if the intention signal is accurately detected, it indicates active participation of the subject during the training protocols.

The rest of this chapter is organized as follows. Section 4.2 explains the experimental protocol including details of the participants, the training protocols, the method of intention detection through the SVM algorithm, and its performance evaluation metrics. The results of the MRCP pattern for healthy subjects and stroke patients during protocols A and B are described in Section 4.3. Section 4.4 explains the results of intention detection during both protocols using the SVM algorithm for healthy and stroke patients. Lastly, Section 4.5 outlines a summary of the chapter.

4.2 Experimental Protocol

4.2.1 Participants' Details

The subjects participating in this experiment consisted of healthy subjects and post-stroke patients. The healthy subjects were four male participants with right hand dominancy and a mean age of 28 years. All healthy subjects reported no history of any neurological disorder. Two post-stroke patients both right hand dominant were initially assessed through two commonly used clinical tests, namely the MAS and FMA scale for hand motor skills. Table 4.1 shows the details of each patient as well as their clinical test scores. Both stroke patients had lesions in their brain stem regions (brain stem pons).

Table 4.1: Stroke patients' details and scores of their clinical tests

Gender	Age	Stroke Onset Duration (Months)	Lesion location	Paretic Hand	MAS-Hand Movement Test Score (0-6)	FMA-Hand Test Score (0-14)
Female	64	7	Left pons	Right	2	9
Male	60	4	Left ponto-medullary junction	Right	2	8

4.2.2 EEG Acquisition and Training Exercise Protocols

Participants were seated upright on a comfortable chair with their right arms attached to the AMADEO hand-arm support unit. The EEG signals were acquired at five selected electrodes namely C3, FC3, Cz, CP3, and T7 during single-session training with FPz used as a ground electrode and CPz as a reference electrode. These five electrodes were selected for signal acquisition because all participants performed motor tasks with their right hand only. The selected electrodes used in this study are highlighted in Figure 4.1. Along with these five single electrodes, the SL channel, which is the linear combination of the other five selected electrodes calculated using the formula [286] mentioned in Equation 4.1, was also used during the data analysis.

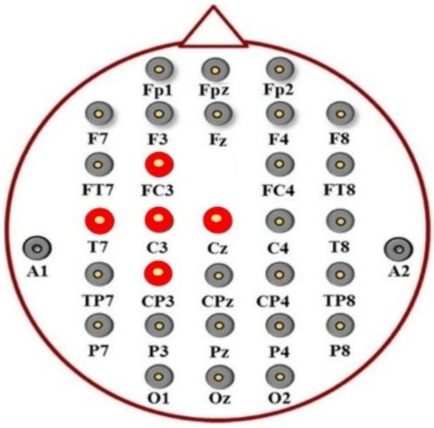


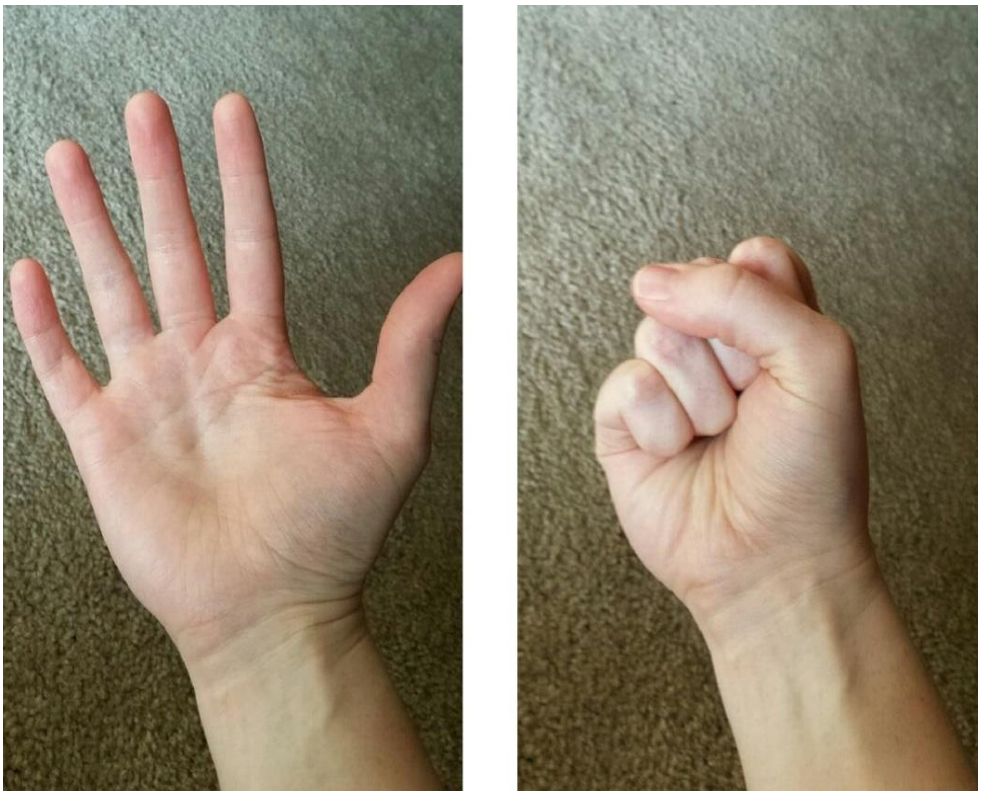
Figure 4.1: Position of selected electrodes during protocols A and B

$$SL = C3 - (FC3 + Cz + CP3 + T7)/4 \tag{4.1}$$

Two distinct training protocols were tested during right hand movement trials as explained below:

(i) Protocol A: Visual-Cues

During protocol A, each participant was trained to focus on visual-cues displayed on a computer screen. Visual-cues displaying hand-opening and hand-closing pictures as shown in Figure 4.2 to alert subjects to perform these specific hand movements. The hand-closing pictures were displayed every 5 s, followed by the hand-opening pictures 1 s later with a 4 s waiting period. This resulted in a 5 s gap between any two hand-closing visual-cues. Each training block comprised 23 trials of hand movements during this protocol.



(a) (b)

Figure 4.2: Visual-cues used in protocol A, (a) Hand-opening cue (b) Hand-closing cue

(ii) Protocol B: AMADEO 2D Game

Of the games available in the AMADEO's active training mode, the Shoot-out was chosen for use in protocol B. The playing screen of the Shoot-out game is shown in Figure 4.3. In this game, the subject closed their hand to shoot the drum coming out at equal time intervals and re-opened their hand to re-load the gun. Subjects had up to 23 trials of hand movements in each block of training.

Figure 4.3: AMADEO Shoot-out game used in protocol B

All participants performed 6 blocks consisting of 23 trials (6 x 23 = 138) for both protocols. At each hand-closing trial, digital event markers were manually sent to the CURRY 8X software (Compumedics, Neuroscan) which was used for EEG acquisition. Protocol B was more interesting and interactive compared to protocol A. The objective of this study was to determine whether the participants would be able to produce a stronger motor intention signal during protocol B than protocol A and whether it could be better detected through the SVM classifier.

4.2.3 Detection of Intention Signal Using SVM

In this study, along with observing variations in MRCP pattern during protocols A and B, the motor intention during hand-closing and rest states was also detected for both healthy and stroke subjects.

SVM is the most commonly employed supervised machine learning algorithm for the intention signal classification and detection of various limb movements according to the literature [105, 108, 113, 116, 120-124]. In this experiment, SVM was used to detect the motor intention of hand-closing trials versus idle state. The complete signal processing steps involved in intention signal detection using SVM are illustrated in Figure 4.4.

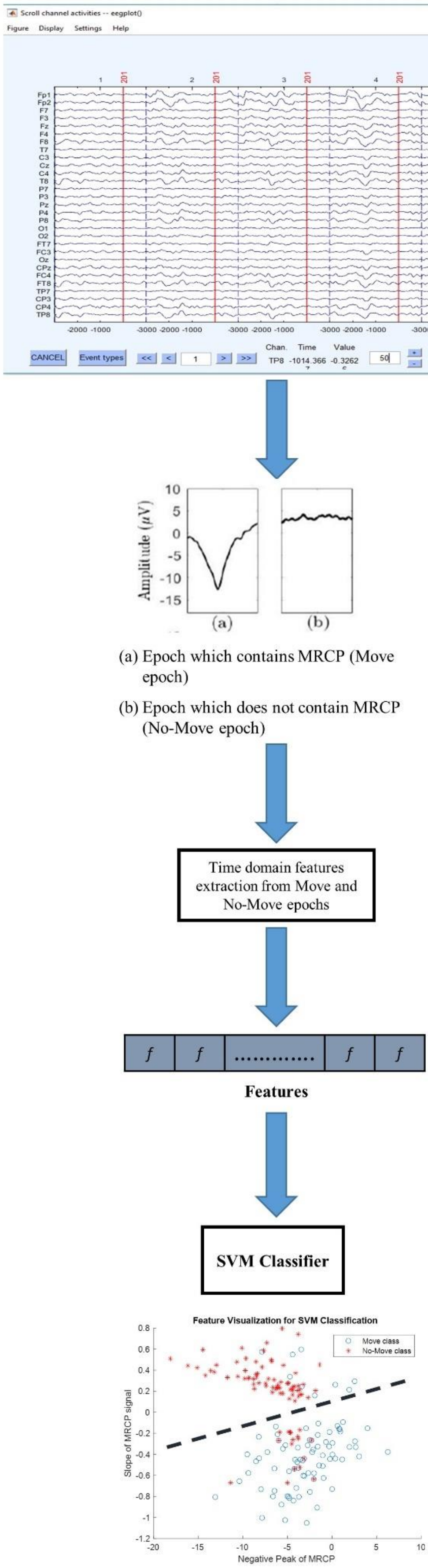


Figure 4.4: Signal processing steps involved in intention signal detection

MRCP patterns produced at the selected single electrodes during hand movement trials were extracted from the raw EEG data using signal processing steps explained in Section 3.4 in Chapter 3. To detect the motor intention of hand-closing versus idle state, the continuous EEG data were divided into epochs i.e. Move epochs from -2 s to 0 s which contained MRCP pattern while the epochs from 0.5 s to 2.5 s which did not contain MRCP pattern was called as No-Move epochs. The Move epochs represent the portion of EEG data that contains the intention signal of hand-closing action while the No-Move epochs represent the idle state conditions of the subjects. From both of these epochs, two time-domain features which include Npeak and slope of MRCP pattern were extracted. The Move epochs have a prominent Npeak and slope of MRCP pattern compared to the No-Move epochs. Based on these time-domain features, the SVM differentiates between both epochs. However, before applying the SVM, both features were plotted and outliers were removed. This prevented biasing the results of SVM due to outliers. In each protocol, an average of 10±2 epochs was rejected per subject. Finally, the Move epoch was marked with a label of class '1', and the No-Move epoch was marked with a label of class '0'. Depending on these input features, the SVM distinguished between classes 1 and 0. Three-fourths of the dataset was utilized for training data while one-fourth was used as test data for intention detection.

4.2.4 Performance Evaluation of SVM

The SVM classifier's performance was determined based on percentage accuracy, TPR − also known as sensitivity and True Negative Rate (TNR) − also called specificity. They were calculated using the relationships given in Equations 4.2, 4.3, and 4.4 where True Positive, False Positive, True Negative and False Negative were abbreviated as TP, FP, TN, and FN respectively.

$$Accuracy = (TP + TN)/(TP + TN + FP + FN) \tag{4.2}$$

$$TPR = TP/(TP + FN) \tag{4.3}$$

$$TNR = TN/(TN + FP) \tag{4.4}$$

All these performance metrics were compared to find the protocol that produced better detection results, indicating stronger motor intention levels in both healthy subjects and stroke patients. In addition, these results could show which electrode was the best choice for intention detection during protocols A and B.

4.3 Results of MRCP Pattern Analysis during Protocols A and B

This section presents the MRCP patterns produced during hand motor tasks in protocols A and B for both healthy participants and stroke subjects. There is an expectation that the MRCP pattern's Npeak and the slope will be more prominent during protocol B for both healthy and stroke subjects.

4.3.1 Results for the Healthy Subjects

Figure 4.5 displays the global MRCP pattern (MRCP pattern averaged with respect to the number of trials) produced during hand movement by healthy subjects for both protocols A and B at all selected electrodes. The visual inspection of the plots shows that MRCP amplitude at all channels starts to decrease around 0.5 s, reaches the maximum negative value around 0 s (movement onset point), and then again starts to increase. Furthermore, the lowest amplitude of the MRCP pattern (termed as Npeak), as well as steepness in the decrease of amplitude (termed as the slope of MRCP pattern), varies for protocols A and B. The Npeak amplitudes at C3, FC3, CP3, and SL appear to be greater during protocol B. Whereas, Npeak values at Cz and T7 electrodes are slightly less in protocol B when compared to that in protocol A. This could be indicative of more engagement of the healthy participants in protocol B compared to protocol A according to four out of six selected electrodes. The slope of the MRCP pattern is also observed to be varied with the change in the training protocols.

4.3.2 Results for the Stroke Patients

The global MRCP pattern at all the six selected channels produced by stroke patients during protocols A and B are presented in Figure 4.6. For stroke patients, the Npeak of MRCP pattern is observed to be slightly greater during protocol B compared to protocol A at all channels except for Cz. It could be inferred that stroke patients are more actively engaged in hand motor tasks during protocol B compared to protocol A. Similar to the healthy participants' group, the stroke patients' group shows the variation in Npeak and slope due to protocol change.

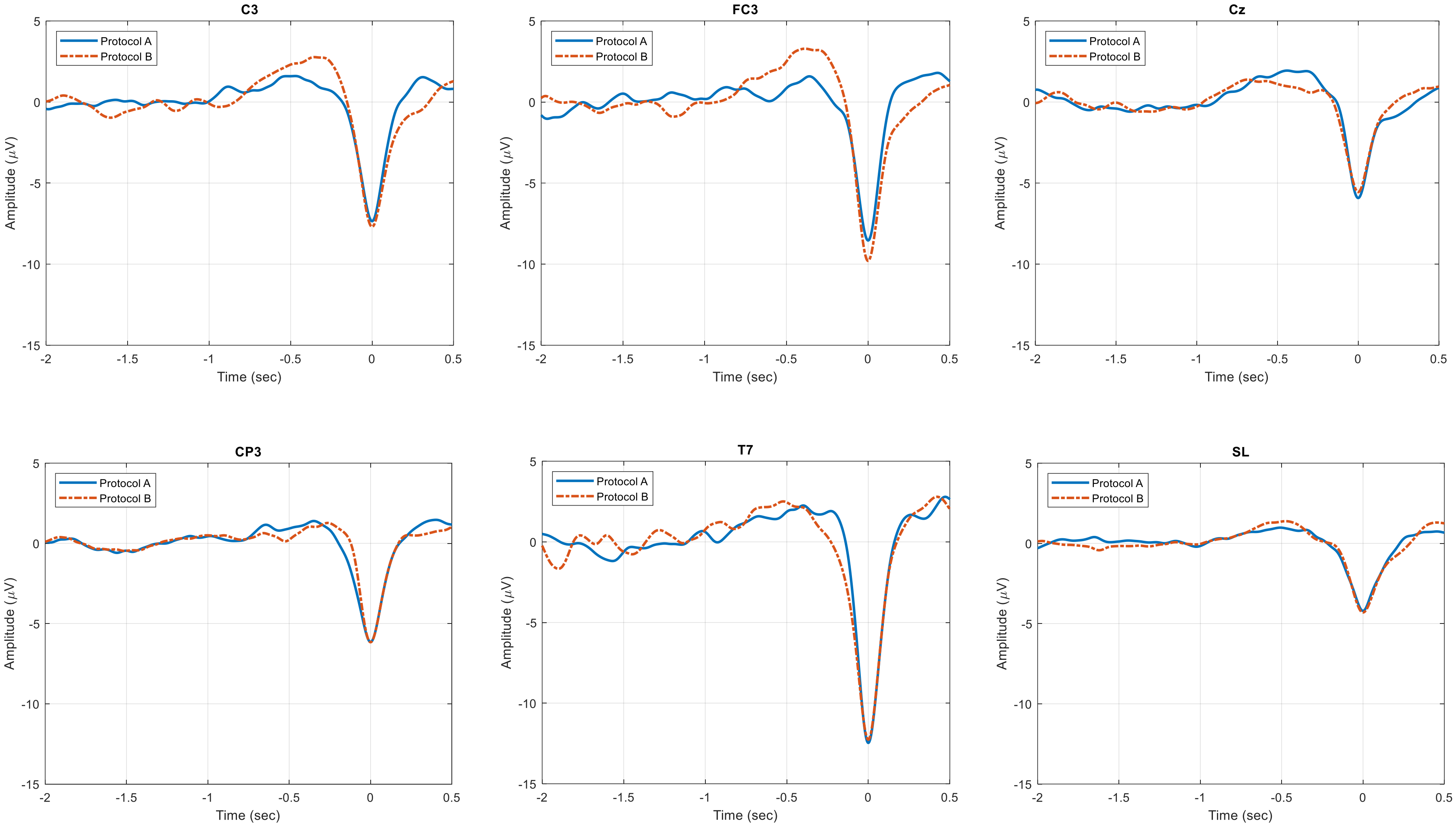


Figure 4.5: Global MRCP pattern produced by healthy subjects during protocols A and B

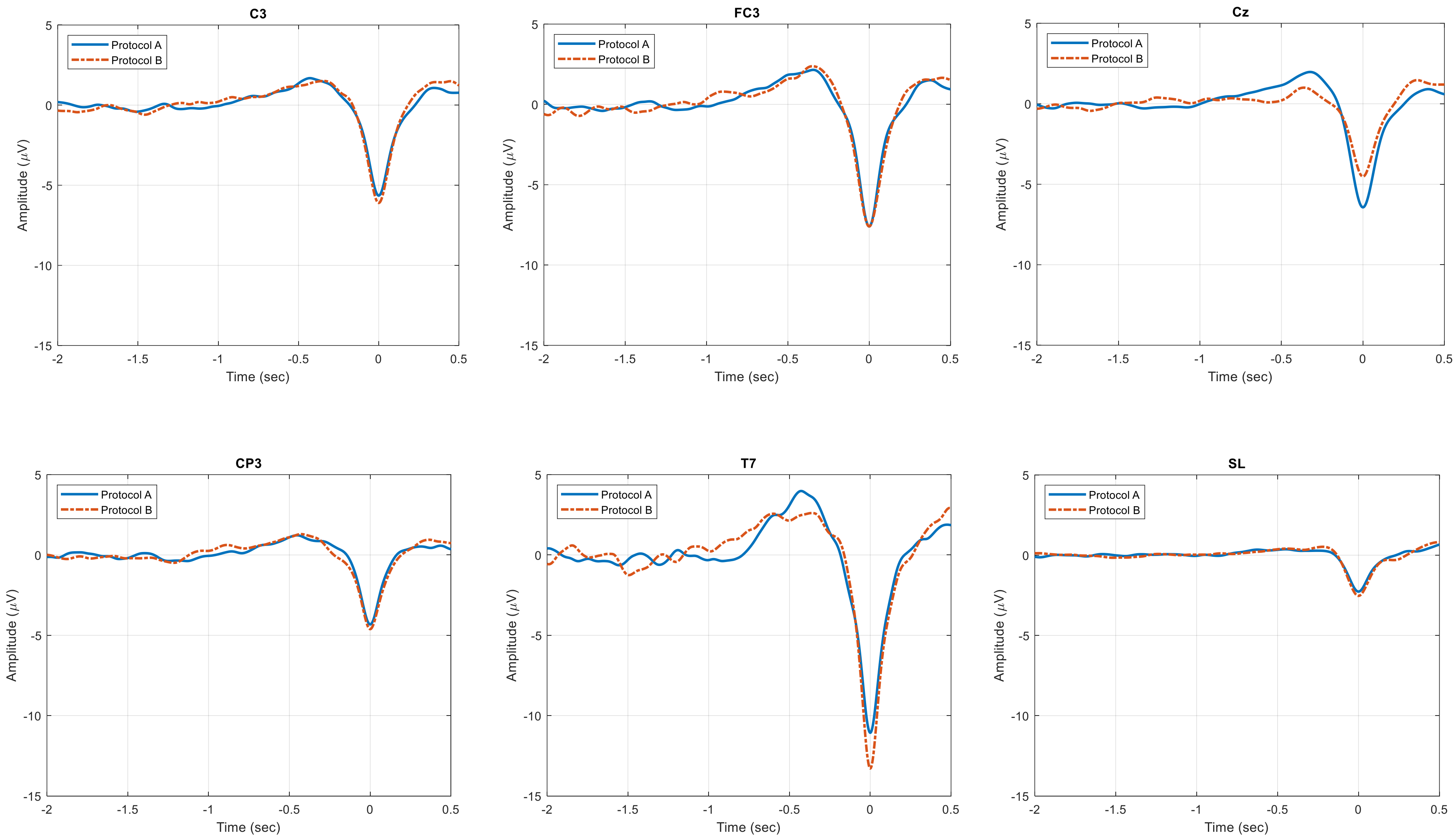


Figure 4.6: Global MRCP pattern produced by stroke patients during protocols A and B

4.4 Results of Intention Detection during Protocols A and B

The MRCP pattern analysis of both healthy and stroke groups showed that the Npeak and slope values at all six channels varied due to change in training protocols. Therefore, the Npeak and slope of the MRCP pattern were extracted from Move and No-Move epochs. They were then used as features for the SVM classifier to differentiate between Move and No-Move epochs.

The MRCP patterns in Figure 4.5 and Figure 4.6 are plotted from -2 s to 0.5 s to get a complete picture of the MRCP features variations due to training protocol change. After 0.5 s, the MRCP pattern stays at a constant amplitude until the start of the next movement trial. Therefore, the Move epoch length was selected from -2 s to 0 s, and the No-Move epoch length was selected from 0.5 s to 2.5 s during the data analysis.

Six electrodes which include C3, FC3, Cz, CP3, T7, and SL were used for intention detection of hand motor tasks during both protocols A and B through SVM. Performance metrics of the SVM classifier including classification accuracy, TPR, and TNR, were calculated and described in this section. Sections 4.4.1 and 4.4.2 present all the results of intention detection for healthy subjects and stroke patients respectively.

4.4.1 Intention Detection for the Healthy Subjects

The results of the SVM classifier accuracy for healthy subjects for protocols A and B are presented in Table 4.2. These results for healthy subjects show that protocol B has better accuracy of SVM classifier than protocol A at all selected channels except for Cz and T7. This supports our hypothesis that during protocol B, subjects are more engaged in performing hand movement and are likely to have greater classification accuracy compared to protocol A. From Table 4.2, it is clear that the classifier's accuracy varies in accordance with the selected electrode, and the highest accuracy for the healthy group is obtained at FC3. According to the results acquired for FC3, protocol B has an SVM classifier's accuracy of 98 % while the classification accuracy of protocol A is 86 %. Furthermore, it is noted that the two electrodes (Cz and T7) which do not show better classification accuracies for protocol B are the same electrodes that showed the smaller Npeak amplitude during protocol B in Figure 4.5. This means it is possible to predict the classifier's performance based on visual inspection of the MRCP patterns.

Table 4.2: Average accuracy of the SVM algorithm across healthy subjects' group

Channel	SVM Classifier's Accuracy (%)	
	Protocol A	Protocol B
C3	64.58	92.86
FC3	86.25	98.0
Cz	73.81	70.0
CP3	57.7	76.3
T7	63	57.69
SL	60.0	83.33

The accuracy alone cannot justify the performance of the classifier, therefore, sensitivity (TPR) and specificity (TNR) parameters are also determined. The TPR and TNR values show whether the extracted features from Move and No-Move classes are distinct enough to be classified accurately by SVM [289]. TPR and TNR values using data of healthy subjects for protocols A and B are shown in Figure 4.7 and Figure 4.8 respectively. In the case of protocol A, Figure 4.7 demonstrates that TPR obtained for C3, FC3, and Cz is lower than its corresponding TNR, whereas, for CP3, T7, and SL, the reverse is the case. Figure 4.8 shows that TPR, for all six electrodes, is higher than its corresponding TNR for protocol B indicating that the Move class contains adequate features to correctly detect motor intention signals.

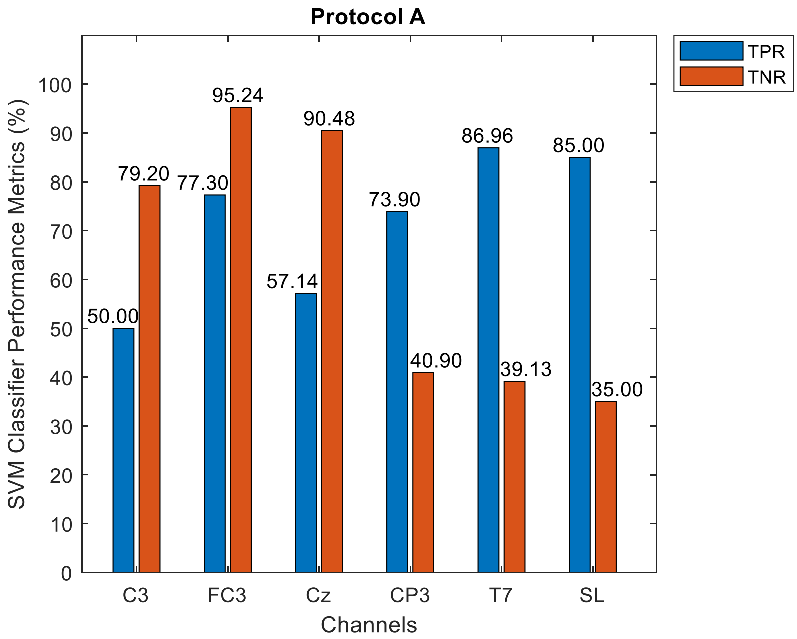


Figure 4.7: Average TPR and TNR values during protocol A across healthy subjects' group

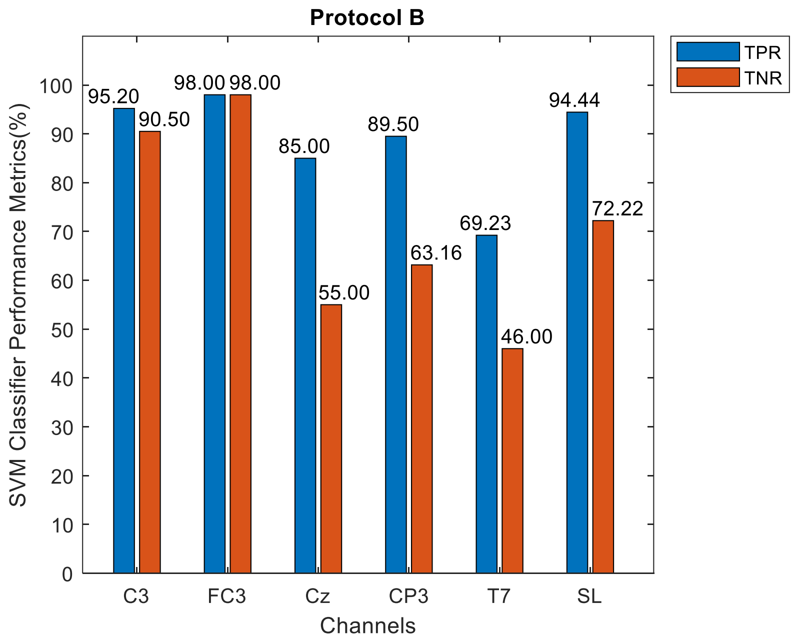


Figure 4.8: Average TPR and TNR values during protocol B across healthy subjects' group

4.4.2 Intention Detection for the Stroke Patients

The performance of the SVM algorithm for the detection of hand motor intention signals produced by stroke patients is discussed in this section. Table 4.3 presents the accuracy of the SVM classifier at all six selected electrodes for stroke patients during protocols A and B. For protocol A, the FC3 electrode shows the maximum accuracy of the SVM classifier of about 72 %. Whereas the same electrode shows classification accuracy of 89 % for intention detection when stroke patients perform the hand movement during protocol B. All other selected electrodes also demonstrate that better classification results for protocol B except for Cz. It is again confirmed from the classifier accuracy results of the stroke group that for both protocols, FC3 shows the maximum classifier's performance. Whereas the Cz electrode shows poor classification performance during protocol B as expected from the visual inspection of MRCP patterns in Figure 4.6.

Table 4.3: Average accuracy of the SVM algorithm across post-stroke patients' group

Channel	SVM Algorithm's Accuracy (%)	
	Protocol A	**Protocol B**
C3	52.88	81.01
FC3	72.22	88.89
Cz	70.45	34.56
CP3	26.25	60.16
T7	49.29	51.43
SL	66.33	83.78

Figure 4.9 shows bar-chart representations of TPR and TNR values obtained using stroke patients' data from protocol A at all six electrodes and that from protocol B in Figure 4.10. For protocol A, Figure 4.9 shows that TNR for FC3, Cz, CP3, and SL is significantly lower than its corresponding TPR. On the other hand, TNR is slightly higher in the case of C3 and slightly lower for T7. However, for protocol B, TNR is higher than TPR for each choice of electrode except for CP3 and T7 as shown in Figure 4.10.

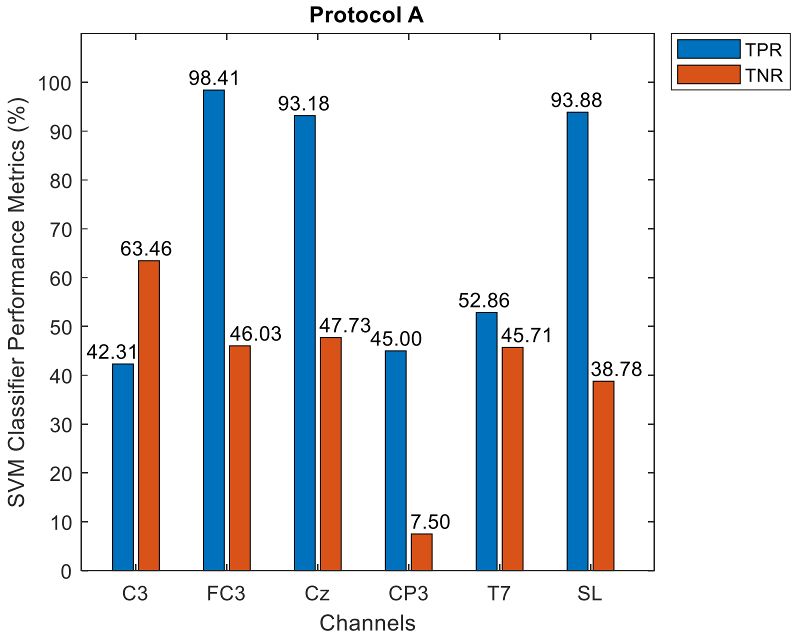


Figure 4.9: Average TPR and TNR values during protocol A across stroke patients' group

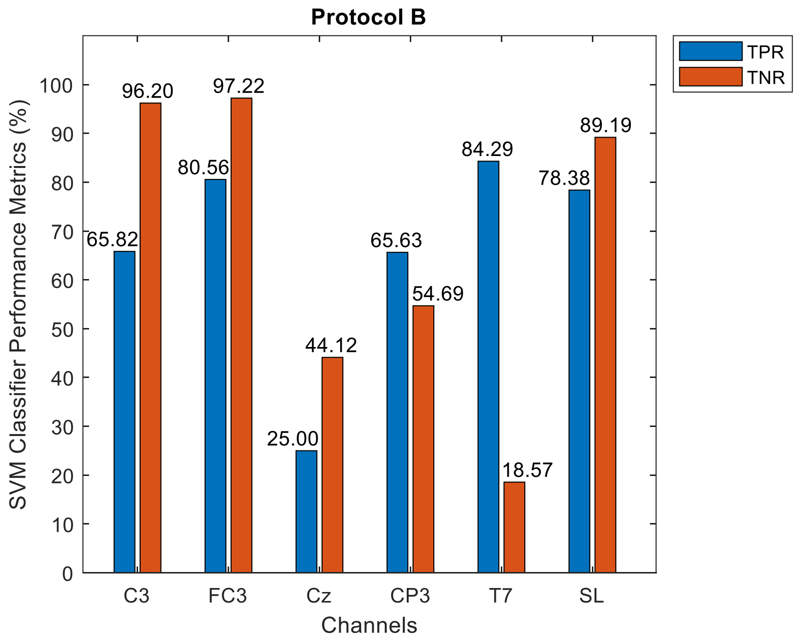


Figure 4.10: Average TPR and TNR values during protocol B across stroke patients' group

In this way, using percentage accuracy, TPR, and TNR metrics were used to determine the classification performance of SVM. The classification accuracy for both protocols A and B at the FC3 channel was found to be greater than the C3 channel in the case of healthy and stroke patients' groups. However, the C3 channel was considered to be the most appropriate channel to detect the motor intention of hand movements [287]. This could be explained by looking at their corresponding TPR and TNR values. The TNR values for the C3 channel were higher in all the cases as compared to the corresponding TNR values for the FC3 channel, that's why the classifier's accuracy for the FC3 channel was found to be more than C3. Hence, the use of TPR and TNR parameters along with the classifier's accuracy is proved to be important in determining the performance of the classifier. These parameters indicate whether good results of the classifier were obtained due to detecting either positive or negative classes accurately.

When the Cz electrode from stroke patients' data as well as the Cz and T7 electrodes from healthy subjects' data were chosen, protocol A had slightly better classification accuracy than protocol B. There could be many possible reasons for this apparent contradiction. The Cz channel is commonly employed to detect foot-related motor intention [148, 290], whereas, T7 acquired brain signal over the temporal lobe while intention signal occurs best at the motor cortex of the brain. Therefore, these results at Cz and T7 electrodes were expected.

4.5 Summary

In this chapter, the deployment of the MRCP pattern to observe the variation in intention signal and to detect it using a machine learning algorithm for hand motor tasks during two different training protocols were performed. These two protocols used in the experimental protocol were based on simple visual-cues and the AMADEO 2D game. The motor intention signals for both healthy participants as well as post-stroke patients were detected using the SVM classifier by selecting six different electrodes. This was followed by an evaluation of the SVM classifier's performance. It was found that MRCP's Npeak amplitude was slightly higher during protocol B compared to that during protocol A. This Npeak amplitude increase could be indicative of the greater active participation of the subjects during protocol B. This was further analyzed using the SVM classification approach. The average classification accuracy of 67.56 % for the visual-cue protocol and 79.7 % for the gaming protocol was achieved for healthy subjects. Similarly, for stroke patients, the average accuracy obtained was 56.24 % and 66.64 % for the visual-cue and the game protocols, respectively. Based on the obtained results, the game protocol was found to be a better option in retaining the concentration of subjects during the training period and showed better overall classification results for both healthy and stroke patients compared to the visual-cues protocol.

It is inferred from this experiment that more complex interactive and engaging exercises such as games available in the AMADEO robot-based rehabilitation device are preferable to promote the active participation of the patients. Therefore, it can be employed for significantly enhancing the effectiveness of rehabilitation therapy for post-stroke patients.

Chapter 5

Quantification of Movement-Related Cortical Potential Associated with Motor Training after Post-Stroke Rehabilitation

5.1 Overview

The study described in this chapter aims to investigate the use of the MRCP pattern as a tool to identify the effect of multi-session motor training on restoring the hand functions of post-stroke patients. The training effect will be observed after the participants complete their rehabilitation training to improve fine finger motor skills. The post-stroke patients underwent multi-session robot-assisted motor training of their affected hand for four weeks with an AMADEO rehabilitation device. An EEG acquisition system was used to record brain activities. These brain activities were used to extract the MRCP pattern’s features from eight selected electrodes.

According to the literature, a decrease in the amplitude of the MRCP pattern is expected to be associated with improvement in hand motor skills due to the repetition of the same training protocol [216, 218-220]. The improvements in motor skills were measured with the help of two commonly employed clinical tests namely FMA and MAS. In addition, hand-kinematic parameters consisted of hand strength measured during flexion (force-flexion), hand strength measured during extension (force-extension), and Hand Range of Movement (HROM) were also selected to assess the rehabilitation training outcomes. AMADEO offers an in-built assessment tool to measure these hand-kinematic parameters. Furthermore, the variation in the features of the MRCP patterns was compared with the results from FMA and MAS clinical tests as well as hand-kinematic parameters.

The rest of the chapter is organized as follows. Section 5.2 describes materials and methods used in the experimental work and contains information on inclusion criteria for participants, motor training protocol, pre and post-training protocols as well as data processing steps. The EEG data analysis results are described in Section 5.3. Results of clinical test and hand-kinematic parameters after a four week study protocol are presented in Section 5.4 and Section 5.5 respectively. Section 5.6 presents results from a study of a subgroup of participants who were given an additional four week training. Section 5.7 summarizes the chapter.

5.2 Materials and Methods

The experimental work was designed to assess the improvements in hand motor skills and corresponding changes in MRCP pattern after post-stroke patients underwent multi-session motor training of their affected hand on the AMADEO robotic device. The basic design of the experiment is illustrated in Figure 5.1. The patients underwent 12 hand motor training sessions on AMADEO over a period of four weeks. The physical improvements in hand motor skills and corresponding changes in MRCP pattern were measured before the start of the experiment and after completing all 12 training sessions.

Figure 5.1: Experimental design of the multi-session hand motor training

5.2.1 Patient Inclusion Criteria

The following inclusion criteria were established before recruiting subjects:

(a) Range of age: 50–85

(b) Clinical stroke within 6 months to enrolment and MRI scan evidence of stroke consistent clinical presentation

(c) Major impairment: hand motor (fine finger motor) deficits

(d) Impairment level: motor abilities suggested by MAS clinical test (Section 7, hand movements, score between 1–5)

(e) Adequate cognition: suggested by widely adopted Rowland Universal Dementia Assessment Scale or Mini-Mental State Examination score of 26 (out of 30) or more [291]

(f) Ability to understand verbal instructions in English

Based on the inclusion criteria, seven ischemic stroke patients all with right hand dominancy were recruited for a robot-assisted motor training study. The characteristics of the stroke patients who participated in this experiment are listed in Table 5.1. Participants signed the written informed consent before the commencement of the experiments. All patients received standard care at a local hospital, in addition to our intervention protocol.

Table 5.1: Important factor information of each stroke patient

Stroke Patient (Gender)	Age (Years)	Stroke Onset Duration (Months)	MAS-Hand Movement Test Score (0-6)	Stroke Location	Affected Hand
SP1* (Male)	82	3	2	Left motor cortex	Right
SP2 (Male)	81	2	3	Left thalamic and internal capsule	Right
SP3 (Male)	67	2	2	Left internal capsule	Right
SP4 (Female)	51	1.3	4	Right basal ganglia	Left
SP5 (Female)	64	4	1	Left pons	Right
SP6 (Male)	60	3	1	Left ponto-medullary junction	Right
SP7 (Female)	63	6	1	Right pons	Left

* SP stands for Stroke Patient

5.2.2 Motor Training Protocol

In this experiment, an AMADEO standard therapy program was used for motor training of the affected hand of all recruited post-stroke patients. In the beginning, the HROM for each patient was set according to the AMADEO protocol to the maximum potential range depending on each patient's hand size. The duration of each training session was 30 minutes and patients received the training one session per day for three sessions per week for four weeks. The total training duration for each patient was 360 minutes in one month. However, patient SP7 completed 10 motor training sessions (300 minutes) instead of 12 due to personal circumstances.

Depending on stroke lesion locations and associated pre-training clinical test values, the patients were divided into two groups: group A consisting of four participants (SP1, SP2, SP3, and SP4); and group B consisting of three participants (SP5, SP6, and SP7). The patients in group A had a stroke in the supratentorial region of the brain and had better baseline finger movements while group B patients had a stroke in the infratentorial region and had limited finger movements due to the location of the lesion in their brain stems. The brain areas above tentorium cerebelli are known as supratentorial and those below tentorium cerebelli are termed as infratentorial areas as shown in Figure 5.2. The designed training strategies for both groups were therefore different. The specific training strategy for both groups is presented in Table 5.2.

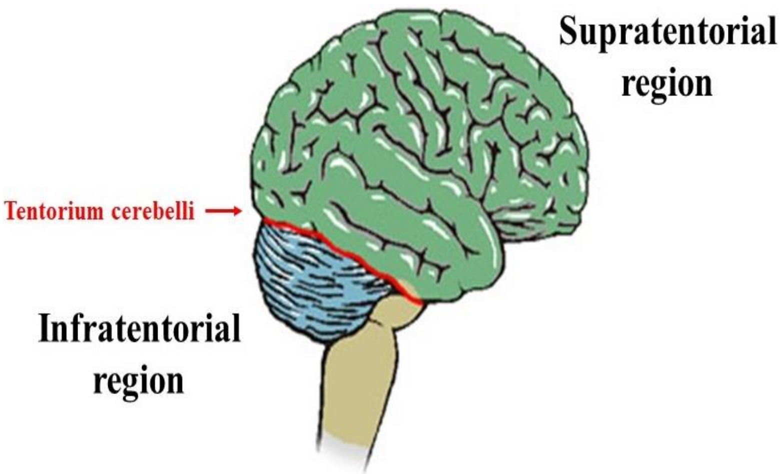


Figure 5.2: Brain's areas according to tentorium cerebelli [292]

Table 5.2: Motor training strategy for group A and group B

Category	Training Strategy
Group A	1) CPM training mode for 5 minutes; 2) CPMplus training mode for 5 minutes; 3) Assistive training mode for 10 minutes; and 4) Active training mode (2D interactive games) for 10 minutes.

Group B	1) CPM training mode for 10 minutes; 2) CPMplus training mode for 10 minutes, and 3) Assistive training mode for 10 minutes.

Although the total duration of motor training for group A was the same as for group B, active training mode was included only in the group A training protocol because stroke patients in group B were unable to play the game with their initial finger movements.

5.2.3 Pre and Post-Training Protocols

Participants were seated on a comfortable chair in an upright posture while baseline measurements were taken. Before the commencement of a multi-session motor training study, three baseline measurements were recorded in week 0:

(1) EEG Acquisition: EEG signals were acquired while the subjects were asked to perform self-paced simple hand-grasping movements with their affected hand in 8 to 10 blocks of 10 trials each. The FPz electrode was used as a ground electrode and a separate electrode was placed on the ipsilateral earlobe as a reference. During signal acquisition, patients were asked to focus on a cross-mark in front of them to avoid random eye-movement artifacts as shown in Figure 5.3. The event markers on each trial were manually sent to the CURRY 8X acquisition software. The time gap between the two trials was randomly varied from 8 s to 10 s.

(2) Clinical Tests: The clinical tests namely the FMA test (wrist and hand sections only) [293] as well as the MAS tests [294], for both hand movement and advanced hand movements, were applied to assess the current hand motor abilities of patients. The details of the tasks performed during all four clinical tests were given in Appendix 4. These clinical tests were denoted as FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements' tests in this thesis.

(3) Hand-Kinematic Parameters: The force-flexion, force-extension, and HROM parameters for the affected hand were measured using the assessment tool on the AMADEO hand rehabilitation device.

All the above-mentioned measurements in week 0 were repeated in week 4 after completion of 12 training sessions and the results were compared (see Figure 5.1).

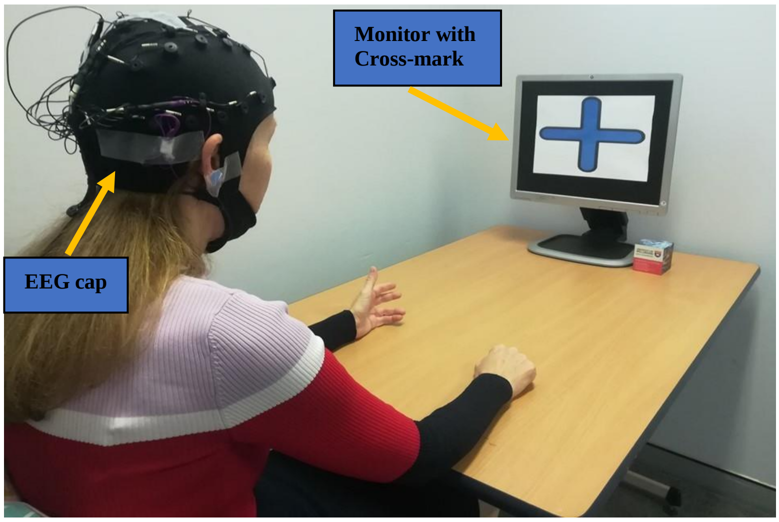


Figure 5.3: Patient performing a self-paced hand-grasping task during pre and post-training protocols

5.2.4 Data Processing and Statistical Analysis

The acquired EEG data were processed to obtain a global MRCP pattern (MRCP patterns averaged with respect to the number of subjects in a group) as explained in Section 3.4 of Chapter 3. During the EOG artefact rejection process, on average, 24 epochs per participant were removed from each pre and post-training data value. However, this removal of epochs still resulted in an acceptable number of trials for averaging. Using global MRCP patterns, five different time-domain features of the MRCP pattern were extracted namely; BP1 amplitude, BP1 onset, BP2 amplitude, BP2 onset, and Npeak amplitude using MATLAB toolbox called 'visualEEG' [74].

The selected EEG channels, located over the sensorimotor and motor cortices of both hemispheres, were FC3, FC4, C3, Cz, C4, CP3, CPz, and CP4. In the literature, the C3, Cz, and C4 electrodes are commonly used to extract MRCP patterns for hand motor tasks [214-220]. In addition, five other electrodes (FC3, FC4, CP3, CP4, and CPz) were also specifically explored in this experiment to get a detailed picture of the MRCP pattern for fine finger motor tasks. The positions of all these selected electrodes in 32-channels Quick-Cap used for this experiment are shown in red color in Figure 5.4.

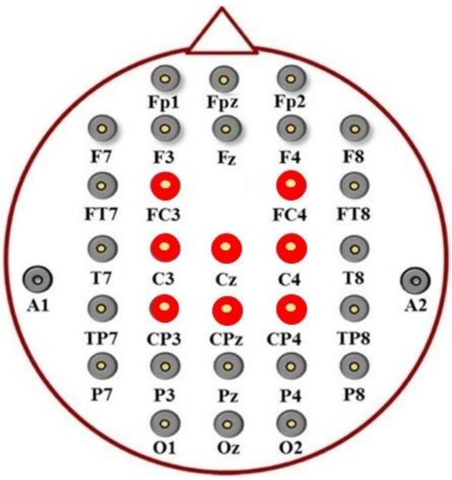


Figure 5.4: Positions of selected electrodes for this experiment

The stroke patients who participated in this experiment received training for either their right or left affected hands. All odd number electrodes (FC3, C3, and CP3) would be contralateral channels for those patients who performed the movement with their right hand and even number electrodes (FC4, C4, and CP4) would be ipsilateral channels. The reverse was true for the patients who performed the left hand movement. Therefore, for group analysis, these electrodes were designated as contralateral FC (CLFC), contralateral C (CLC), and contralateral CP (CLCP) to indicate the contralateral representation for both right hand and left hand movements. Similarly, to represent the ipsilateral side of both hand movements, the electrodes were designated as ipsilateral FC (ILFC), ipsilateral C (ILC), and ipsilateral CP (ILCP). The electrodes Cz and CPz are central channels and therefore do not need to have their labels based on ipsilateral or contralateral positions. Hence, the electrodes used in the analysis were CLFC, CLC, CLCP, ILFC, ILC, ILCP, Cz, and CPz.

Along with EEG data analysis, clinical tests, and hand-kinematic parameters' measurements were also performed. The clinical tests (FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements) were performed by patients three times by each patient and the best scores were recorded according to the general rule of administration for these clinical tests. Whereas hand-kinematic parameters were also measured three times using the AMADEO assessment tool and their average values were used to ensure the validity and consistency of the results.

The statistical significance was measured in all the defined three measurement parameters (MRCP pattern analysis, clinical tests, as well as hand-kinematic parameters) using a two-tailed paired t-test. The significance level of the t-test is reported at the alpha value of $p < 0.05$.

5.3 EEG Data Analysis Results

In this section, results obtained from EEG data analysis for groups A and B are presented. For both groups, visible global MRCP patterns were obtained using the post-stroke patients' data at all eight selected electrodes for pre and post-training periods. The global MRCP patterns for all ipsilateral channels (ILFC, ILC, ILCP), contralateral channels (CLFC, CLC, CLCP), and central channels (Cz, CPz) obtained from EEG data acquired during pre and post-training protocols for group A and group B are shown in Figure 5.5 and Figure 5.6 respectively. The MRCP patterns at all electrode sites are plotted for the time interval -1 to 1 s for better visualization of the changes that occur in the MRCP patterns during motor training.

For group A, visual inspection of the global MRCP patterns indicates that the post-training values of Npeak of MRCP patterns are prominently decreased at all selected electrodes compared to their corresponding pre-training values. Whereas global MRCP patterns for group B show that the post-training Npeak is considerably increased at ipsilateral electrodes (ILFC, ILC, ILCP), slightly decreased at contralateral electrodes and one of the central electrodes (CLFC, CLC, CLCP, CPz) but remains the same at Cz central electrode. The individual features of the MRCP pattern and their statistical analysis for both groups are discussed in Sections 5.3.1 to 5.3.3.

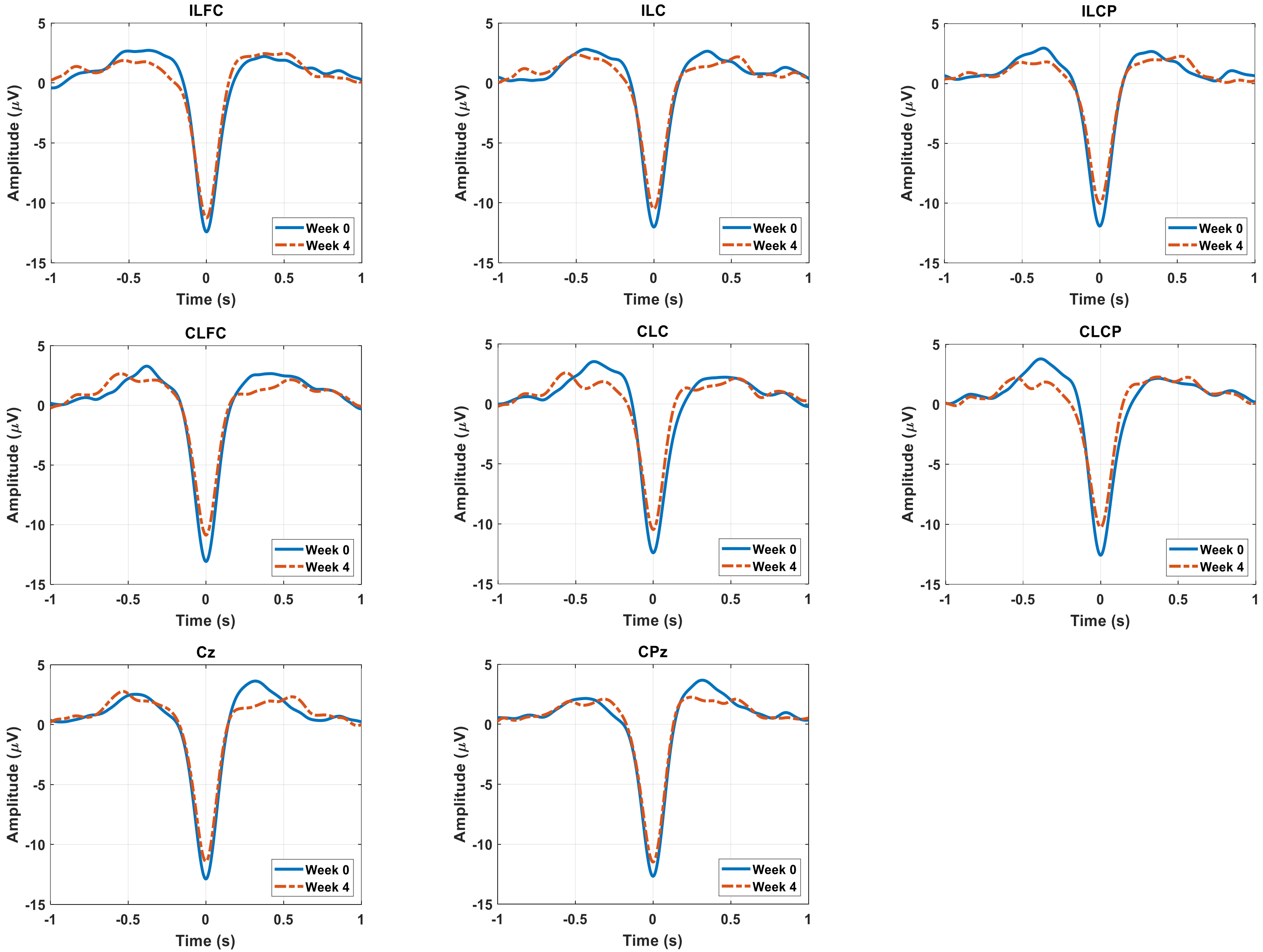


Figure 5.5: Global MRCP patterns for group A at all channels after 12 motor training sessions. Legend Week 0 represents the pre-training period, and legend Week 4 shows the post-training period in all figures.

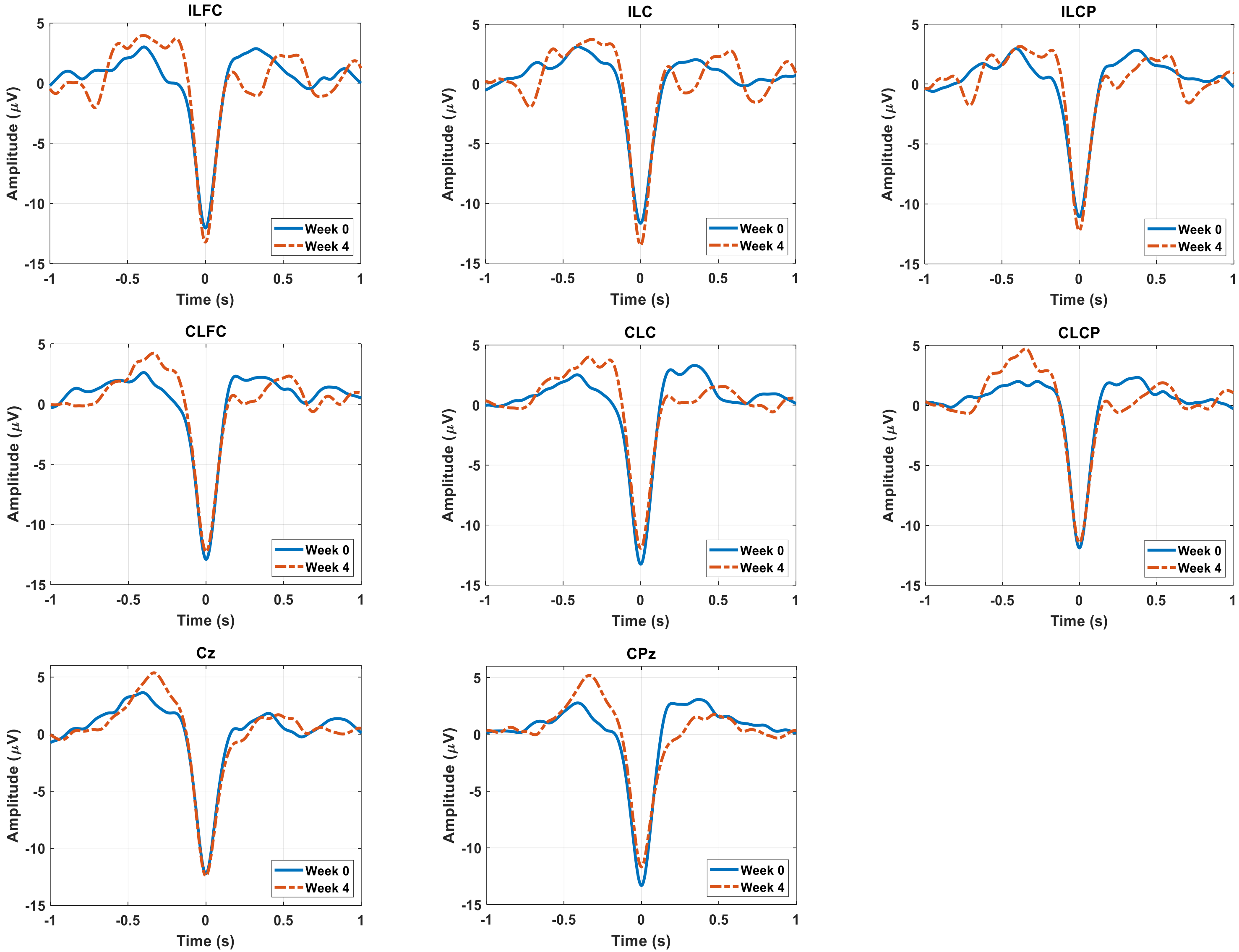


Figure 5.6: Global MRCP patterns for group B at all channels after 12 motor training sessions. Legend Week 0 represents the pre-training period, and legend Week 4 shows the post-training period in all figures.

5.3.1 Bereitschaftspotential 1 (BP1) Amplitude and Onset

The BP1 amplitude was calculated as the absolute amplitude difference between the BP1 amplitude and BP2 amplitude. Figure 5.7 shows the mean absolute values of BP1 amplitude using column charts with error bars for each electrode position for group A. The error bars were calculated using the Standard Deviation (SD) values across subjects for each of the eight electrodes. The post-training BP1 amplitude values are found to be decreased at all electrodes with respect to their corresponding post-training values. The paired t-test shows that the changes between pre and post-training values in BP1 amplitude at all electrodes are not statistically significant ($p > 0.05$). Table 5.3 shows the BP1 onset for group A in the form of the mean (± SD) for its pre-training and post-training values. The mean BP1 onset before training was -1.48 (± 0.364) s compared to -1.559 (± 0.375) s after completion of training for the participants in group A. Application of paired t-test shows that the change between the pre and post-training values of BP1 onset for group A is not statistically significant ($p > 0.05$).

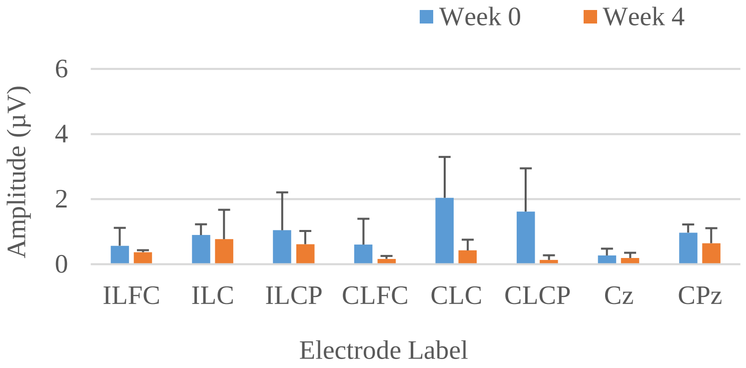


Figure 5.7: Mean absolute BP1 amplitude at week 0 and week 4 for group A. The error bars represent SD values across subjects for each electrode.

Table 5.3: Mean values for BP1 onset at week 0 and week 4 for group A (Mean (± SD))

Channels	**BP1 Onset for group A**	
	BP1 Onset values at Week 0 (s)	**BP1 Onset values at Week 4 (s)**
ILFC	-1.562 (± 0.253)	-1.158 (± 0.138)
ILC	-1.336 (± 0.281)	-1.528 (± 0.641)
ILCP	-1.393 (± 0.238)	-1.483 (± 0.545)
CLFC	-1.652 (± 0.431)	-1.429 (± 0.184)
CLC	-1.172 (± 0.206)	-1.189 (± 0.137)
CLCP	-1.418 (± 0.552)	-1.842 (± 0.471)
Cz	-1.743 (± 0.319)	-1.783 (± 0.549)
CPz	-1.562 (± 0.631)	-2.059 (± 0.338)

In the case of group B, the mean absolute values of BP1 amplitude for all electrodes are shown in Figure

5.8. It is observed that post-training BP1 amplitude is higher at all electrode positions except at ILFC and ILCP compared to pre-training values. Table 5.4 presents the pre and post-training values of BP1 onset for group B. For this group, the mean BP1 onset was found to be -1.466 (± 0.504) s for pre-training and -1.467 (± 0.185) s for post-training periods. When the paired t-test was applied, no statistically significant change was found between the pre and post-training values of both BP1 amplitude and BP1 onset for group B (p > 0.05).

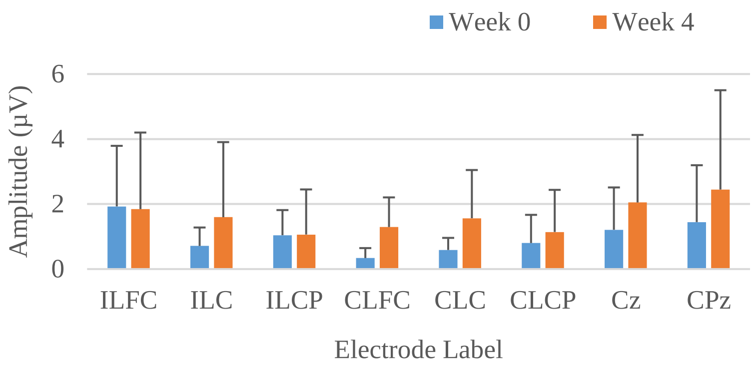


Figure 5.8: Mean absolute BP1 amplitude at week 0 and week 4 for group B. The error bars represent SD values across subjects for each electrode.

Table 5.4: Mean values for BP1 onset at week 0 and week 4 for group B (Mean (± SD))

Channels	**BP1 Onset for group B**	
	BP1 Onset values at Week 0 (s)	**BP1 Onset values at Week 4 (s)**
ILFC	-1.378 (± 0.344)	-1.405 (± 0.122)
ILC	-1.202 (± 0.232)	-1.33 (± 0.151)
ILCP	-1.253 (± 0.406)	-1.568 (± 0.158)
CLFC	-1.535 (± 0.561)	-1.423 (± 0.109)
CLC	-1.636 (± 0.579)	-1.548 (± 0.047)
CLCP	-1.497 (± 0.617)	-1.613 (± 0.15)
Cz	-1.744 (± 0.62)	-1.455 (± 0.395)
CPz	-1.484 (± 0.676)	-1.393 (± 0.351)

5.3.2 Bereitschaftspotential 2 (BP2) Amplitude and Onset

The mean absolute values of BP2 amplitude for group A, calculated as an absolute difference of the amplitude between BP2 and Npeak amplitudes, are shown in the form of a column chart in Figure 5.9. The BP2 amplitude at all electrodes is considerably higher than the BP1 amplitude. Moreover, it is noted that the BP2 amplitude is decreased in all channels after the training for group A participants. The pre and post-training values of the BP2 onset for the participants of group A are shown in Table 5.5. The average value of BP2 onset for group A was calculated to be -0.233 (± 0.079) s before the commencement of the training sessions and was reduced to -0.197 (± 0.042) s after completion of 12 training sessions. However, when the paired t-test was applied, it did not show statistical significance between pre and post-training values of BP2 amplitude and onset for group A ($p > 0.05$).

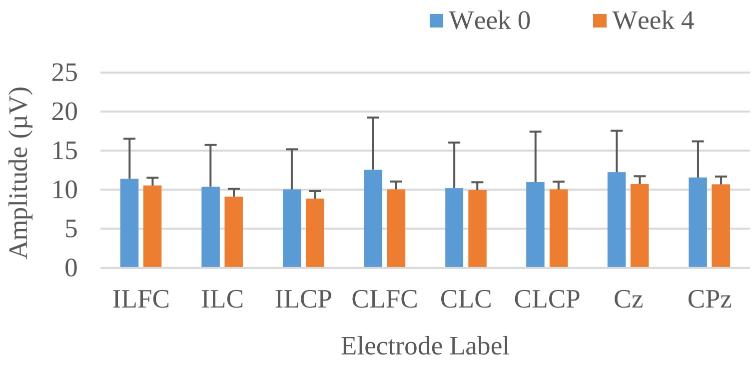


Figure 5.9: Mean absolute BP2 amplitude at week 0 and week 4 for group A. The error bars represent SD values across subjects for each electrode.

Table 5.5: Mean values for BP2 onset at week 0 and week 4 for group A (Mean (± SD))

Channels	**BP2 Onset for group A**	
	BP2 Onset values at Week 0 (s)	**BP2 Onset values at Week 4 (s)**
ILFC	-0.187 (± 0.021)	-0.229 (± 0.095)
ILC	-0.251 (± 0.109)	-0.217 (± 0.067)
ILCP	-0.226 (± 0.049)	-0.203 (± 0.044)
CLFC	-0.206 (± 0.039)	-0.186 (± 0.025)
CLC	-0.233 (± 0.138)	-0.181 (± 0.04)
CLCP	-0.22 (± 0.098)	-0.2 (± 0.031)
Cz	-0.222 (± 0.079)	-0.176 (± 0.022)
CPz	-0.236 (± 0.099)	-0.183 (± 0.015)

For group B, the mean absolute values for BP2 amplitude and pre and post-training values for BP2 onset for all eight electrodes are presented in Figure 5.10 and Table 5.6 respectively. The post-training BP2 amplitude is increased at ILFC, ILC, and ILCP, whereas, it is decreased at CLFC, CLC, CLCP, Cz, and CPz when compared with the corresponding pre-training values. The mean BP2 onset before the start of motor training was found to be -0.199 (± 0.074) s which then slightly decreased to -0.156 (± 0.021) s after training completion. When the paired t-test was applied, no statistical significance was found for both BP2 amplitude and onset at any electrode's position for group B ($p > 0.05$).

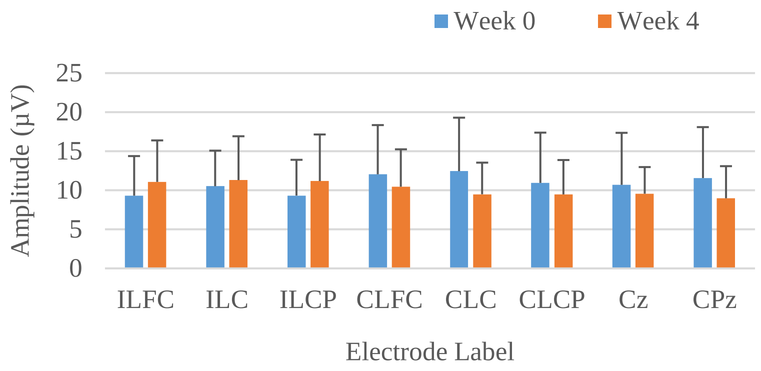


Figure 5.10: Mean absolute BP2 amplitude at week 0 and week 4 for group B. The error bars represent SD values across subjects for each electrode.

Table 5.6: Mean values for BP2 onset at week 0 and week 4 for group B (Mean (± SD))

Channels	**BP2 Onset for group B**	
	BP2 Onset values at Week 0 (s)	**BP2 Onset values at Week 4 (s)**
ILFC	-0.3 (± 0.161)	-0.144 (± 0.017)
ILC	-0.182 (± 0.036)	-0.167 (± 0.036)
ILCP	-0.241 (± 0.121)	-0.141 (± 0.022)
CLFC	-0.159 (± 0.017)	-0.173 (± 0.031)
CLC	-0.206 (± 0.111)	-0.154 (± 0.015)
CLCP	-0.138 (± 0.019)	-0.165 (± 0.023)
Cz	-0.226 (± 0.111)	-0.149 (± 0.01)
CPz	-0.143 (± 0.019)	-0.155 (± 0.01)

5.3.3 Negative Peak (Npeak) Amplitude

Figure 5.11 shows the column chart representation of the mean absolute pre and post-training values of the Npeak features of the MRCP pattern for group A. The Npeak amplitude at all eight electrode positions decreased compared to pre-training values. The application of paired t-test on Npeak amplitude revealed that its post-training decreases were statistically significant at ILC (p=0.005), ILCP (p=0.03), CLFC (p=0.035), CLC (p=0.027), CLCP (p=0.019), Cz (p=0.035) as well as CPz (p=0.014) compared to pre-training values as indicated by a '*' sign in Figure 5.11. However, the decrease in post-training Npeak amplitude is statistically not significant at ILFC (p=0.118) according to paired t-test. Hence, it can be concluded that group A participants show a statistically significant decrease in Npeak amplitude in seven of eight selected electrodes after completion of the rehabilitation training strategy.

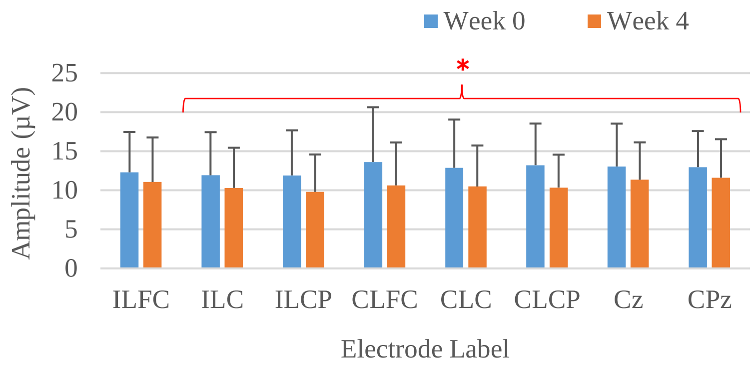


Figure 5.11: Mean absolute Npeak amplitude at week 0 and week 4 for group A. The error bars represent SD values across subjects for each electrode. The symbol '' indicates a significant decrease in Npeak amplitude at week 4 compared to that at week 0.*

For group B, Figure 5.12 displays the bar-chart representation for mean absolute pre and post-training values for Npeak amplitude. An increase in all ipsilateral electrodes (ILFC, ILC, and ILCP) for post-training Npeak amplitude values are observed compared to their pre-training values. On the other hand, Npeak amplitudes at all contralateral and central electrodes (CLFC, CLC, CLCP, Cz, and CPz) are either remained constant or decreased after the training. However, these changes were not statistically significant at any electrode position with respect to the paired t-test ($p > 0.05$).

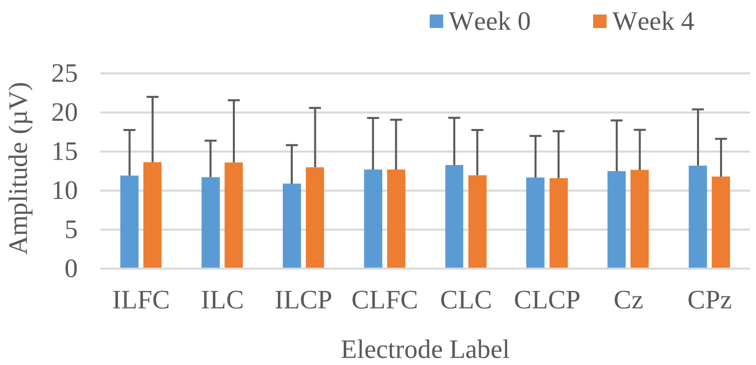


Figure 5.12: Mean absolute Npeak amplitude at week 0 and week 4 for group B. The error bars represent SD values across subjects for each electrode.

The EEG data analysis revealed that all participants in both groups A and B were able to generate MRCP patterns during the self-paced motor task of their affected hand at all eight selected electrode positions. Five features of the MRCP pattern namely; BP1 amplitude, BP1 onset, BP2 amplitude, BP2 onset, and Npeak amplitude were investigated for group A and group B separately to explore whether a significant change in the MRCP pattern's features occurred after the completion of 12 motor training sessions by the stroke patients. Npeak amplitude of group A participants showed a statistically significant decrease in Npeak amplitude after four weeks of training. Group B participants did not show a statistically significant change in Npeak. BP1 and BP2 amplitudes for all eight electrodes in both groups did not change significantly with training. BP1 and BP2 represent the preparation phase of voluntary movement [71]. In this experiment, they have smaller amplitudes compared to Npeak amplitudes, and hence detecting a significant change in the BP1 and BP2 amplitudes are less expected. The pre and post-training values of BP1 onset for both groups A and

B lie between -2 s to -1.1 s consistent with the previous work [71]. Similarly, the pre and post-training values of BP2 onset for both groups are less than -0.5 s which is also consistent with the results reported in [71].

5.4 Clinical Test Results

FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements' tests were executed on week 0 and week 4 of the designed robot-assisted training for each stroke patient in group A and group B. These clinical tests were used to determine the physical improvements in the hand motor abilities of the patients due to the training.

Table 5.7 shows the average values for four clinical tests of group A in the mean (± SD) form. There is an average increase of 1.8 in the FMA-wrist test, as well as an average increase of 3.7 obtained for the FMA-hand test. For MAS-hand movement and MAS-advanced hand movement tests, the average increase is 1.7 and 1.0 respectively. The paired t-test was applied between pre and post-training values of all four clinical tests. The significant change is indicated by bold values and a '*' sign on the values in Table 5.7. For group A, FMA-wrist (p=0.006), FMA-hand (p=0.043) as well as MAS-hand movements (p=0.035) clinical tests showed statistically significant improvement after the completion of 4-weeks of hand motor training. However, the MAS-advanced hand movement clinical test did not show statistically significant improvement according to paired t-test (p=0.252).

Table 5.7: Average clinical test results for group A after four weeks of motor training (Mean (± SD)). The symbol '' indicates a significant increase in clinical test results at week 4 compared to that at week 0.*

Assessment Period	FMA-Wrist Score (0-10)	FMA-Hand Score (0-14)	MAS-Hand Movements Score (0-6)	MAS-Advanced Hand Movements Score (0-6)
Week 0	6.5 (± 2.4)	8.3 (± 2.6)	2.8 (± 1)	3.3 (± 2.8)
Week 4	**8.3 (± 2.1)***	**12 (± 1.2)***	**4.5 (± 1.3)***	4.3 (± 1.5)

For group B, the average clinical test results are presented in Table 5.8 in the form of the mean (± SD). The average increase in FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements' clinical tests are calculated to be 1.4, 3.0, 0.3, and 0 respectively for this group. The paired t-test was applied and the significance level is indicated as bold values and a '*' sign on the values in Table 5.8. The paired t-test revealed that only the FMA-hand test (p=0.035) showed statistically significant improvement for the patients in group B. Whereas, the FMA-wrist test (p=0.27), MAS-hand movements test (p=0.423), and MAS-advanced hand movements test did not show any statistically significant improvements in their post-training values compared to their corresponding pre-training values.

Table 5.8: Average clinical test results for group B after four weeks of motor training (Mean (± SD)). The symbol '' indicates a significant increase in clinical test results at week 4 compared to that at week 0.*

Assessment Period	FMA-Wrist Score (0-10)	FMA-Hand Score (0-14)	MAS-Hand Movements Score (0-6)	MAS-Advanced Hand Movements Score (0-6)
Week 0	1.3 (± 1.2)	2.7 (± 1.5)	0.7 (± 0.6)	0.3 (± 0.6)
Week 4	2.7 (± 2.5)	**5.7 (± 2.1)***	1 (± 1)	0.3 (± 0.6)

Hence, according to the results of clinical tests obtained after four weeks of robot-assisted hand training sessions, group A showed statistically significant improvement in three out of four clinical tests whereas, group B revealed improvement in only one clinical test.

5.5 Results of Hand-Kinematic Parameters

The AMADEO assessment tool allows the measurement of force-flexion, force-extension, and HROM of fingers and thumb. Therefore, these hand-kinematic parameters were measured at the pre and post-training periods for group A and group B.

For group A, Table 5.9 shows the mean (± SD) values of force-flexion, force-extension, and HROM obtained during pre and post-training protocols. It is noted that patients in group A achieved an average increase of 20.2 N in force-flexion and an average increase of 12.7 N in force-extension. The HROM parameter shows a mean increase of 36.6 % after the completion of 12 motor training sessions. The statistical significance levels between pre and post-training values of all three hand-kinematic parameters were calculated using the paired t-test. The pre and post-training values of all these hand-kinematic parameters (force-flexion, p=0.028; force-extension, p=0.048; HROM; p=0.039) for hand movement recovery showed statistically significant improvement as a result of the 12 motor training sessions.

Table 5.9: Average hand-kinematic parameters for group A after four weeks of motor training (Mean (± SD)). The symbol '' indicates a significant increase in hand-kinematic parameters at week 4 compared to that at week 0.*

Assessment Period	Force-Flexion (N)	Force-Extension (N)	HROM (%)
Week 0	38.9 (± 14)	6.9 (± 8)	52.8 (± 34.9)
Week 4	**59.1 (± 8.4)***	**19.6 (± 8)***	**89.4 (± 15.9)***

Table 5.10 presents the average force-flexion, force-extension, and HROM values obtained from the AMADEO assessment tool for group B in the mean (± SD) form. The participants of this group showed an average increase of 16 N in force-flexion, 3.5 N in force-extension, and 27.8 % in HROM parameters. Application of paired t-test between pre and post-training values of all three hand-kinematic parameters showed that improvements in any of these parameters were not statistically significant ($p > 0.05$).

Table 5.10: Average hand-kinematic parameters for group B after four weeks of motor training (Mean (± SD))

Assessment Period	Force-Flexion (N)	Force-Extension (N)	HROM (%)
Week 0	15.1 (± 15.9)	2.1 (± 2.6)	11.9 (± 18.3)
Week 4	31.1 (± 30.3)	5.6 (± 6.4)	39.7 (± 34.4)

The results of hand-kinematic parameters showed that post-stroke patients in group A gained significant improvements in the force-flexion, force-extension, and HROM parameters after completion of four weeks of the motor training. However, group B stroke patients did not show significant improvement in any of the hand-kinematic parameters after a similar amount of training to group A.

5.6 Extended Training for Group B

The results discussed in Sections 5.3 to 5.5 revealed that, apart from the FMA-hand score, four weeks of motor training did not have a significant rehabilitation effect on post-stroke patients in group B. They neither showed a statistically significant change in the features of the MRCP pattern, nor substantial improvements in the other three clinical tests or any of the hand-kinematic parameters. Therefore, it was decided to extend the training period for all participants in group B for another four weeks (12 sessions) to determine whether the extension of the hand motor training has any effect on the MRCP pattern's features, clinical tests, and hand-kinematics parameters.

5.6.1 Extended Training Protocol

All three brain stem stroke patients in group B underwent another phase of motor training that consisted of 12 sessions (three sessions/week) of advanced training protocols using the AMADEO device. The complete training protocol consisting of two training phases I and II for stroke patients in group B is shown in the form of a flowchart in Figure 5.13. During this extended training (phase II mentioned in Figure 5.13), patients received four levels of training each day consisting of CPM training mode for 5 minutes, CPMplus training mode for 5 minutes, assistive training mode for 10 minutes, and Active training mode for 10 minutes. During the active training mode, subjects played 2D interactive games using their affected hand. In this way, group B participants received two-phases of training using the AMADEO device in which phase II of training was slightly more intense compared to phase I as it included training on active training mode.

The same three assessment procedures were conducted at the end of eight weeks (week 8) of the designed robot-assisted training of hand as performed during the beginning of training (week 0) and at the end of phase I of training (week 4) (see Figure 5.13). The three assessment procedures consisted of EEG signal acquisition during self-paced simple hand-grasping movements using the affected hand to extract MRCP pattern, conducting FMA-wrist, FMA-hand, MAS-hand movement, and MAS-advanced hand movement clinical tests, and measuring the force-flexion, force-extension, and HROM parameters of the affected hand using AMADEO assessment tool.

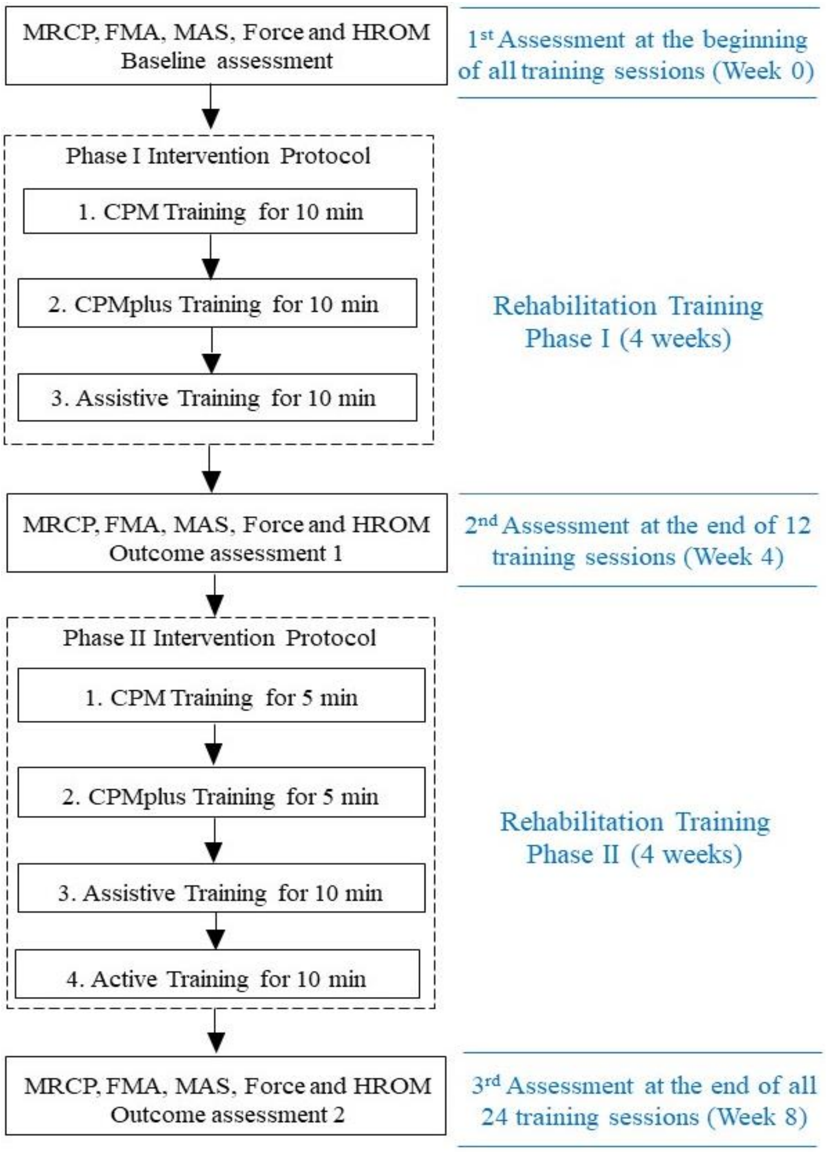


Figure 5.13: Flow diagram of a complete motor training strategy for group B and assessment periods

5.6.2 Results

In this section, the results obtained from the data analysis on week 8 will be compared to those obtained during week 0 and week 4 to measure the effect of extending the training on MRCP pattern changes and physical improvement in hand motor skills.

Figure 5.14 shows the global MRCP pattern plots at all eight electrodes, extracted from EEG data acquired during the self-paced hand-grasping task for infratentorial stroke patients (brain stem stroke patients) of group B. This figure represents the MRCP plots for the pre-training period before the start of any rehabilitation training session (week 0) and after the completion of both phases (phases I and II) of training (week 8). Visual inspection of the plots reveals that the Npeak amplitude of the MRCP pattern is decreased at week 8 with respect to the corresponding value at week 0 for all electrode positions. Whereas, as described in Section 5.3, the Npeak amplitude for group B at week 4 is increased at ipsilateral electrodes, slightly decreased at contralateral and CPz electrodes and remains the same at the Cz electrode compared to week 0. In order to assess the significance of these variations, individual MRCP features are analyzed.

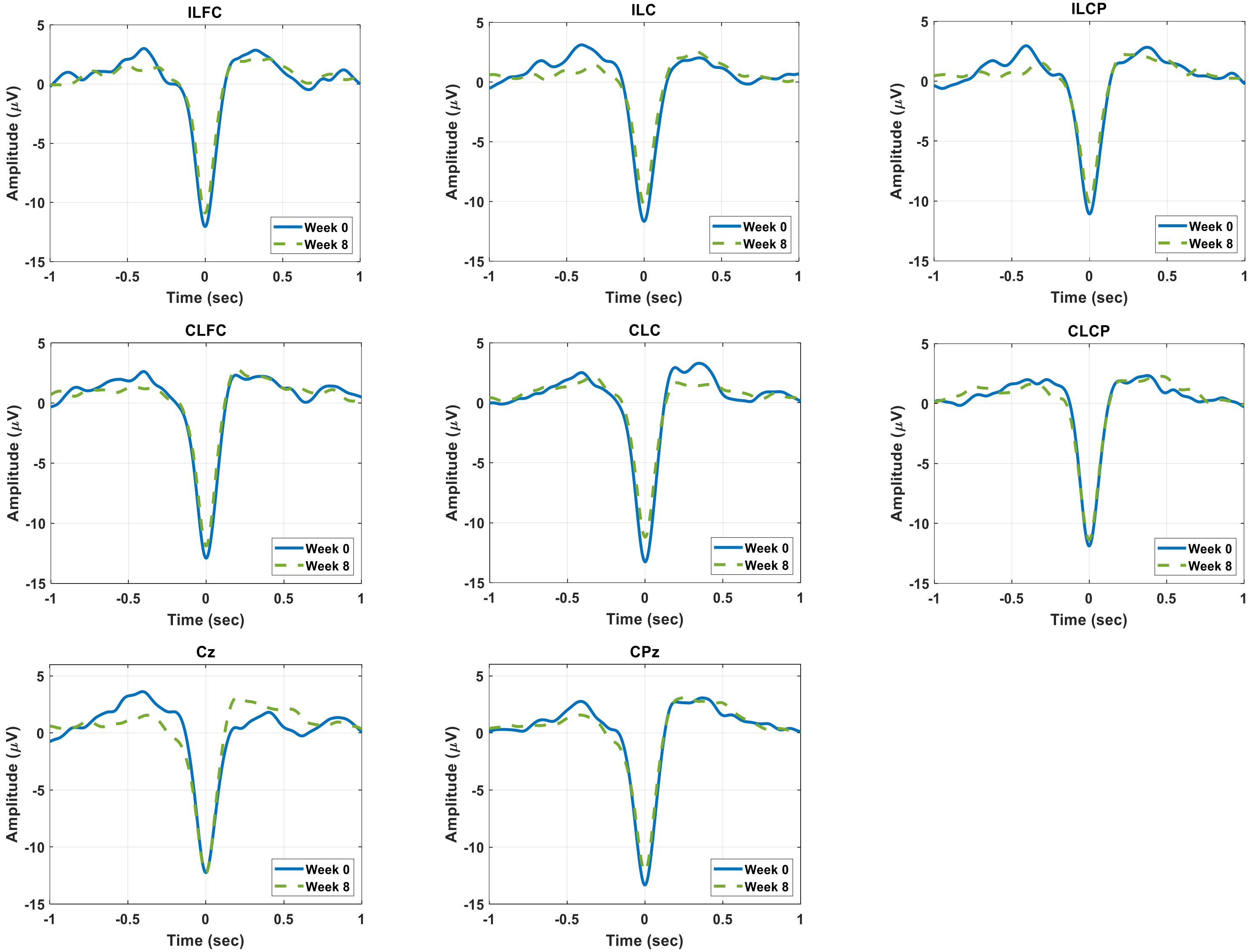


Figure 5.14: Global MRCP patterns for group B at all channels after 24 motor training sessions. Legend Week 0 represents the pre-training period before the beginning of any training session, and legend Week 8 shows the post-training period after the end of 24 training sessions in all figures.

As observed in Section 5.3, of five features of the MRCP pattern, only Npeak amplitude showed a significant change in group A. Therefore, for extended study results analysis for group B, only Npeak amplitude of the MRCP pattern is analyzed. Figure 5.15 shows the bar-chart representation of average Npeak amplitudes at all eight electrodes for group B. A consistent decrease in the Npeak amplitude was observed for all selected electrodes after a total of eight weeks of training when it is compared with week 0. When the paired t-test was applied, a significant change in Npeak was obtained at CLC (p=0.01) and CPz (p=0.04) electrode positions. The significance level is indicated by a '*' symbol in Figure 5.15.

In contrast to these results, the change in Npeak amplitude at all eight electrodes was not consistently decreased after the first four weeks of motor training compared to week 0 (see Figure 5.12). These results suggest that four weeks of rehabilitation is not a sufficient time to obtain consistent MRCP patterns' changes for the brain stem stroke patients in group B. This outcome is consistent with clinical observations that patients with brain stem strokes are typically slower to recover motor function than patients with supratentorial strokes [295].

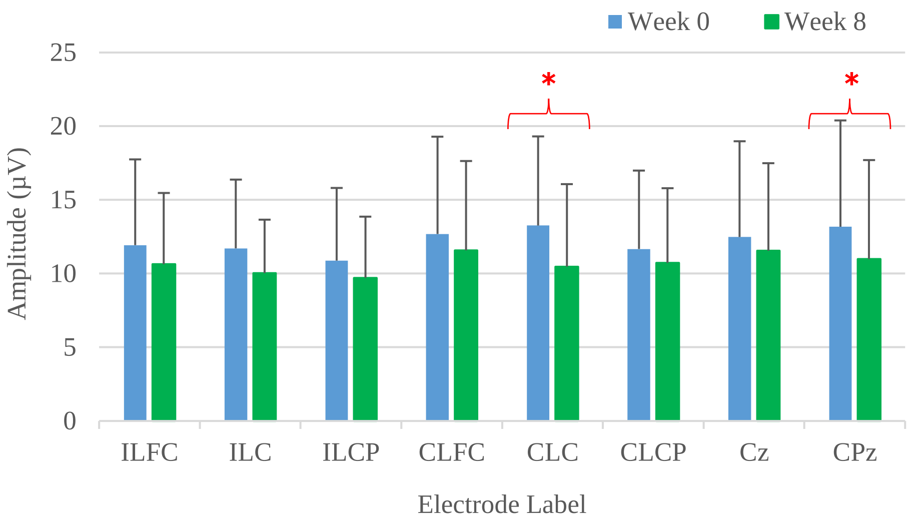


Figure 5.15: Mean absolute Npeak amplitude at week 0 and week 8 for group B. The error bars represent SD values across subjects for each electrode. The symbol '' indicates a significant decrease in Npeak amplitude at week 8 compared to that at week 0.*

Table 5.11 shows the average results of FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movement tests. The two-tailed paired t-test was applied to clinical test results obtained at week 0 and week 8. The results are presented in the form of the mean (± SD) and the significant change between these tests is indicated by bold values and a '*' symbol on the values. It is observed earlier that only the FMA-hand test shows a significant change in all patients when they complete phase I (four weeks) of the intervention protocol (see Table 5.8). However, after phase II (eight weeks) of training, the patients show statistically significant improvement in two clinical tests i.e., FMA-hand and MAS-hand movements' tests.

Table 5.11: Average clinical test results for group B after eight weeks of training (Mean (± SD)). The symbol '' indicates a significant increase in clinical test results at week 8 compared to that at week 0.*

Assessment Period	Clinical Test Results			
	FMA-Wrist Score (0-10)	**FMA-Hand Score (0-14)**	**MAS-Hand Movements Score (0-6)**	**MAS-Advanced Hand Movements Score (0-6)**
Week 0	1.3 (± 1.2)	2.7 (± 1.5)	0.7 (± 0.6)	0.3 (± 0.6)
Week 8	3.7 (± 2.3)	**8 (± 2.6)***	**2.3 (± 0.6)***	1.3 (± 0.6)

Table 5.12 shows the average values of the hand-kinematic parameters which include force-flexion, force-extension, and HROM for group B obtained at week 0 and week 8. The values are presented in mean (± SD) and the statistical significance change is indicated by bold values and a '*' sign on the values. According to Table 5.10, none of the hand-kinematic parameters show any significant change after motor training in phase I (four weeks). Whereas Table 5.12 shows that a statistically significant improvement in all the force-flexion, force-extension, and HROM parameters is observed when the patients completed their eight weeks of training (phases I and II).

Table 5.12: Average hand-kinematic parameters for group B after eight weeks of training (Mean (± SD)). The symbol '' indicates a significant increase in hand-kinematic parameters at week 8 compared to that at week 0.*

Assessment Period	Hand-Kinematic Parameters		
	Force-Flexion (N)	**Force-Extension (N)**	**HROM (%)**
Week 0	15.1 (± 15.9)	2.1 (± 2.6)	11.9 (± 18.3)
Week 8	**42.2 (± 24.9)***	**13.9 (± 6.8)***	**64.6 (± 24.8)***

The results of clinical tests and hand-kinematic parameters show that group B patients regained significant hand motor functions after eight weeks of extended training. As mentioned before, these outcomes are consistent with clinical observations for this category of patients [295].

5.7 Summary

The main purpose of this study was to investigate possible changes in the features of the MRCP pattern when post-stroke patients gained improvements in motor skills of their impaired hands after robot-assisted rehabilitation training on the AMADEO device. The reported results reveal that the Npeak amplitude of the MRCP pattern is decreased consistently in patients with supratentorial strokes (group A) after four weeks of training and decreased consistently in patients with brain stem strokes (infratentorial stroke) after eight weeks of training. These results suggest that four weeks of rehabilitation is not sufficient time to induce significant MRCP signal changes for the infratentorial stroke patients. The clinical evidence about infratentorial stroke rehabilitation also demonstrates that the recovery speed of such patients is slower compared to supratentorial stroke patients [295].

The changes in MRCP patterns are also associated with improvements in clinical tests and hand-kinematic parameters. According to the results of clinical tests obtained after four weeks of robot-assisted training, group A showed statistically significant improvement in three out of four clinical tests. Whereas group B showed improvement in only one clinical test after the first four weeks of training and two clinical tests after eight weeks of training. Whereas the analysis of hand-kinematic parameters showed that post-stroke patients in group A gained significant improvements in all force-flexion, force-extension, and HROM values after the completion of four weeks of the training program. Group B showed significant improvement in all the hand-kinematic parameters only after completing eight weeks of training.

The decrease in MRCP's Npeak amplitude after the designed robot-assisted motor training reflects that neurological pathways become more established so that fewer cortical resources are needed for motor planning and execution of tasks. This hypothesis is also supported by studies in healthy participants available in the literature [216-220]. However, further investigations are required to validate the occurrence of neuroplasticity.

To the best of our knowledge, this study is the first attempt to use the MRCP pattern as an assessment tool to determine the effect of the rehabilitation training strategy on the brain activities acquired from the actual stroke patients. The results of this study also indicate that EEG has future potential clinical utility in post-stroke rehabilitation.

Chapter 6

Adaptive Robot-Assisted Stroke Rehabilitation Guided by EEG − Two Case Studies

6.1 Introduction

In Chapter 5, the effect of motor training on the features of the MRCP pattern was established. The post-stroke patients were engaged in robot-aided training on the AMADEO device for a couple of weeks. A simple palmar grasping task was deployed for EEG acquisition during pre-training and post-training periods to measure the effect of the training using the MRCP pattern. It was shown that the Npeak amplitude of the MRCP pattern was significantly decreased post-rehabilitation training with the improvements in clinical tests and hand-kinematic parameters. The motor training strategy used in that experiment comprised an amalgamation of four training modes and remained constant throughout the experiment. Although this rehabilitation training proved to be beneficial, the question of the degree of engagement of the patient during the protocol was still unanswered. The effect of individual training mode on hand motor skills should also be determined. Therefore, the need for an intelligent, adaptive, dynamic, and more engaging training regime is warranted. This would require a regime that changes the training modes according to the degree of subjects' engagement during the training sessions as measured by variations in the features of the MRCP pattern.

It was assumed in Chapter 5 that reduced Npeak amplitude represented the reconnection of the neurological pathways, automatic performance of the task, and less intentional engagement of the subject. This, in turn, lessened the number of cortical resources required to plan and execute motor tasks. In this chapter, this assumption is further validated, and it is shown that making the rehabilitation training more challenging for a subject requires the more intentional engagement of the subject during the training sessions, resulting, in turn, an increase in the Npeak amplitude.

The training strategy, used in the experimental work described in this chapter, deploys a chain of training modes that advances to more challenging tasks as the Npeak amplitude decreases. According to our findings so far, this represents that the motor skills associated with the task are restored through neuroplasticity phenomena, requiring less engagement from the subject during training sessions. Moving to the next challenging level of training mode demands once again higher engagement of the subject making Npeak amplitude more pronounced. Such a training strategy should result in a more effective and time-efficient rehabilitation process for post-stroke patients.

The work presented in this chapter represents the conceptual framework of a feasibility study for an adaptive and dynamic robot-assisted rehabilitation strategy. The efficacy of the proposed training strategy is also verified through the measurement of the hand-kinematics parameters and clinical tests. The organization of the chapter is as follows. Section 6.2 describes the characteristics of the patients, EEG acquisition process, adaptive motor training strategy details, as well as hand-kinematic parameters and clinical test measurement methods. All experimental results for case study 1 are presented in Section 6.3 and that for case study 2 in

Section 6.4. A comparison between hand-kinematic parameters and clinical test results for the fixed-training strategy (described in Chapter 5) with that for the adaptive-training strategy is explained in this chapter in Section 6.5. Finally, a summary of the results and their implications is provided in Section 6.6.

6.2 Materials and Methods

6.2.1 Participants' Characteristics

This study was conducted on two right hand dominant stroke patients. The patient inclusion criteria were the same as described in Section 5.2.1 of Chapter 5. Based on the inclusion criteria, two patients who experienced a supratentorial stroke were identified and their stroke-related details are listed in Table 6.1. Both patients received standard care at a local hospital in addition to the adaptive robot-based rehabilitation training for their affected hands. The participants gave their written informed consent before the experiment commencement.

Table 6.1: Details of stroke patients

Stroke Patient (Gender)	Age (Years)	Onset Duration (Months)	Lesion Location	Affected Hand
SP1 (Female)	62	3	Right striatocapsular infarct	Left
SP2 (Male)	73	2	Right middle cerebral artery infarct	Left

6.2.2 EEG Acquisition Process

The EEG signals were measured over eight electrode sites of FC4, C4, CP4, Cz, CPz, FC3, C3, and CP3 during each training day using 32-channel Ag/AgCl Quick-Cap (Compumedics-Neuroscan) according to the 10–20 electrode positioning system. The electrodes FC4, C4, and CP4 are contralateral channels, Cz and CPz are central channels, as well as FC3, C3, and CP3 are ipsilateral channels for both patients because they used their left affected hand during training. Whereas, FPz electrode and ipsilateral mastoid point were used as ground and reference electrodes respectively. The Grael 4K EEG amplifier was set to a sampling frequency of 2048 Hz and the impedance of each electrode was set below 5 kΩ before the signal acquisition. At each hand closing movement during training, digital event markers were manually sent to the data acquisition software, CURRY 8X (Compumedics-Neuroscan). The acquired EEG data were processed to extract the MRCP pattern as explained in Section 3.4 of Chapter 3. The extracted MRCP patterns were averaged out with respect to the number of trials to obtain a global MRCP pattern at all selected electrodes. Those global MRCP patterns were then used to extract the Npeak amplitude feature. Only Npeak amplitude is considered for this experiment because based on the experimental results presented in Chapters 4 and 5, Npeak amplitude is the only component of MRCP that shows considerable changes after training.

6.2.3 Adaptive Motor Training Strategy

The training strategy consisted of 30 minutes of robot-assisted hand therapy three days a week for four weeks resulting in 12 training sessions overall. The patients received training for their affected hands using the AMADEO device. AMADEO offers four training modes with increasing intensity; Mode 1: CPM; Mode 2: CPMplus; Mode 3: Assistive training; and Mode 4: Active training. The active training consists of 2D games, the most interactive training mode available in AMADEO, which requires the maximum engagement of the patient. The Shoot-out game was chosen during the active training mode. The EEG acquisition process during each AMADEO training mode of subjects SP1 and SP2 is shown in Figure 6.1 and Figure 6.2 respectively.

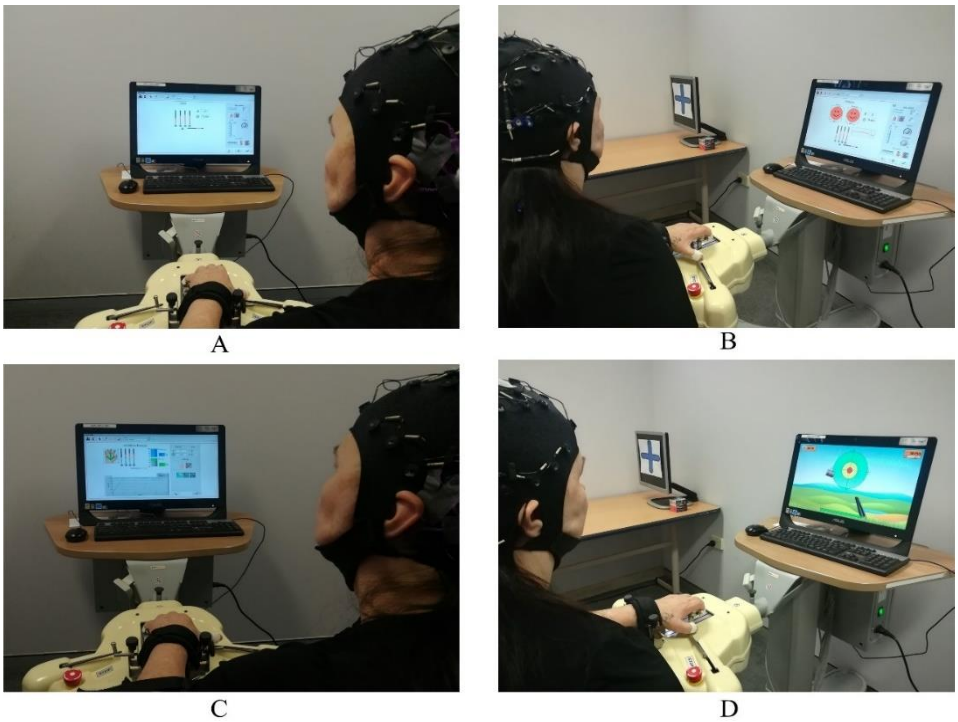


Figure 6.1: Hand motor training of SP1 with EEG acquisition during each AMADEO training mode; (A) CPM, (B) CPMplus, (C) Assistive training, (D) Active training

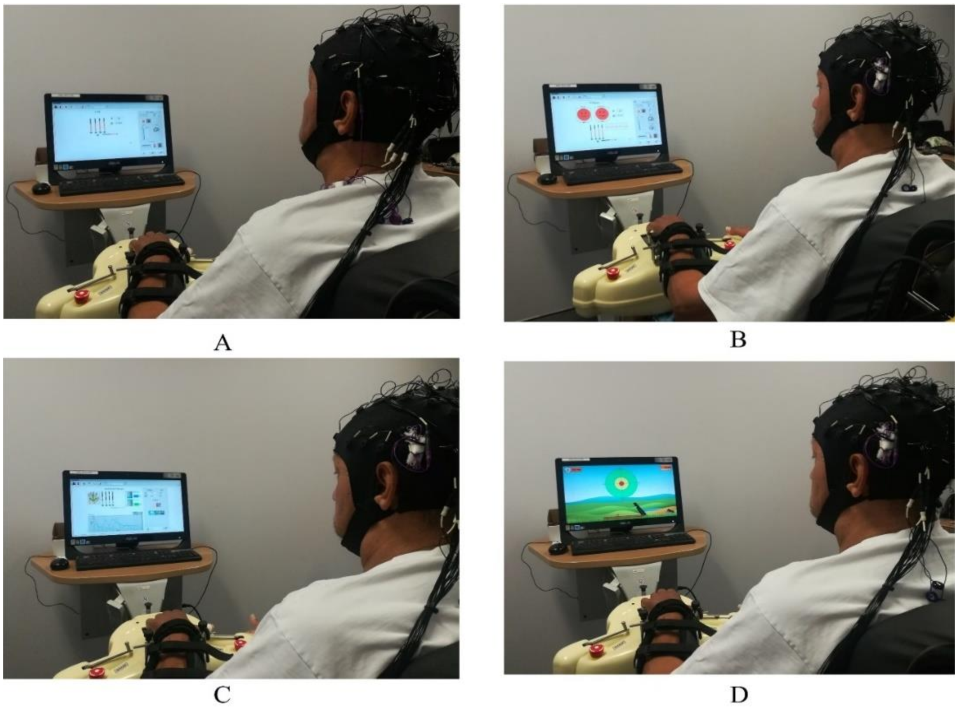


Figure 6.2: Hand motor training of SP2 with EEG acquisition during each AMADEO training mode; (A) CPM, (B) CPMplus, (C) Assistive training, (D) Active training

The training during each day was executed in three blocks of 10 minutes; each termed as T1, T2, and T3. The EEG data were acquired for all three blocks of training to extract the Npeak amplitude of MRCP patterns at all selected electrodes. One minute of rest was given to the subject between the training blocks. Each subject started motor training with CPM for two consecutive days. Equation 6.1 was developed for this experiment as a condition to change training mode for each stroke patient in which T3Npeak denotes the Npeak during the T3 period at any given electrode. More specifically, the Npeak amplitude of the MRCP pattern was compared for any two consecutive training days at each selected electrode by calculating the difference as depicted in Equation 6.1. As all Npeak values are negative in amplitude, if T3Npeak on the current training day is decreased or remained the same compared to the previous training day then their difference will be positive and the condition in Equation 6.1 will be true. When this condition is true at all selected electrodes, the training mode is progressed to the next level (i.e. CPMplus). This process is repeated until the end of 12 training sessions for each stroke subject. In this way, they performed a specific number of days on any training mode in accordance with their level of engagement.

$$T3Npeak_{day_n} - T3Npeak_{day_{n-1}} \geq 0 \tag{6.1}$$

6.2.4 Measurements of Hand-Kinematic Parameters and Clinical Tests

To determine the effect of the designed adaptive rehabilitation training strategy on hand motor skills, hand-kinematic parameters measurements, and clinical tests were performed. Hand-kinematic parameters that include force-extension, force-flexion, and HROM for fingers and thumb, were measured after each training session. Three measurements of each of these hand-kinematic parameters were taken and their average values were used during analysis. Clinical tests comprised FMA-wrist, FMA-hand, MAS-hand movement as well as MAS-advanced hand movement tests. These clinical tests were conducted during pre and post-training periods and demonstrated the overall effect of the designed motor training strategy on hand motor skills.

6.3 Case Study 1: Experimental Results

This section presents all the experimental results of subject SP1.

6.3.1 Selection of Training Mode Based on MRCP's Npeak Amplitude

The SP1 started training of the affected hand on the CPM mode for the first two days of the training. Once the Npeak amplitude values of the MRCP pattern for day 1 and day 2 of CPM training were obtained, the difference in Npeak amplitude during their T3 periods was calculated using Equation 6.1. Figure 6.3 shows the values of the T3Npeak difference between any two consecutive days at all electrode positions.

The condition in Equation 6.1 is not true on day 2 of the training. This indicates that the patient is still learning the CPM training mode and the same training is continued on day 3. On day 3, the condition is true for all electrodes (see the second set of column-bars in Figure 6.3) which means it is time to progress to the second training mode, i.e. CPMplus on day 4. The same comparison method is applied to Npeak values on day 4 and further on to determine when the condition in Equation 6.1 holds. It is found that the condition is true on day 7, day 10, and day 12 of the training strategy after spending four training days on CPMplus, three days on assistive training, and two training days on active training respectively.

In this way, the number of training days on any AMADEO training mode for SP1 was determined by the Npeak amplitude comparison according to Equation 6.1 at all selected electrode sites. In total, the patient SP1 received 360 minutes of AMADEO training for four weeks in which the SP1 spent 90 minutes on CPM, 120 minutes on CPMplus, 90 minutes on assistive training, and 60 minutes on active training.

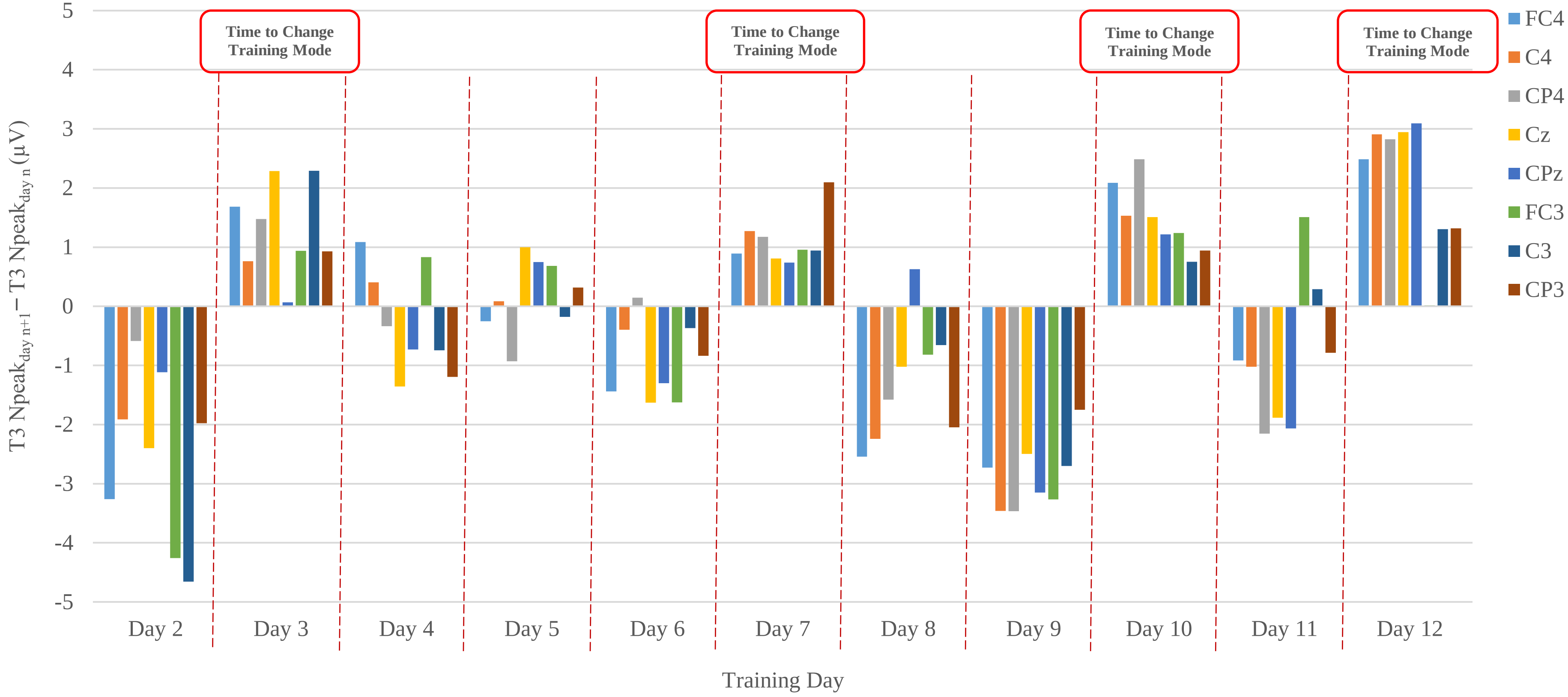


Figure 6.3: Progression of training modes based on the difference of Npeak amplitudes between any two consecutive days for SP1

6.3.2 Variations in MRCP's Npeak on Progression of Training Mode

After executing the adaptive-training strategy, the effect of the progression of the training mode on the Npeak amplitude was also observed. This was done by calculating the difference between Npeak amplitudes during T3 of the last day of one training mode and that during T1 of the first day of the next training mode at all electrode sites as represented in Equation 6.2.

$$Npeak_{diff} = T3Npeak_{day_{n-1}} - T1Npeak_{day_n} \tag{6.2}$$

The $\text{Npeak}_{\text{diff}}$ values are shown in Table 6.2 when SP1 progressed over four training modes. All the $\text{Npeak}_{\text{diff}}$ due to the progression of training modes are found to be negative at all electrode sites which shows an increase in Npeak amplitudes. This means that when the patient SP1 is introduced to a new training mode, Npeak amplitudes increase which is, in turn, an indication of an increase in the engagement of the subject. Furthermore, during the game playing mode (active training mode), the subject has the maximum engagement that is shown by the maximum negative difference at all electrode positions in the third column of Table 6.2.

Table 6.2: Effect of training mode progression on MRCP's Npeak for SP1

Electrode label	**$\text{Npeak}_{\text{diff}}$ values due to Training Mode Progression (μV)**		
	CPM to CPMplus	***CPMplus to Assistive***	***Assistive to Active***
FC4	-0.712	-1.147	-4.488
C4	-1.633	-1.489	-4.662
CP4	-2.677	-2.052	-4.566
Cz	-2.881	-2.324	-6.136
CPz	-2.158	-2.041	-4.912
FC3	-0.57	-1.37	-4.613
C3	-2.183	-1.364	-5.556
CP3	-2.598	-2.986	-4.873

6.3.3 Analysis of Npeak Amplitude based on Electrode Position

The analysis of Npeak amplitude based on selected electrode positions was also performed to determine whether the amplitude of Npeak varies at different electrode locations. Figure 6.4 shows the Npeak amplitudes during the T3 block of all 12 training days for SP1. It is noted that the Npeak amplitude values at contralateral channels (FC4, C4, and CP4) are larger than the corresponding ipsilateral channels (FC3, C3, and CP3) for any training day. Moreover, both central channels (Cz, and CPz) also show higher values for Npeak amplitudes compared to the ipsilateral channels (FC3, C3, and CP3) for a training day. This confirms the primary origin of Npeak is the contralateral (with respect to the movement) side of the brain [71, 220].

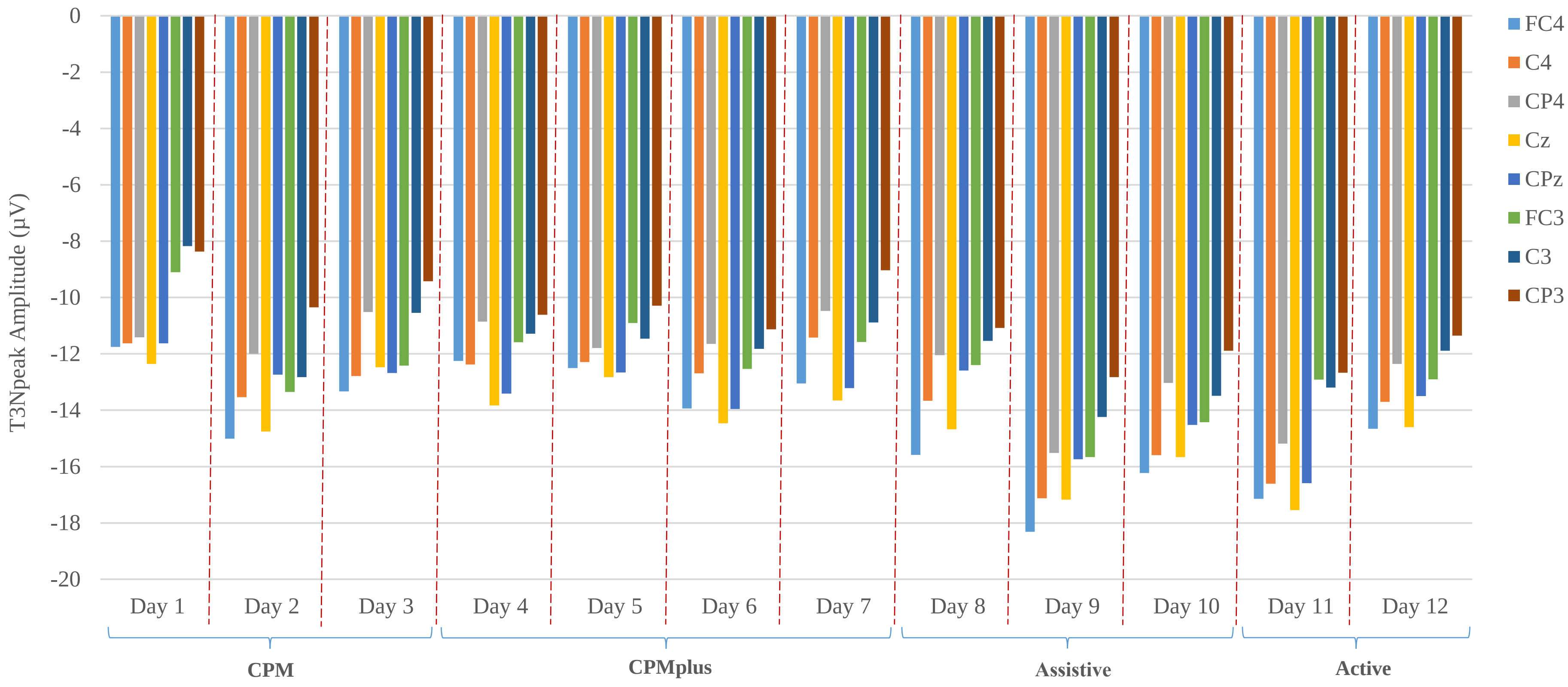


Figure 6.4: MRCP's Npeak amplitudes during T3 block of each training day at all eight electrode sites for SP1

6.3.4 Outcomes of Hand-Kinematic Parameters due to Individual Training Mode

In order to measure the effect of adaptive-training strategy on the physical improvements in hand motor skills, three hand-kinematics parameters which include force-extension, force-flexion, and HROM, were measured for SP1 after every training session. These parameters were obtained using the AMADEO assessment tool. The effect of individual training mode on all hand-kinematic parameters was measured by calculating the percentage change and cumulative change.

After completing three days of training on CPM, the force-extension, force-flexion, and HROM average values for SP1 were found to be 7.33 N, 17.77 N, and 71.13 % respectively. The percentage change in all these parameters after completing training on CPMplus, assistive, and active training modes were calculated and presented in Table 6.3. The maximum percentage change in force-extension, force-flexion, and HROM values is achieved by the patient after completion of active training. This is expected because, when the active training mode is introduced, the patient SP1 has maximum engagement which is indicated by the maximum increase in Npeak amplitude (see column 3 of Table 6.2). It is inferred that the stroke patient can gain maximum improvement in hand motor skills when he/she has maximum engagement during training.

Table 6.3: Percentage change in hand-kinematic parameters due to individual training mode for SP1

Training Modes	***Force-Extension (%)***	***Force-Flexion (%)***	***HROM (%)***
CPMplus	9.14	5.63	5.16
Assistive training	17.88	40.81	5.21
Active training	37.86	39.42	9.02

The average cumulative change in all the hand-kinematic parameters was also calculated for SP1 and shown in the form of a bar-chart in Figure 6.5. It is noted that force-extension, force-flexion and HROM values for SP1 are progressively increasing till the active training mode. This shows that the subject continues to improve in the hand-kinematic parameters until the end of the adaptive-training strategy.

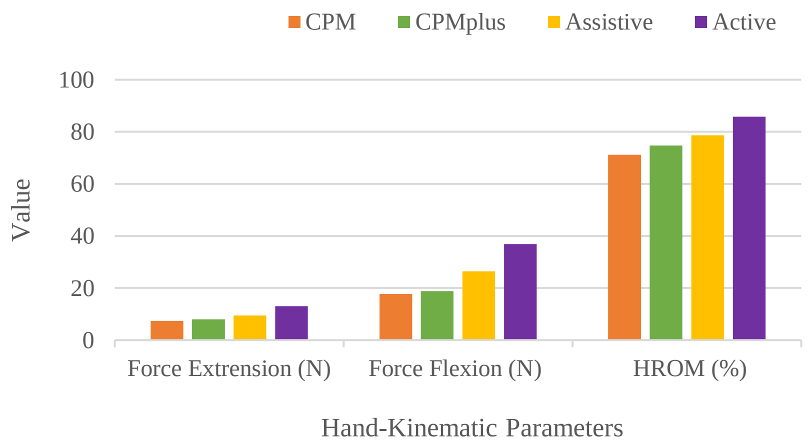


Figure 6.5: Cumulative change in hand-kinematic parameters with respect to training modes for SP1

6.3.5 Clinical Test Results

The four clinical tests were conducted pre and post-adaptive hand motor training for SP1. The bar-chart representation of the pre and post-training values for FMA-wrist, FMA-hand, MAS-hand movements, and MAS-advanced hand movements tests are shown in Figure 6.6. It is observed that all four clinical tests show a prominent increase in their post-training values which demonstrates that patient SP1 gains considerable improvement in the hand movements after completing the adaptive rehabilitation training strategy.

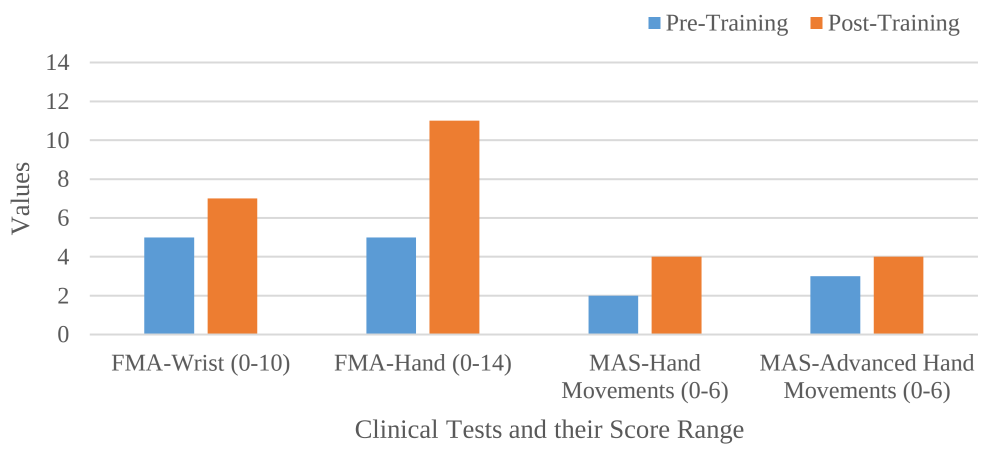


Figure 6.6: Clinical test results for SP1

6.4 Case Study 2: Experimental Results

In this section, all the experimental results for SP2 are presented.

6.4.1 Selection of Training Mode Based on MRCP's Npeak Amplitude

Similar to SP1, the patient SP2 started the training on Mode 1 i.e. CPM for the first two days. The same condition expressed in Equation 6.1 is used to compare Npeak amplitudes between two consecutive days for the progression of training modes for SP2. The difference of T3Npeak values between any two consecutive training days at all selected channels for SP2 is shown in Figure 6.7. It is found that SP2 shows a decrease in Npeak amplitudes (positive T3Npeaks difference) after two days of training on CPM, four days of training on CPMplus, and four days of training on assistive training. In this way, SP2 completes 10 days of the total training strategy. Finally, Mode 4 (active training mode) is selected for training on day 11 and the patient SP2 spends the last two training days (day 11 and day 12) on active training mode.

Out of 360 minutes, SP2 spent 60 minutes on CPM, 120 minutes on CPMplus, 120 minutes on assistive training mode, and the last 60 minutes on active training mode.

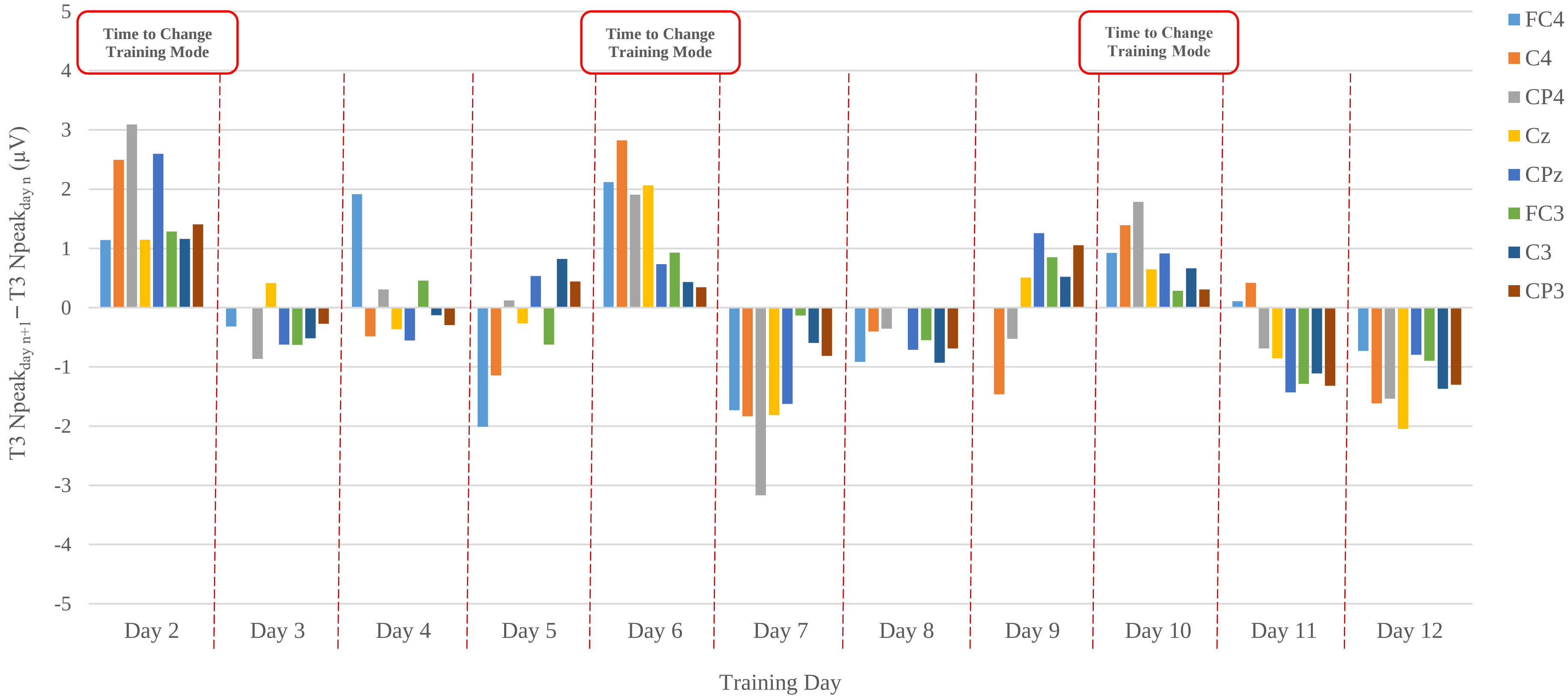


Figure 6.7: Progression of training modes based on the difference of Npeak amplitudes between any two consecutive days for SP2

6.4.2 Variation in MRCP's Npeak on Progression of Training Mode

The training mode progression effect on Npeak amplitude for SP2 was calculated using Equation 6.2 and the results are presented in Table 6.4. The $\text{Npeak}_{\text{diff}}$ values due to progression between any two training modes are found to have negative values at all electrode positions which indicates that the Npeak amplitude is increased when the new training mode is introduced to the subject SP2 similar to the SP1. The maximum Npeak amplitude increase is found when the patient SP2 starts training on active training mode (see column 3 of Table 6.4). Hence, SP2 also shows maximum engagement, and in consequence maximum increase in Npeak during active training mode similar to SP1.

Table 6.4: Effect of training mode progression on MRCP's Npeak for SP2

Electrode label	$\text{Npeak}_{\text{diff}}$ values due to Training Mode Progression (μV)		
	CPM to CPMplus	***CPMplus to Assistive***	***Assistive to Active***
FC4	-1.581	-0.768	-2.223
C4	-0.263	-1.097	-1.874
CP4	-1.486	-0.374	-1.624
Cz	-0.277	-0.866	-2.174
CPz	-1.324	-0.074	-1.517
FC3	-1.425	-1.043	-2.677
C3	-0.878	-0.749	-2.14
CP3	-1.214	-0.534	-1.76

6.4.3 Analysis of Npeak Amplitude based on Electrode Position

Figure 6.8 presents the average Npeak amplitudes during the T3 blocks of all training days for SP2. It is noted that for any training day, Npeak amplitudes at contralateral channels (FC4, C4, and CP4) as well as central channels (Cz and CPz) are greater in magnitude compared to that at ipsilateral channels (FC3, C3, and CP3). Hence, the Npeak amplitude analysis of SP2 also confirms that MRCP's Npeak primary origin is the contralateral side of the brain with respect to the movement.

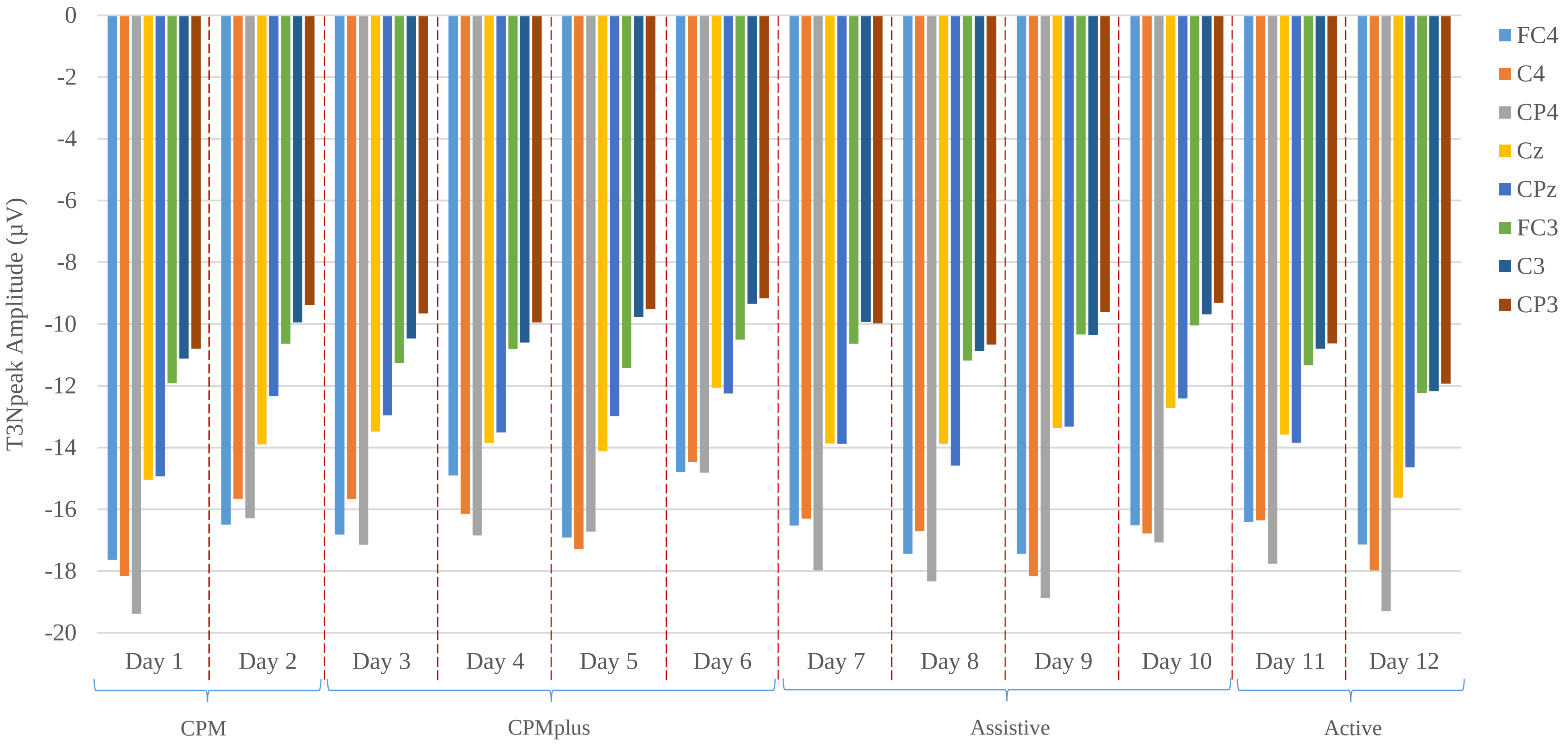


Figure 6.8: MRCP's Npeak amplitudes during T3 block of each training day at all eight selected electrode sites for SP2

6.4.4 Outcomes of Hand-Kinematic Parameters due to Individual Training Mode

When the subject SP2 completed two days of training on CPM, the hand-kinematic parameters i.e. force-extension, force-flexion, and HROM values were calculated to be 7.35 N, 12.35 N, and 72 % respectively. Table 6.5 shows the percentage change in all hand-kinematic parameters when the patient SP2 completed training on CPMplus, assistive training, and active training modes. It is noted that the highest percentage change in force-extension, force-flexion, and HROM values of SP2 is obtained when the patient undergoes the active training mode similar to SP1.

Table 6.5: Percentage change in hand-kinematic parameters due to individual training mode for SP2

Training Modes	***Force-Extension (%)***	***Force-Flexion (%)***	***HROM (%)***
CPMplus	2.45	30.36	9.72
Assistive training	7.3	36.21	9.18
Active training	17.57	40.67	9.8

For SP2, the cumulative average change in all three hand-kinematic parameters (force-extension, force-flexion, and HROM) is presented in the bar-chart form in Figure 6.9. A steady increase in all these parameters during training on Mode 1 through Mode 4 is observed which indicates that the patient continues to improve throughout the training strategy.

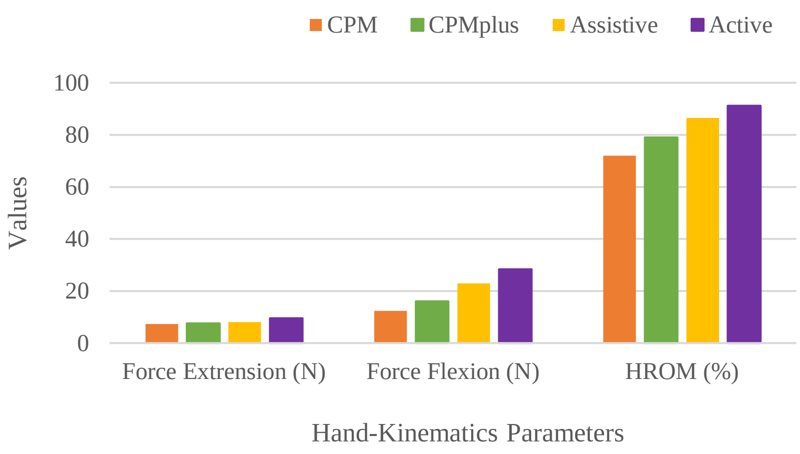


Figure 6.9: Cumulative change in hand-kinematic parameters with respect to training modes for SP2

6.4.5 Clinical Test Results

The results for all four clinical tests obtained before the commencement and after completion of the adaptive-training strategy of SP2 are shown in the form of a bar-chart in Figure 6.10. Considerably high post-training values of all FMA-wrist, FMA-hand, MAS-hand movement and MAS-advanced hand movements tests compared to their corresponding pre-training values are observed. The clinical test results prove that SP2 also gains prominent physical improvement in the hand motor skills after completing this adaptive rehabilitation program similar to SP1.

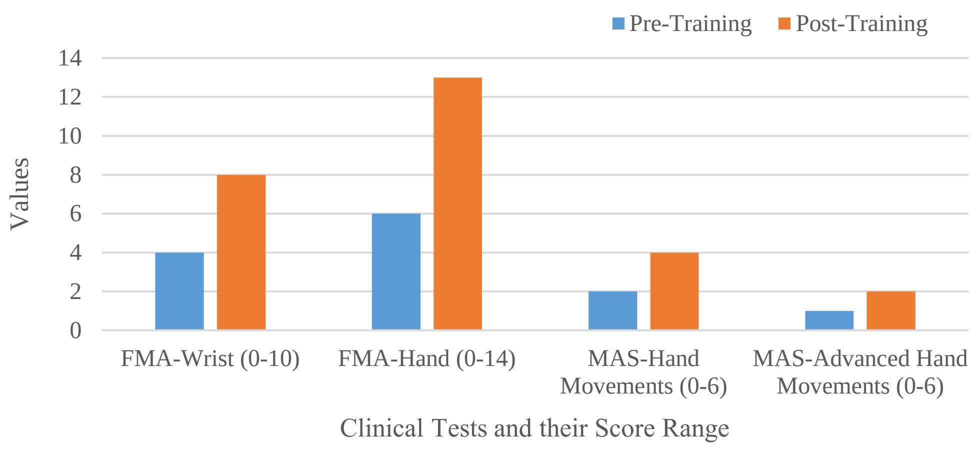


Figure 6.10: Clinical test results for SP2

6.5 Comparison of Fixed-Training and Adaptive-Training Strategies on Improvements of Hand Motor Skills

In Chapter 5, group A consists of supratentorial stroke patients who completed four weeks of motor training on AMADEO which remained fixed throughout the rehabilitation training strategy. While in this chapter, two other supratentorial stroke patients underwent adaptive-training strategies where training modes of AMADEO were changed based on MRCP's Npeak variations. In this section, the comparison between fixed-training and adaptive-training strategies is made on hand-kinematic parameters and clinical test results.

6.5.1 Comparison of Hand-Kinematic Parameters

The average hand-kinematic parameter results for group A patients after a fixed-training strategy are re-produced in Table 6.6 from Table 5.9 in Chapter 5.

Table 6.6: Average hand-kinematic parameters for group A after four weeks of fixed-training strategy (Mean)

Assessment Period	Force-Extension (N)	Force-Flexion (N)	HROM (%)
Pre-training	6.9	38.9	52.8
Post-training	19.6	59.1	89.4

While, the average values of hand-kinematic parameters for two subjects who performed adaptive-training strategy, as explained in this chapter, are calculated and presented in Table 6.7.

Table 6.7: Average hand-kinematic parameters after four weeks of adaptive-training strategy (Mean)

Assessment Period	Force-Extension (N)	Force-Flexion (N)	HROM (%)
Pre-training	5.5	11.15	53.15
Post-training	15.7	33.15	91

The percentage change between pre and post-training values of all three hand-kinematic parameters for fixed-training participants as well as that for those who underwent adaptive-training strategy is calculated using mean values given in Table 6.6 and Table 6.7, respectively. These values of percentage change for all three hand-kinematic parameters are presented in Table 6.8. These results provide preliminary evidence that the adaptive-training strategy may provide some benefits beyond those obtained through the fixed-training strategy, particularly in relation to the force-flexion parameter. This suggests that stroke patients are more responsive to adaptive-training strategy. However, further research is required.

Table 6.8: Percentage change in hand-kinematic parameters

Training Type	**Force-Extension (%)**	**Force-Flexion (%)**	**HROM (%)**
Fixed-Training	184.06	51.93	69.32
Adaptive-Training	185.45	197.3	71.21

6.5.2 Comparison of Clinical Test Results

For group A in Table 5.7 of Chapter 5, the average clinical test values at pre and post-training periods of fixed-training strategy are re-produced in Table 6.9. While the average clinical test results for the patients who participated in adaptive-training are calculated and present in Table 6.10.

Table 6.9: Average clinical test results for group A after four weeks of fixed-training strategy (Mean)

Assessment Period	**FMA-Wrist Score (0-10)**	**FMA-Hand Score (0-14)**	**MAS-Hand Movements Score (0-6)**	**MAS-Advanced Hand Movements Score (0-6)**
Pre-training	6.5	8.3	2.8	3.3
Post-training	8.3	12	4.5	4.3

Table 6.10: Average clinical test results after four weeks of adaptive-training strategy (Mean)

Assessment Period	**FMA-Wrist Score (0-10)**	**FMA-Hand Score (0-14)**	**MAS-Hand Movements Score (0-6)**	**MAS-Advanced Hand Movements Score (0-6)**
Pre-training	4.5	5.5	2	2
Post-training	7.5	12	4	3

Using the mean values of clinical test results for fixed-training and adaptive-training groups from Table 6.9 and Table 6.10, the percentage changes in their pre and post-training values are calculated and given in Table 6.11. Similar to hand-kinematic parameters, the percentage change of the clinical tests for the adaptive-training group is higher compared to that for the fixed-training group. Therefore, the results of both physical hand improvement parameters (hand-kinematic parameters and clinical tests) show the advantages of implementing the adaptive-training strategy for post-stroke rehabilitation.

Table 6.11: Percentage change in clinical test results

Training Type	FMA-Wrist Test (%)	FMA-Hand Test (%)	MAS-Hand Movements Test (%)	MAS-Advanced Hand Movements Test (%)
Fixed-Training	27.69	44.58	60.71	30.30
Adaptive-Training	66.67	118.18	100	50

6.6 Summary

The feasibility of a patient-specific and adaptive robotic-based training strategy for stroke rehabilitation was explored in this chapter. Two post-stroke patients underwent 12 training sessions (three days per week) on AMADEO robotic device for their affected hand while brain activities were recorded by an EEG acquisition system. The analysis of the EEG signals clearly showed a decrease in the Npeak amplitude of the MRCP pattern at all selected electrodes when the patient mastered a specific training mode on AMADEO. When the new training modes were introduced to both patients, the Npeak amplitude was increased at all selected electrodes indicating the enhanced engagement of the patients. In this way, by observing MRCP's Npeak variations, the AMADEO training modes were changed.

The physical improvements in hand motor skills were determined by measurements of hand-kinematic parameters and clinical tests. The hand-kinematic parameters which include force-extension force-flexion and HROM were measured at the end of each training session. During the active training mode of AMADEO, patients showed a maximum improvement in all three hand-kinematic parameters compared to all other training modes. This indicates that the selection of appropriate training mode at the correct time, not only maintains the concentration of the patient during the training sessions but also influences the hand-kinematic parameters. Lastly, results of clinical tests showed a noticeable improvement in hand motor skills achieved by patients after completing the adaptive rehabilitation training strategy.

The comparison of hand-kinematic parameters and clinical tests for supratentorial stroke patients performed 12 sessions of fixed-training strategy with the patients who underwent 12 sessions of this adaptive-training strategy was also made. It was revealed that the adaptive-training group achieved better improvements in both hand-kinematic parameters and clinical tests than the fixed-training group. Based on these preliminary results, the adaptive-training group showed accelerated motor recovery in comparison to the fixed-training group for the same duration of 12 sessions. This could be because the current training mode was moved to the more challenging mode when the patient attained competency in the current task. This was also verified by the variation in MRCP's Npeak during the training. After all, patients are more fully engaged and so progress to the higher training levels more quickly. Therefore, this adaptive-training strategy is a preferable training strategy because it can provide patient-specific training that is more time-efficient. However, further investigations are required with larger sample size.

The proposed adaptive rehabilitation training strategy has many practical implications in clinical settings. EEG set-up is a user-friendly, cost-effective, scalable, and practical method compared to other methods such as fMRI for monitoring brain activities during rehabilitation exercises. Therefore, this adaptive rehabilitation training strategy could potentially be utilized by therapists as an aid to prescribing individualized exercises that can continuously challenge patients, keeping them engaged for more of the time. Furthermore, this training strategy can guide therapists to decide the optimum time to move to more advanced training exercises during the rehabilitation period of post-stroke patients. Ultimately, it is likely to promote faster motor and functional recovery of post-stroke patients which is in the best interests of both patients and rehabilitation centres.

Chapter 7

Conclusion and Future Work

7.1 Overview

Stroke generally diminishes the ability of the brain to send commands to the affected limb(s) to perform a required motor task. Therefore, clinical and research activities in the field of post-stroke rehabilitation are applying reverse engineering to address this problem. There is an ongoing effort to apply therapeutic training to the affected body limb(s) of stroke patients so that the damaged area of the brain can recover using the neuroplasticity phenomenon. The study reported in this thesis was a contribution to this area of research for post-stroke rehabilitation.

The project was focused on the recovery of motor disabilities of stroke-affected hands and the primary aim was to establish the relationship between the MRCP pattern, the engagement level of patients, and the rehabilitation outcomes. More specifically, this thesis aimed to enhance the outcomes of robot-assisted rehabilitation for post-stroke patients by maintaining their active engagement throughout the training sessions. Towards achieving this aim, a series of training strategies were designed, conducted and the results were validated clinically.

The major contributions of this study were three-fold:

(1) The application of the MRCP pattern as a motor intention signal was established by designing a single-session motor training strategy. It was validated on both healthy and stroke-affected subjects.

(2) The effect of a designed multi-session training strategy on the MRCP pattern and the corresponding physical improvements in hand motor skills for post-stroke patients were determined.

(3) A novel adaptive-training strategy that maximizes the rehabilitation outcomes by monitoring the variations of the MRCP pattern throughout the training period was proposed and validated on post-stroke patients.

As a conclusion to this work, this chapter reviews the major achievements of the research and presents its generic outcomes with potential benefits to others who work in this field. Several suggestions for future work are also provided in this chapter. The rest of the chapter is organized as follows. The major findings of the literature review and the adopted research design based on the research gaps are summarized in Section 7.2. The major contributions of the work are covered in Sections 7.3 to 7.6. Recommendations for future work are detailed in Section 7.7.

7.2 Comprehensive Literature Review and Research Design

The study was informed by a comprehensive literature review conducted on various applications of EEG-derived patterns (ERD/ERS and MRCP) for motor rehabilitation of post-stroke patients as described in Chapter 2. This literature review also identified research gaps in the discipline which helped in formulating the research design.

Three distinct research fields were identified in the literature search, which was further categorized into sub-fields. The first category includes intention signal classification during different or same limb movements, intention signal detection, and intention signal decoding into various kinematic properties of the limb. The second category consists of EEG-BCI applications for motor rehabilitation and contains studies that utilize EEG-derived patterns to either control the movement of robotic devices or apply different stimulations using the EEG-BCI system for motor recovery of post-stroke patients. The last category contains literature that determines the effect of motor training on EEG-derived patterns by either comparing these patterns' variation between skilled and non-skilled subjects or by studying such variations during pre and post-training periods or during the actual training period.

It is found after a comprehensive review of the literature, the most commonly used upper limb for movement classification and detection problem is the hand [109, 112, 119, 121, 123, 124, 135, 136, 138, 287, 296-298]. The reason for this preference of hand tasks for intention classification and detection problem is that the hand plays the most vital role in our daily life activities as well as it has greater complexity of movements as compared to other upper limbs. Therefore, keeping the importance of hand motor recovery in stroke rehabilitation, this project targeted the rehabilitation training for hand and finger impairments of stroke patients using AMADEO rehabilitation device.

Another aspect of post-stroke rehabilitation investigated in this project is to determine the effect of the designed training protocol on the MRCP pattern. There are conflicting reports in the literature about the changes in the features of the MRCP pattern resulted from the achievement in task competency due to motor training. The studies, investigating the effect of motor skill acquisition through training, reported different variations in the features of the MRCP pattern. Furthermore, all these studies investigated the effect of learning of simple motor tasks on the MRCP pattern for healthy subjects in non-clinical applications. These research gaps were addressed in Chapter 5 by determining the effect of re-learning of lost fine motor skills of fingers and hand through a specific rehabilitation training strategy for the post-stroke patient on the MRCP pattern. As well as by designing and validating the novel and adaptive rehabilitation strategy for the post-stroke motor recovery of hand in Chapter 6.

7.3 Measurement of Subject Engagement Level through MRCP

Robot-assisted rehabilitation training promises to provide task-oriented, high-intensity, and repetitive treatments to patients with motor deficits [40]. However, the effectiveness of such rehabilitation training mainly depends on the active participation of the subjects. This is because robot-assisted devices can provide excessive assistance to the patients that may have a negative effect on the re-learning of their motor skills. Moreover, active participation of post-stroke patients is considered to be a core reason for neuroplasticity induction [18]. Therefore, at the first stage of this research project, a single-session experiment was designed for the intention signal detection for hand motor tasks during two distinct training protocols as explained in Chapter 4.

The knowledge from available literature was used to detect the selected hand motor task related to this research project. This project requires the understanding of intention signal detection during hand-grasping tasks using the AMADEO device, therefore, the hand closing action was detected using features of the MRCP pattern and SVM algorithm. Moreover, this detection of intention signal was used as a tool to determine the active participation of both healthy subjects and post-stroke patients. The experimental results revealed that the Npeak amplitude of the MRCP pattern was more pronounced when subjects performed hand motor tasks using a 2D game training protocol compared to that during the visual-cue protocol. The greater Npeak amplitude depicted better engagement of subjects during game-based training protocols. Moreover, when the features of the MRCP pattern were fed to the SVM classifier, the intention detection for motor tasks during the 2D game had greater classifier accuracy compared to that performed during the visual-cue protocol. The average classification accuracies for the visual-cues protocol were 67.56 % for healthy subjects and 56.24 % for stroke patients, whereas the accuracies for the game protocol were 79.7 % for the healthy participants and 66.64 % for the post-stroke patients. These results helped in understanding the MRCP pattern variations due to different exercise protocols and it was then used in designing further robot-assisted training strategies for this research project.

7.4 Decrease in MRCP's Npeak with Achievement in Task Competency

In Chapter 5, it was shown that after multi-session robot-assisted training, the MRCP's Npeak amplitude decreased. This decrease in Npeak amplitude means that patients required fewer cortical resources for the planning and execution of the motor tasks when the participants achieved competency in the practiced motor task. With the achievement in task competency, the hand motor skills of stroke patients were also improved. The improvements in hand motor skills were verified by two methods. The first method was the use of the commonly employed clinical tests which include FMA (wrist and hand sections) and MAS (hand movements and advanced hand movements sections) tests. While the second method was the measurement of hand-kinematic parameters (force-flexion, force-extension, and HROM) using the AMADEO assessment tool. This study advanced the literature by performing and evaluating a longitudinal study with post-stroke patients and determining the decrease in MRCP's Npeak amplitude when the patients achieve competency in task performance. Moreover, the training protocol used for the stroke patients was carefully designed to improve their hand strength as well as the range of movements of their fingers and thumb.

The aforementioned training protocol was validated with seven post-stroke patients. A larger number of participants and the inclusion of the control group in the study would have strengthened our confidence in the result. However, the number of potential participants was limited by the clinical availability of suitable participants within the time frame of the study. Participants in the study were relatively heterogeneous with regard to the level of impairments as well as the time length from stroke onset to the intervention commencement among the recruited stroke patients. It may be the case that with a more homogeneous group of participants more uniform and statistically significant data could have been extracted. However, our inclusion criteria had to be wide; otherwise, clinical availability would have not allowed us to recruit a sufficient number of participants.

7.5 Training Strategy Design and its Outcomes Based on Lesion Location

Many authors, in the literature, concluded that the post-stroke recovery of motor skills depends upon the stroke lesion location. For instance, Shelton and Reding [299], demonstrated that the probability of isolated upper limb recovery decreased progressively with lesion locations from cortex to corona radiata, and the posterior limbs of the internal capsule. Similarly, Schiemanck et al. [300] showed that stroke patients having lesion locations in internal capsules have the lowest probability of isolated motor recovery compared to lesion locations at the cortex, sub-cortex, and corona radiata after one-year post-stroke. After performing a longitudinal study on stroke patients, Feydy et al. [301] concluded that their motor recovery was subjected to whether the primary motor cortex was involved in the lesion location or not. Moreover, some authors reported the effect of stroke lesion location on brain activities. For example, Park et al. [266] used ERD/ERS analysis of the EEG signal to show that the hemispheric asymmetry and topographic characteristics of the beta band power significantly varied among stroke patients' groups with different lesion locations. Similarly, in [267], the authors showed that the amplitude of ERD decreased for stroke patients having lesion locations involving the motor cortex. The authors in [299-301] demonstrated that stroke recovery depends on stroke lesion location and the studies described in [266, 267] show how ERD/ERS pattern differs due to variable stroke lesion locations. However, there is no consensus on how MRCP patterns vary as a result of motor training in post-stroke patients with variable lesion locations. This was found from the experimental results presented in Chapter 5.

The multi-session robot-based training strategy, explained in Chapter 5, was tested for stroke patients having lesion locations in the supratentorial or infratentorial region of their brain. The supratentorial and the infratentorial stroke patients took part initially for four weeks of the designed rehabilitation training strategy. The supratentorial stroke patients demonstrated a significant recovery in their hand motor skills as well as the corresponding decrease in the MRCP's Npeak amplitude. Whereas, the infratentorial stroke patients could not obtain significant results after the first four weeks of training and their training was extended for a further four weeks. When the results of the extended training strategy were analyzed for the infratentorial stroke group, a significant decrease in the Npeak amplitude of the MRCP pattern and substantial improvement in hand motor skills were obtained. Hence, it was inferred from the experimental results that the intensity of the rehabilitation training strategy (training protocol design and its duration) should be formulated according to the lesion locations of the stroke patients included in the study.

7.6 Novel Adaptive Rehabilitation Training Strategy

A novel strategy for a patient-specific and adaptive robot-based stroke rehabilitation was explored in Chapter 6. This strategy started with a simple training mode available in AMADEO and progressed to its more advanced training modes based on the patient's level of engagement. AMADEO offers four modes of rehabilitation training with increasing intensity; Mode 1: CPM; Mode 2: CPMplus; Mode 3: Assistive training; and Mode 4: Active training. It has been learned from the literature and confirmed by the experimental results described in Chapter 4 that MRCP's Npeak amplitude varies based on the patient's level of engagement while performing motor tasks during different training protocols. Moreover, it is also found from the experimental results in Chapter 5 that the Npeak decreases when the patients achieve competency in the current training mode. Therefore, the patient's engagement was monitored constantly in the adaptive rehabilitation training strategy and when the patient gained competency in the current training mode, the next training mode was selected.

This adaptive rehabilitation technique was tested on two post-stroke patients with supratentorial lesion location who underwent four weeks of training (three training sessions per week) on the AMADEO device for their affected hands. This experiment revealed the following results; firstly, a decrease in the Npeak of MRCP pattern was observed when the patient mastered a specific training mode on AMADEO. This determined the number of days for which a patient underwent a particular training mode. Secondly, when any new training mode was introduced to the patient, the Npeak was increased indicating the enhanced engagement of the patient during the training session. Thirdly, the maximum improvement in all hand-kinematic parameters was gained by the patients during the active training mode when they had maximum engagement level.

Using this rehabilitation technique, the number of days for each training mode was determined by the patient's MRCP pattern variations. In total, both patients received 360 minutes of adaptive robot-assisted training as follows: one patient spent 90 minutes on CPM, 120 minutes on CPMplus, 90 minutes on assistive training, and 60 minutes on active training while the other patient spent 60 minutes on CPM, 120 minutes on CPMplus, 120 minutes on assistive training, and the last 60 minutes on active training.

A comparison of the motor skill improvements between the fixed-training strategy performed in Chapter 5 and the adaptive-training strategy proposed in Chapter 6 revealed noteworthy outcomes. It shows that the hand-kinematic parameters and clinical tests for supratentorial stroke patients who performed the fixed-training strategy were inferior to those supratentorial stroke patients who underwent the adaptive-training strategy. The adaptive-training group achieved 145.37 %, 1.39 %, and 1.89 % more improvements in force-flexion, force-extension, and HROM respectively compared to the fixed-training group. While the percentage improvement in the FMA-wrist, FMA-hand, MAS-hand, and MAS-advanced hand movements' clinical tests were 38.98 %, 73.6 %, 39.29 %, and 19.7 % respectively. It is, therefore, concluded that the adaptive rehabilitation training strategy is more effective because it provides patient-specific training resulting in a significantly better enhancement in hand-motor skills.

The implementation of adaptive-training strategy at rehabilitation centres can provide valuable guidance to therapists on when it is appropriate to stimulate patients with more challenging tasks to keep them engaged. It is likely to promote rapid neuroplasticity changes leading to a faster functional and motor recovery of the patients. In future work, this approach needs to be applied to a large cohort of post-stroke patients to investigate the efficacy of the method.

7.7 Future Work Recommendations

There can be an exploration of various other training strategies to enhance the outcomes of stroke rehabilitation along with the strategies demonstrated in this thesis. This includes the use of more immersive technologies for motor training with wearable robotic devices, the design of an online EEG-BCI system for active stroke rehabilitation, neuroplasticity measurement using fMRI as well as utilizing stimulation techniques to augment neuroplasticity for stroke recovery. These promising advances and plausible future directions of the developments in the field of stroke rehabilitation are described in this section.

7.7.1 Use of VR Games and Wearable Hand Robotic Devices

VR is a computer-based technology that provides real-time simulation of activity, environment, or scenario that allows users to interact by providing augmented sensory feedback in a safe, ecological, and individualized 2D or 3D environment. The patients then perform specific actions or motor tasks to achieve a goal using these environments [302]. Moreover, such VR interventions can provide patients with enjoyable exercises and games towards their rehabilitation which, in turn, increases their motivation level [14].

It is confirmed from the experimental work of this project that the active participation of stroke patients is one of the essential elements for a fast recovery of lost motor skills. However, there is still room for future research to enhance the engagement level of patients during rehabilitation exercises. In Chapter 4, it was demonstrated that stroke patients showed better engagement levels during 2D games compared to visual-cue protocol. This engagement level can be further enhanced by the use of VR-based games and simulated environments. This could be confirmed by comparing the variations in EEG-derived patterns during hand motor tasks using VR-based 2D and 3D games with that during a simple 2D game(s).

Furthermore, AMADEO is an end-effector-based stationary system for hand physiotherapy whereas, there are other 5-DOF hand robotic devices that are more portable and work well with the VR-based rehabilitation gaming system. These devices include CyberGrasp by CyberGlove Systems LLC [303], Hand of Hope by Rehab-Robotics Company, and Gloreha by Idrogenet srl. Therefore, these more portable devices can also be incorporated while designing hand-based rehabilitation strategies for post-stroke patients in the future.

7.7.2 Online EEG-BCI System Design for Active Post-Stroke Training

Various BCI systems have been explored extensively in the field of stroke rehabilitation. They can provide direct communication and control paths between the brain and the external devices without using the peripheral nerves or muscles [57]. MRCP pattern can be used as feedback to the closed-loop BCI system as mentioned in Section 2.4 of Chapter 2. Therefore, an online EEG-BCI system for active rehabilitation training of post-stroke patients could be designed in the future.

In an adaptive rehabilitation training strategy proposed in this project, the decision to progress to the next AMADEO training mode was made based on offline EEG data analysis, and the new training mode was implemented on the next training day. If the intention signal is measured continuously during the training session through online analysis of the EEG data, then it is possible to progress to the next training mode as soon as the patient achieves competency in the current training mode. For such protocol, a closed-loop EEG-BCI system needs to be designed in which the MRCP pattern is used in the feedback loop as a measure of the engagement level of the patient. This training scheme will ensure the active participation of the patient throughout the training period, therefore increasing the recovery speed as well as reducing the required overall duration for post-stroke rehabilitation.

7.7.3 Neuroplasticity Measurements using fMRI

Recent advancements in non-invasive technologies lead to a more profound understanding of neuroplasticity and its relationship to post-stroke recovery [26, 304-306]. Many novel stroke rehabilitation strategies, such as the adaptive rehabilitation training strategy developed in this research project, envisage triggering changes in the neural pathways of the brain due to the neuroplasticity phenomena. However, the use of EEG alone cannot measure the neuroplasticity changes occurring during stroke recovery. Therefore, the use of other modalities is required for quantifying these neuroplasticity changes.

fMRI is one of the modalities that is being explored for measuring the neuroplasticity effect during and after the stroke recovery period [307-310]. fMRI is a non-invasive technique used to map human brain activities by measuring changes in the blood flow that occurs as a result of an increase in neural activity [311, 312]. Recently, authors in [313] determined brain activations during the hand-grasping task using fMRI with healthy subjects. This builds the confidence of developing a similar protocol for the hand motor recovery of the actual stroke patients. Therefore, for future work, fMRI measurement can be used as an assessment method for rehabilitation training strategies. In this way, the neuroplasticity phenomena underlying this recovery mechanism in stroke patients as a result of rehabilitation can be verified.

7.7.4 Augmentation of Neuroplasticity using Stimulation Techniques

The neuroplasticity in the affected brain of the post-stroke patients can be augmented using various types of stimulation techniques [314-316]. One of these techniques is transcutaneous neuromuscular stimulation also called FES which is commonly applied in the stroke rehabilitation period. FES application can strengthen muscles, improve motor control of the affected limb, decrease pain, reduce spasticity as well as increase the range of movement of the affected limb(s) [317-319]. Furthermore, researchers have explored FES application based on intention detection using EEG-BCI system for wrist and hand movements [192], for arm [194, 320] or they use FES signal in the feedback to improve the performance of EEG-BCI systems [195, 196]. Different brain activities are also being modulated using FES application for both UE and LE recovery of post-stroke patients [197-199, 207, 208]. However, there is still a research gap of how to use FES for augmentation of fine finger motor skill improvement of stroke patients to induce neuroplasticity.

The other category of stimulation techniques is Non-Invasive Brain Stimulation (NIBS) which includes repetitive TMS and tDCS. Such stimulation techniques improve the motor deficits in the patients by either increasing the cortical excitation of the affected hemisphere or by decreasing the excitation of the unaffected hemisphere [321-323]. Furthermore, the increase in motor cortex excitation appears to be linked to the re-learning of the lost motor functions in post-stroke patients [324, 325]. Also, the combination of rehabilitation training coupled with NIBS protocols can have better rehabilitation outcomes when compared to the effect of motor training or stimulation alone [326-328]. Although the use of TMS and tDCS application for stroke rehabilitation has been demonstrated in the literature [228-232], the application of NIBS at different stroke rehabilitation stages, as well as the most effective protocols for NIBS applications, can be explored in future.

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Appendices

Appendix 1

1. Ethics Application Approvals

(i) From March 2017 to March 2018

Dear Professor Naghdy,

Thank you for submitting the progress report. I am pleased to advise that renewal of the following Human Research Ethics application has been approved.

Please note that, as this can only take effect from the date of approval and as the previous approval expired on 10 November 2016, if any data was collected between 10 November 2016 and 8 march 2017 it was collected without ethics approval. This is in breach of your obligation as a researcher to maintain approval from appropriate ethics committees (Australian Code for the Responsible Conduct of Research 2007).

Ethics Number:	2014/400
AuRed Number:	HREC/14/WGONG/91
Project Title:	Robotic-assisted upper extremity rehabilitation for post-stroke patients
Researchers:	Butt Maryam; Carmody John; Du Haiping; Huang Xianwei; Murray Geoffrey; Naghdy Golshah; Ros Montse; Naghdy Fazel
Renewed From:	07/03/2017
New Expiry Date:	08/03/2018

Please note that approvals are granted for a twelve month period. Further extension will be considered on receipt of a progress report prior to the expiry date.

This certificate relates to the research protocol submitted in your original application and all approved amendments to date. Please remember that in addition to completing an annual report, the Human Research Ethics Committee also requires that researchers immediately report:

- proposed changes to the protocol including changes to investigators involved
- serious or unexpected adverse effects on participants
- unforeseen events that might affect continued ethical acceptability of the project

A condition of approval by the HREC is the submission of a progress report annually and a final report on completion of your project. This progress report must be submitted by accessing the IRMA system prior to the expiry date.

Yours sincerely,
Susan Thomas

Dr Susan Thomas,
Chair, UOW & ISLHD Health and Medical Human Research Ethics Committee
The University of Wollongong and Illawarra and Shoalhaven Local Health District Health and Medical HREC is constituted and functions in accordance with the NHMRC National Statement on Ethical Conduct in Human Research. The processes used by this HREC to review multi-centre research proposals have been certified by the National Health and Medical Research Council.

1. Ethics Application Approvals

(ii) From March 2018 to March 2019

Dear Professor Naghdy,

Thank you for submitting the progress report. I am pleased to advise that renewal of the following Human Research Ethics application has been approved.

Ethics Number:	2014/400
AuRed Number:	HREC/14/WGONG/91
Project Title:	Robotic-assisted upper extremity rehabilitation for post-stroke patients
Researcher/s:	Huang Xianwei; Naghdy Golshah; Ros Montse; Naghdy Fazel; Murray Geoffrey; Butt Maryam; Carmody John; Du Haiping
Renewed From:	09/03/2018
New Expiry Date:	08/03/2019

Please note that approvals are granted for a twelve month period. Further extension will be considered on receipt of a progress report **prior to the expiry date**.

This certificate relates to the research protocol submitted in your original application and all approved amendments to date. Please remember that in addition to completing an annual report, the Human Research Ethics Committee also requires that researchers immediately report:

- proposed changes to the protocol including changes to investigators involved
- serious or unexpected adverse effects on participants
- unforeseen events that might affect continued ethical acceptability of the project

A condition of approval by the HREC is the submission of a progress report annually and a final report on completion of your project. This progress report must be submitted by accessing the IRMA system prior to the expiry date.

Yours sincerely,

Susan Thomas

Dr Susan Thomas,
Chair, UOW & ISLHD Health and Medical Human Research Ethics Committee

The University of Wollongong and Illawarra and Shoalhaven Local Health District Health and Medical HREC is constituted and functions in accordance with the NHMRC National Statement on Ethical Conduct in Human Research. The processes used by this HREC to review multi-centre research proposals have been certified by the National Health and Medical Research Council.

1. Ethics Application Approvals

(iii) From March 2019 to March 2020

Dear Professor Naghdy,

Thank you for submitting the progress report. I am pleased to advise that renewal of the following Human Research Ethics application has been approved.

Ethics Number:	2014/400
AuRed Number:	HREC/14/WGONG/91
Project Title:	Robotic-assisted upper extremity rehabilitation for post-stroke patients
Researchers:	Butt Maryam; Carmody John; Du Haiping; Huang Xianwei; Murray Geoffrey; Naghdy Golshah; Ros Montserrat; Naghdy Fazel
Renewed From:	09/03/2019
New Expiry Date:	08/03/2020

Please note that approvals are granted for a twelve month period. Further extension will be considered on receipt of a progress report **prior to the expiry date**.

This certificate relates to the research protocol submitted in your original application and all approved amendments to date. Please remember that in addition to completing an annual report, the Human Research Ethics Committee also requires that researchers immediately report:

- proposed changes to the protocol including changes to investigators involved
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2. Participation Consent Form

CONSENT FORM

TITLE: BCI Integration in Robot-Assisted Rehabilitation for Post Stroke Patients
RESEARCHER'S NAME: Maryam Butt
SITE: University of Wollongong (UOW)/Port Kembla Hospital

I have been given information about "**BCI Integration in Upper Extremity Robot-Assisted Rehabilitation for Post Stroke Patients**" and discussed the research project with Mrs Maryam Butt who is conducting this research as a part of PhD project supervised by Associate Prof. Golshah Naghdy in the School of Electrical, Computer and Telecommunications Engineering at University of Wollongong.

I have been advised of the potential risks and burdens associated with this research, which includes up to 2 hours of my time, the possibility of feeling tired during training. I have had the opportunity to ask Mrs Maryam Butt any question I may have had about the research and my participation.

I understand that my participation in this research is voluntary, I am free to refuse to participate and I am free to withdraw from the research at any time. My refusal to participate or withdrawal of consent will not affect my relationship with the Faculty of Informatics or my relationship with the University of Wollongong, Wollongong Hospital, or Port Kembla Hospital.

If I have any enquiries about the research, I can contact Maryam Butt on or Prof. Golshah Naghdy on or if I have any concern or complaint regarding the way the research is or has been conducted, I can contact the Ethics Officer, Human Research Ethics Committee, Office of Research, University of Wollongong on 02-4221 4457.

By signing below I am indicating my consent to participate in the project. I understand that my information will be kept confidential.

I understand that the data collected from my participation will be used for a PhD thesis and will be used in summary form in journal or conference papers, and I consent for it to be used in that manner.

Signed *Date*

..../....../......

Name (please print)

....

3. Honorary Research Appointment Application Approval

Health
Illawarra Shoalhaven
Local Health District

NSW GOVERNMENT

Research Support Office
Telephone: 02 4253 4800
Facsimile: 02 4253 4803

TRIM NO: DT17/147210
Ref: 2014/400
APPROVAL

Ms Maryam Butt

Dear Ms Butt

I wish to advise that your application for Appointment of Honorary Research Associate with the Illawarra Shoalhaven Local Health District (ISLHD) has been approved.

This appointment is for the purpose of conducting the following project and specifically for activities, approved by ISLHD, undertaken as part of the project and is only valid with a current Human Research Ethics Committee approval and receipt of an annual report:

HREC project number: 2014/400
Project Title: Robotic-assisted upper extremity rehabilitation for post-stroke patients

Please note if you wish to seek an extension of your appointment for further projects you will need to provide details, in writing to this office, of the proposed project and associated ISLHD clinician(s).

Yours faithfully

KRISTY PIERCE
Research Governance Officer

12 October 2017

c.c A/Prof John Carmody, HOD – Neurology Department

Research Support Office
Level 8, Block C West, Wollongong Hospital
(LMB 8808, SCMC NSW 2521)

Appendix 2

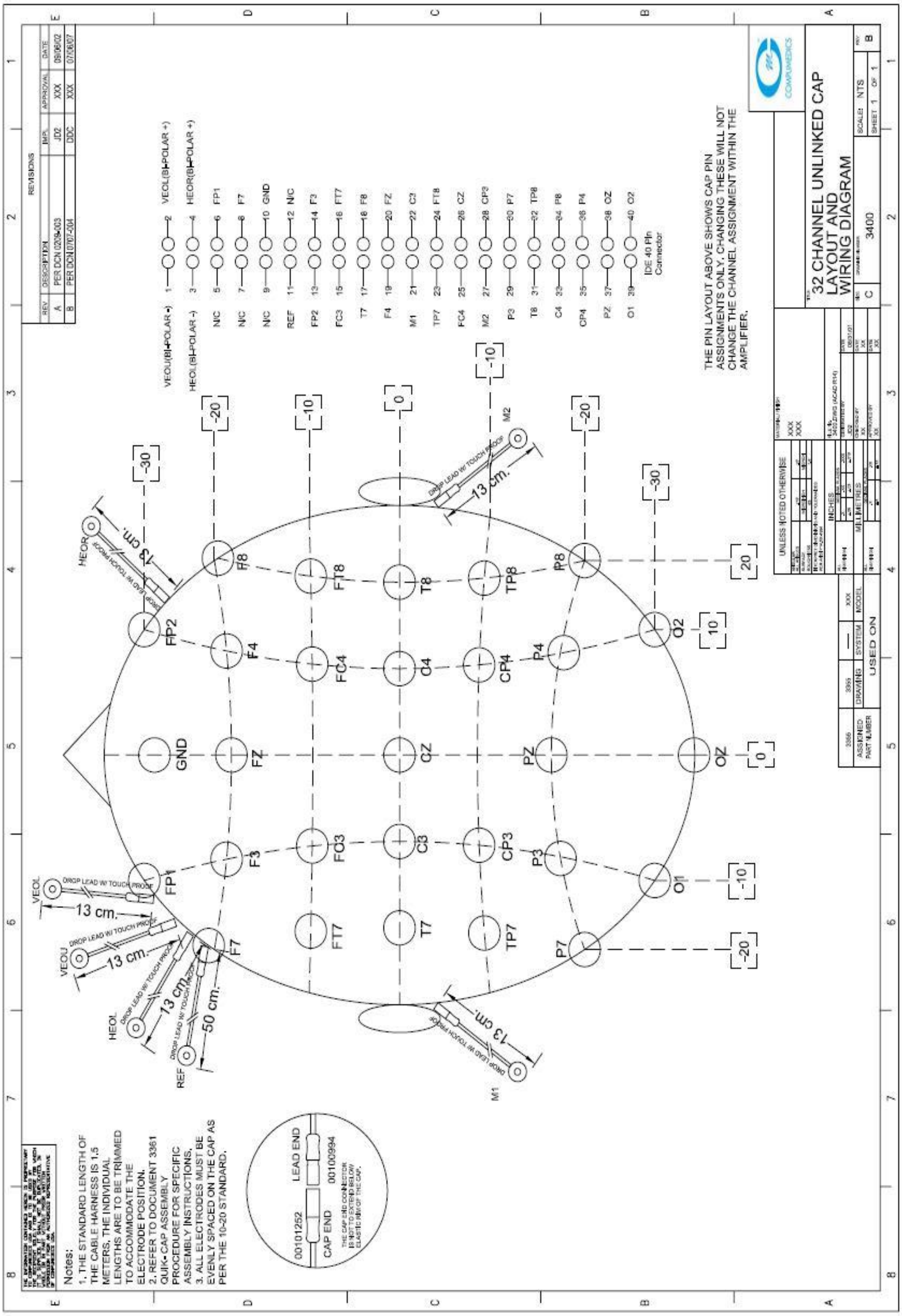
1. IP Addresses

(i) The IP address for the host PC is 192.168.10.1

(ii) The IP address for the Grael 4K amplifier is 192.168.10.201

Appendix 3

1. Wiring Diagram of 32-Channel Quick-Cap by Compumedics Neuroscan



Appendix 4

1. Fugl-Meyer Assessment Upper Extremity (FMA-UE)

(i) FMA-Wrist Clinical Test

WRIST support may be provided at the elbow to take or hold the position, no support at wrist, check the passive range of motion prior testing		**none**	**partial**	**full**
Stability at 15° dorsiflexion elbow at 90°, forearm pronated shoulder at 0°	less than 15° active dorsiflexion dorsiflexion 15°, no resistance is taken maintains position against resistance	0	1	2
Repeated dorsiflexion / volar flexion elbow at 90°, forearm pronated shoulder at 0°, slight finger flexion	cannot perform volitionally limited active range of motion full active range of motion, smoothly	0	1	2
Stability at 15° dorsiflexion elbow at 0°, forearm pronated slight shoulder flexion/abduction	less than 15° active dorsiflexion dorsiflexion 15°, no resistance is taken maintains position against resistance	0	1	2
Repeated dorsifexion / volar flexion elbow at 0°, forearm pronated slight shoulder flexion/abduction	cannot perform volitionally limited active range of motion full active range of motion, smoothly	0	1	2
Circumduction	cannot perform volitionally jerky movement or incomplete complete and smooth circumduction	0	1	2
	Total B (max 10)			

(ii) FMA-Hand Clinical Test

HAND support may be provided at the elbow to keep 90° flexion, no support at the wrist, compare with unaffected hand, the objects are interposed, active grasp		**none**	**partial**	**full**
Mass flexion from full active or passive extension		0	1	2
Mass extension from full active or passive flexion		0	1	2
	GRASP			
A – flexion in PIP and DIP (digits II-V) extension in MCP II-V	cannot be performed can hold position but weak maintains position against resistance	0	1	2
B – thumb adduction 1-st CMC, MCP, IP at 0°, scrap of paper between thumb and 2-nd MCP joint	cannot be performed can hold paper but not against tug can hold paper against a tug	0	1	2

C - opposition pulpa of the thumb against the pulpa of 2-nd finger, pencil, tug upward	cannot be performed can hold pencil but not against tug can hold pencil against a tug	0	1	2
D – cylinder grip cylinder shaped object (small can) tug upward, opposition in digits I and II	cannot be performed can hold cylinder but not against tug can hold cylinder against a tug	0	1	2
E – spherical grip fingers in abduction/flexion, thumb opposed, tennis ball	cannot be performed can hold ball but not against tug can hold ball against a tug	0	1	2
Total C (max 14)				

2. Motor Assessment Scale (MAS)

(i) Hand Activities

1. Sitting at a table (Wrist Extension): Affected forearm resting on table. Place cylindrical object in palm of patient's hand. Patient asked to lift object off table by extending the wrist – no elbow flexion allowed.

2. Sitting at a table (Radial Deviation of Wrist): Therapist should place forearm with ulnar side on table in mid-pronation/supination position. Thumb in line with forearm and wrist in extension. Fingers around cylindrical object. Patient is asked to lift hand off table. No wrist flexion or extension.

3. Sitting (Pronation / Supination): Affected arm on table with elbow unsupported at side. Patient asked to supinate and pronate forearm (¾ range acceptable).

4. Place a 5 inch ball on the table so that the patient has to reach forward with arms extended to reach it. Have the patient reach forward with shoulders protracted, elbows extended, and wrist in neutral or extended, pick up the ball with both hands and put it back down in the same spot.

5. Have the patient pick up a polystyrene cup with their affected hand and put it on the table on the other side of their body without any alteration to the cup.

6. Continuous opposition of thumb to each finger 14 x in 10 seconds. Each finger in turn taps the thumb, starting with the index finger. Do not allow thumb to slide from one finger to the other or go backwards.

Task No.	1	2	3	4	5	6
Score						
Total MAS- Hand Movements Score			/ 6			

(ii) Advanced Hand Activities

1. Have the patient reach forward to pick up the top of a pen with their affected hand, bring the affected arm back to their side and put the pen cap down in front of them.

2. Place 8 jellybeans, (beans), in a teacup an arm's length away on the affected side. Place another teacup an arm's length away on the intact side. Have the patient pick up one jellybean with their affected hand and

place the jellybean in the cup on the intact side.

3. Draw a vertical line on a piece of paper. Have the patient draw horizontal lines to touch the vertical line. The goal is 10 lines in 20 seconds with at least 5 lines stopping at the vertical.

4. Have the patient pick up a pen/pencil with their affected hand, hold the pen as for writing, and position it without assistance and make rapid consecutive dots (not strokes) on a sheet of paper. Goal: at least 2 dots a second for 5 seconds.

5. Have the patient take a dessert spoon of liquid to their mouth with their affected hand without lowering the head toward the spoon or spilling.

6. Have the patient hold a comb and comb the back of their head with the affected arm in abduction and external rotation, forearm in supination.

Task No.	1	2	3	4	5	6
Score						
Total MAS- Advanced Hand Movements Score				/ 6		