MEASUREMENT OF ENGAGEMENT AND CORTICAL REORGANIZATION IN BRAINS OF STROKE PATIENTS VIA ELECTROENCEPHALOGRAPHY (EEG) AS A RESULT OF VISUAL FEEDBACK THERAPY

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DECLARATION

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

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STATEMENT 1

This thesis is the result of my own investigations, except where otherwise stated.
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ABSTRAK

Selaras dengan kemajuan bidang perubatan baru-baru ini, terdapat pelbagai inovasi yang diaplikasikan di dalam bidang pemulihan strok untuk mengurangkan kebosanan pesakit sambil meningkatkan penglibatan mereka di dalam latihan pemulihan yang berulang. Ini termasuk terapi yang menggunakan maklum balas visual dalam persekitaran realiti maya. Selain itu, pengukuran keadaan otak sebelum dan selepas pemulihan juga penting untuk memantau proses pemulihan pesakit. Kajian ini secara amnya merangkumi dua aspek utama, kesan terapi maklum balas visual terhadap penglibatan pesakit strok di dalam latihan pemulihan mereka, serta reka bentuk algoritma pengukuran pemulihan fungsi otak melalui Elektroensefalografi (EEG). EMOTIV EPOC + ialah peranti EEG yang digunakan dalam penyelidikan ini untuk mengukur indeks penglibatan serta pemulihan fungsi otak melalui isyarat EEG yang direkodkan.

Satu eksperimen dilakukan terhadap lima orang sihat yang menggunakan mesin pemulihan iLLSRM dengan dan tanpa maklum balas visual. Indeks penglibatan (EI) diukur menggunakan formula $\boldsymbol{EI} = \frac{\beta}{\alpha + \theta}$. Hasil daripada eksperimen, nilai purata EI bagi subjek sihat menggunakan mesin ini dengan maklum balas visual adalah 24.53% lebih tinggi daripada tanpa maklum balas visual. Ini menunjukkan bahawa penggunaan terapi maklum balas visual dapat digunakan untuk membantu pesakit-pesakit strok untuk fokus dan menglibatkan diri dalam sesi pemulihan dan seterusnya menguatkan laluan neuromotor. Untuk pengukuran pemulihan fungsi otak pula, nilai koheren dikira antara isyarat EEG yang direkodkan daripada elektrod yang terletak di atas korteks motor. Sistem ini kemudiannya dibandingkan dengan teknik yang berdasarkan pengimejan resonans magnet fungsian (fMRI). Indeks koheren bagi orang sihat ialah 0.494 ± 0.0591, sedangkan indeks purata fMRI antara korteks motor utama kiri dan kanan subjek sihat ialah 0.537 ± 0.0958. Peratusan perbezaan adalah hanya 8.01%. Oleh itu, disimpulkan bahawa EEG boleh digunakan sebagai alternatif kepada fMRI di dalam mengukur pemulihan fungsi otak. Dalam masa depan, kajian klinikal akan dijalankan untuk melibatkan pesakit strok di dalam menilai keberkesanan rawatan maklum balas visual bagi merangsang pemulihan strok serta untuk mengesahkan kegunaan indeks koheren beta EEG sepanjang tempoh pemulihan mereka.

ABSTRACT

In line with recent advancement in medical field, there are various innovations in the stroke rehabilitation field in order to reduce the boredom of patients while enhancing their participation in the repetitive rehab exercises. This includes the visual feedback therapy. Besides, the measurement of the state of brains before and after rehab is important in monitoring the recovery of patients. This research covers two major aspects, the influence of the goal-oriented visual feedback rehab system on the engagement of stroke patients in their rehabilitation exercises, as well as the design of brain functional recovery quantification algorithm via Electroencephalography (EEG). EMOTIV EPOC+ is the EEG device used in this research to quantify engagement index as well as the brain functional recovery through its recorded EEG signals.

An experiment is carried out on five healthy subjects using an iLLSRM rehab machine with and without visual feedback display. Engagement index (EI) is measured using formula $\boldsymbol{EI = \frac{\beta}{\alpha+\theta}}$. At the end of the experiment, the mean value of engagement index of healthy subjects using this machine with visual feedback was found 24.53% higher than without visual feedback. This indicated that the use of visual feedback can help stroke patients to be more engaged during the rehab session and hence strengthening the neuromotor pathways. For the brain functional recovery quantification, coherence values are computed among the EEG signals recorded from electrodes lying above motor cortex. The system is then compared with the established technique based on the functional magnetic resonance imaging (fMRI). From the results, the resting-state EEG beta coherence index of healthy subjects was found to be 0.494±0.0591, whereas the average fMRI functional connectivity between left and right primary motor areas of healthy subjects was 0.537±0.0958. The percentage difference was only 8.01% and this shows that the two methods are comparable. Hence, it is deduced that EEG is capable to be used as an alternative to fMRI in quantifying the brain functional recovery. For the future work, a clinical trial will be carried out to involve stroke patients in assessing the efficacy of the visual feedback treatment in facilitating stroke recovery as well as to further validate the reliability of EEG brain beta coherence index throughout their recovery processes.

CHAPTER 1: INTRODUCTION

1.1 Overview of Stroke

According to the World Heart Federation, 15 million people worldwide suffered from stroke and nearly five million are left permanently disabled with paralysis and weaknesses every year [1]. For instance, approximately 50,000 Canadians and 780,000 Americans suffered from stroke each year, resulting in disabilities, reduced mobility, independence, and quality of life [2, 3]. This has made stroke as one of the leading causes of disability. The motor function can be affected by stroke, accident or aging. One-sided paralysis is a common effect of stroke which diminishes the strength and control of the motor system, including upper and lower limbs. About 80% of patients with stroke experience motor weakness/hemiparesis [4].

Generally, there are two major kinds of stroke, namely ischemic and hemorrhagic stroke. The ischemic stroke is due to an obstruction within a blood vessel supplying blood to the brain, because of the presence of blood clot. Blood clot is often due to atherosclerosis, which is a build-up of fatty deposits on the inner lining of a blood vessel. Consequently, a portion of the brain becomes deprived of oxygen and will stop functioning [5]. This type of stroke accounts for 87 percent of all stroke cases. On the other hand, a hemorrhagic stroke occurs when a blood vessel carrying oxygen and nutrients to the brain bursts and spills blood into the brain. The most common cause of hemorrhagic stroke is uncontrolled hypertension or high blood pressure [5].

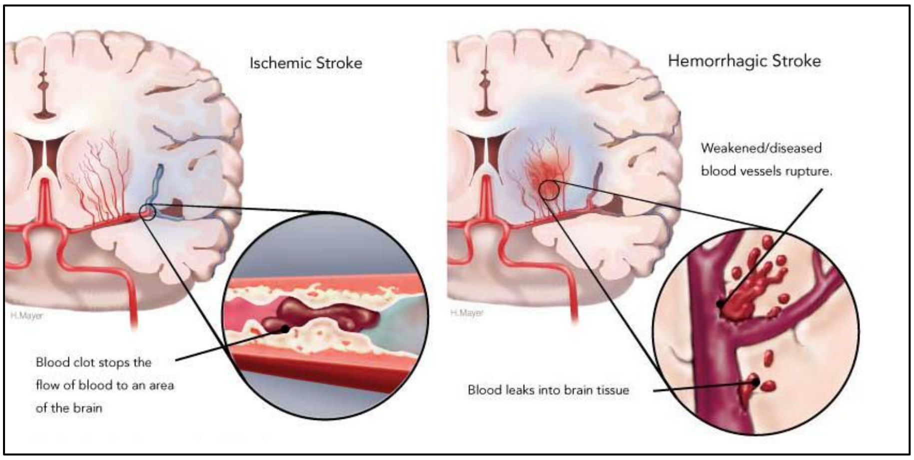


Figure 1.1: Occurrence of ischemic and hemorrhagic stroke [5]

1.2 Electroencephalography (EEG)

In 1929, a German Psychiatrist called Hans Berger conducted an experiment by placing electrodes on his daughter's scalp while his daughter was doing mental arithmetic questions. His intention is to prove his hypothesis concerning the electrical activity of brains [6]. Eventually, he discovered that the brain activity increased when his daughter was doing difficult mathematic calculation involving multiplication. This changed the view of the whole world because he proved that it is possible to measure and quantify human brain electrical activity. Subsequently, in 1935, a neuroscientist named Adrian demonstrated the recording technique of brain activity in live during the meeting of the Physiological Society in London [6].

Since then, the electroencephalography (EEG) became the hot topic in the biomedical research. It is proven to be a non-invasive electrophysiological monitoring technique to record electrical activity of the brain. By placing small metal discs with thin electrodes on the scalp of human, EEG is able to track and capture brainwave patterns. Technically, it measures fluctuations of voltage as a result of ionic current within the neurons in the brain [7]. The signals will then be sent to a computer for further analysis to indicate brain activity. Thus, it is capable and usually be used to find or identify problems and diseases based on the abnormalities of electrical activity happening in the brain. The Figure 1.2 below shows the transmission mechanism of signals between two neurons. The cell body of a neuron communicates with its own terminals via electrical signals or called action potentials along the axon, whereas communication between neurons is achieved via chemical synapses [7].

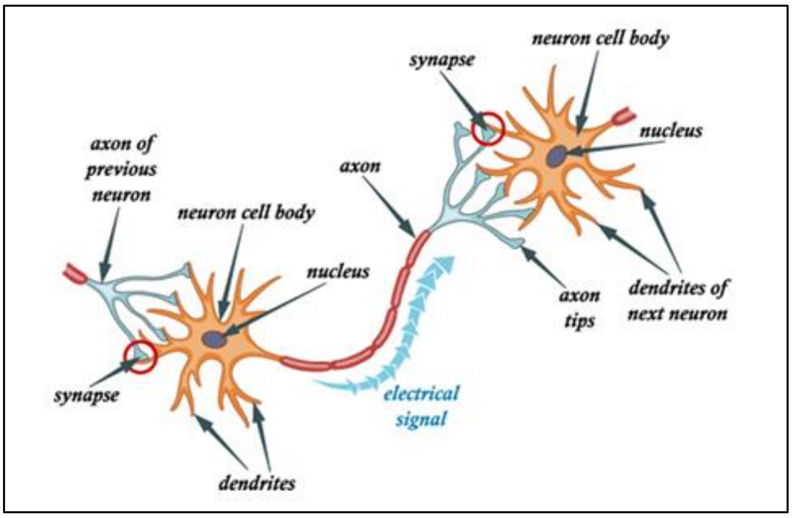


Figure 1.2: Signal transmission between two neurons [7]

1.3 Problem Statement

Commonly, stroke rehabilitation guidelines recommend the intensive and repetitive practice of functional tasks after stroke [8]. However, for many patients, sole repetition can be unmotivating and frustrating. One way of encouraging motivation is by providing patients with visual feedback of their movement in real-time. This kind of therapy can be further developed, by incorporating it in a goal-oriented virtual environment [9]. Also, since enhancing engagement of patients during stroke rehabilitation are in the focus of current research [10], thus, it is important to determine the relationship between visual feedback therapy and the engagement of patients in their rehabilitations.

In the monitoring of stroke recovery, there is always one common challenge which is to have a direct measurement of the state of the brain before and after the rehabilitation process. According to Marcos Rios-Lago [11], recovery of functions can take several forms, namely the reorganization of functional interactions within an existing network of brain regions, the recruitment of new areas into the network and the plasticity in regions of cortex surrounding the damaged area and this is determined by calculating the correlation coefficients over the motor cortex of brain from the functional magnetic resonance imaging (fMRI) [12]. This has been well demonstrated in connectivity studies using fMRI, where greater motor deficits were associated with reduced connectivity across cortical motor regions [12]. However, the fMRI machines are usually available only in hospitals of big cities and limit the accessibility. In addition, the cost of service in getting the fMRI scanning is also very expensive with a cost of about RM800 per scan [13].

1.4 Objectives

In order to tackle the stated problems, two main objectives have been identified as below:

- To investigate the effect of goal-oriented visual feedback on the engagement of stroke patients in rehabilitation exercises.
- To develop an algorithm to calculate the functional connectivity using electroencephalogram (EEG) data as an indicator of brain functional recovery.

1.5 Scope of the Project

In this project, the effectiveness of the implementation of goal-oriented visual feedback therapy in enhancing the engagement of stroke patients in rehabilitation is investigated. The engagement measurement is done by via EEG signals as recorded by EMOTIV EPOC+ device as shown in Figure 1.3 below. Besides that, this project also aims to focus on designing an EEG recovery monitoring system in order to overcome the low accessibility and high cost of fMRI in quantifying the cortical reorganization or functional recovery of brains. Connectivity measurement can be made based on the data obtained from the brain EEG signals which are able to measure the electrical signals or activities from the underlying cortical regions. In more specific, the quantification algorithm is called EEG brain beta coherence index. This will lower the cost significantly to RM 40 per measurement making the solution to be highly accessible and affordable as compared to fMRI. In order to verify the EEG algorithm, comparison with connectivity from existing fMRI library is used as the validation tool.

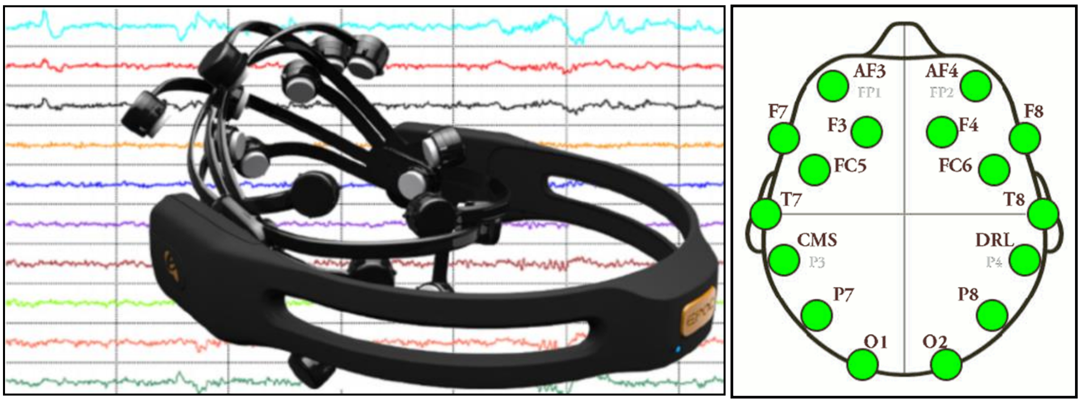


Figure 1.3: EMOTIV EPOC+ [14]

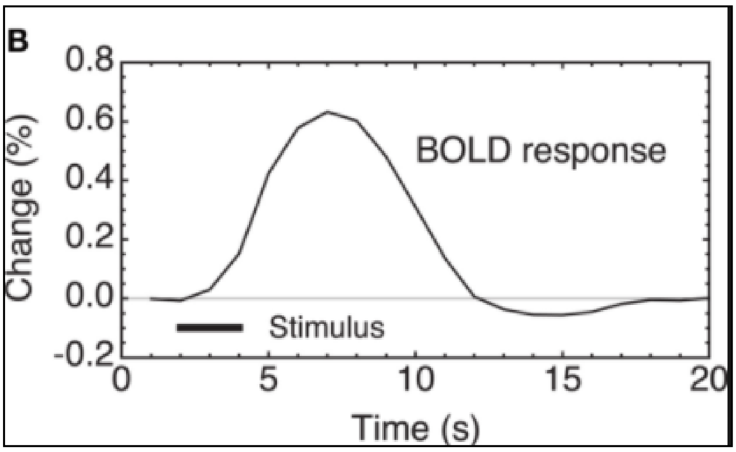


Figure 1.4: fMRI BOLD signal [15]

CHAPTER 2: LITERATURE REVIEW

2.1 Application of Visual Feedback in Stroke Rehabilitation

In stroke rehabilitation, visual feedback gives patients knowledge of their movements and is known to promote movement re-education [16]. It can be particularly useful for proximal limb segments, which can be hard to see by the individual without contorting the body [9]. Also, since maintaining and enhancing engagement of patients during stroke rehabilitation exercises are the focus of current research, real-time visual feedback is believed to play an important role [10].

With visual feedback, the subject can focus on the improvement of his or her performance in an interactive virtual composition. The system can communicate to the subject about the measures of performance and direction for improvement related to his or her movement, while maintaining engagement in the repetitive task-oriented therapy. Engaging within an active rehabilitation experience promotes neural plasticity for recovery of motor and cognitive function [17]. An example of research using visual feedback has been conducted for upper extremities as shown in Figure 2.1 below where three Inertial Measurement Units (IMUs) were placed in each segment of the upper extremity, allowing the determination of the special orientation of the limb. The IMUs were secured to the patient through elastic straps. Then, real-time visual feedback is shown in the mobile app with a bar displaying the progress in each one of the movements, along with the specified goal, repetition count, remaining exercise time and posture [18].

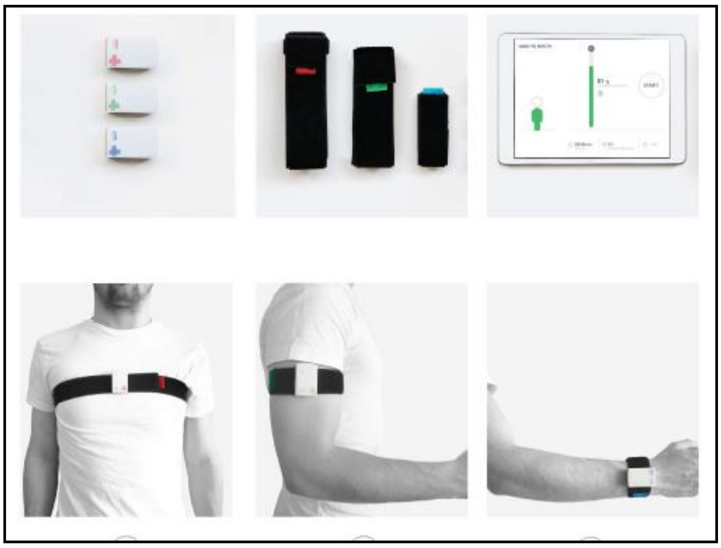


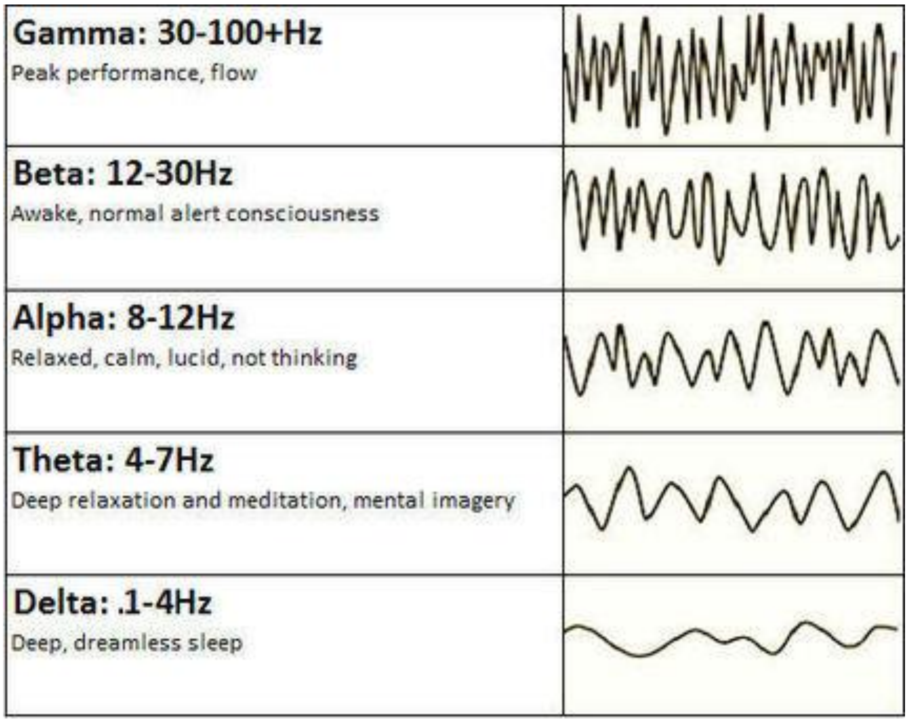
Figure 2.1: System components and integration [18]

2.2 Characteristics of EEG Signals

EEG signals are also called brainwaves. They are produced by synchronised electrical pulses from billions of neurons which are continuously communicating with each other. As shown in Table 2.1 below, brainwaves are divided into slow, moderate, and fast waves [19]. Delta (δ) has the highest amplitude compared to all other brainwaves. Its frequency range is 4 Hz or below. Delta activity is only normal in an adult patient if they are in a moderate to deep sleep. Meanwhile, the frequency range of the Theta (θ) is within 4 to 7 Hz. For Theta activity, it is normal if the patient is in deep relaxation. Alpha (α) waves are dominant during quietly flowing thoughts. The frequency range of the Alpha is in between 8 and 12Hz and usually is observed in the posterior area of the skull.

Beta (β) wave is known as a normal waveform in human brain and it is an obvious signal in most patients who are alert or conscious. The frequency range of the Beta is between 12 to 30 Hz. The local field potential activity in motor cortical and basal ganglia regions exhibit prominent Beta oscillation during muscular contraction, reaching, grasping and attention tasks [20]. Lastly, the frequency range of the Gamma (γ) wave is associated between 30 Hz to 100 Hz [19]. This wave is dominant during tasks requiring peak performance.

Table 2.1: Types of brainwaves [19]



Gamma: 30-100+Hz Peak performance, flow	
Beta: 12-30Hz Awake, normal alert consciousness	
Alpha: 8-12Hz Relaxed, calm, lucid, not thinking	
Theta: 4-7Hz Deep relaxation and meditation, mental imagery	
Delta: .1-4Hz Deep, dreamless sleep	

2.3 Pre-processing for EEG Signals

Before the interpretation and analysis of clinical EEG signals, there are undoubtedly the presence of artefact problems which are the unwanted disturbances not originating from the brains. EEG artefacts can be divided in two categories. The first one is the non-stereotyped artefacts due to subject's movements or external sources of interference, whereas stereotyped artefacts are for instance ocular eye movements, blinks and heart beats [21]. Since the spatial distribution of non-stereotyped artefacts is extremely variable, thus it relies on visual inspection in removing them before further pre-processing. Meanwhile, stereotyped artefacts can be easily removed by Independent Component Analysis (ICA) as they have a highly reproducible spatial distribution and temporal profiles [21]. The concept of ICA is defined as the procedure of maximizing the degree of statistical independence among outputs based on the contrast functions and is proceeded with the removal of unwanted components [22].

In the research of Lisha, Ying and Beadle (2005), four signals were generated and passed through a linear system with random mixed matrix. The mixed signal was processed with the proposed ICA algorithm in order to assess the performance of the decomposition. As shown in the last column of Figure 2.2 below, it can be seen that the ICA method effectively separated the independent sources and recovered the original signals without artefacts [22]. In short, ICA is very effective in decomposing the artefacts from the relevant signals and further separating the mixed signals into a series of subcomponents.

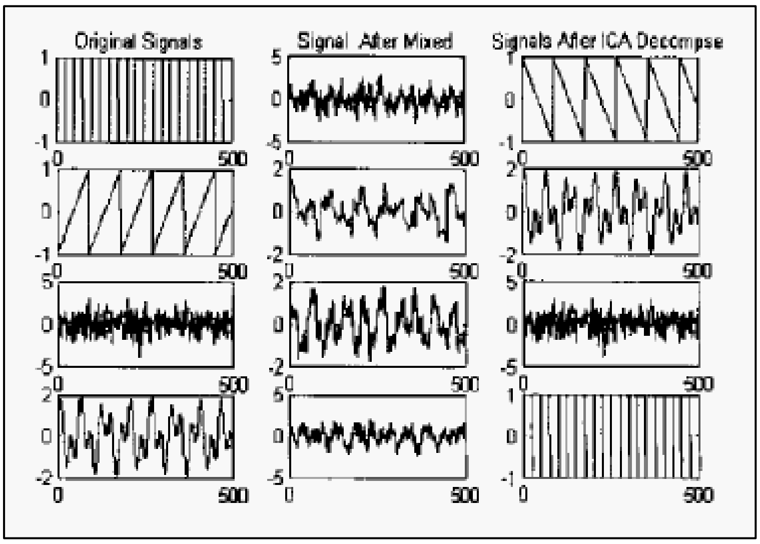


Figure 2.2: Simulation results of separating the mixed sources using ICA [22]

2.4 Measurement of Engagement via EEG

EEG is nowadays a common technique for the measurement of task engagement. According to Berka et al. (2007), engagement index implies the efficiency and involvement of people in information-gathering, visual scanning and sustained attention [23]. Regarding the measurement, Pope et al. [24] and Freeman et al. [25] proposed that engagement index can be calculated by computing the ratio of (Beta/(Alpha + Theta)). Meanwhile, Smith and Gevins showed the increase of theta response in frontal lobe along with the decrease of alpha response in the parietal lobe when the difficulty of given tasks increased [26]. Other works also showed that increment in engagement index was correlated with increased number of completed tasks as well as the time a person can stay awake and conscious. On the other hand, Yamada [27] researched on children playing video games showed that a higher theta activity is associated with a high degree of blink inhibition.

Table 2.2: Three different formulas for measurement of engagement index

Researcher	**EEG Engagement Index**	**Description**
Pope et al. [24] and Freeman et al. [25]	$\frac{\text{Beta}}{\text{Alpha} + \text{Theta}}$	Averaged across all sensor locations
Smith and Gevins [26]	$\frac{\text{Theta}}{\text{Alpha}}$	Average frontal midline theta and average parietal alpha
Yamada [27]	Theta	Averaged frontal theta

McMahan et al carried out experiment to compare these three engagement indices by using EMOTIV EPOC device [28]. In their experiment, higher engagement was expected for the game with more critical challenges. They concluded that (Beta/(Alpha + Theta)) is the preferred algorithm for calculating the engagement levels via this EEG device. The reason is due to the lesser number of electrodes of EMOTIV EPOC in which the sensors may not have enough resolution to support individual sensor measurements that the other two indices require for calculating engagement levels [28].

2.5 Neuroplasticity

In the study of neuroscience, neuroplasticity is defined as the brain's ability to reorganize itself by forming new neural connections throughout life or in short is called as the cortical reorganization [29]. Neuroplasticity allows the neurons in the brain to compensate for disease and to adjust their activities in response to changes in their environment. The two most plausible forms of plasticity are collateral sprouting of new synaptic connections and unmasking of previously latent functional pathways. Recent progress in neuroscience has established that the plasticity is a continuous state whereby the brain is constantly being modified by changes in setting and situations.

2.6 Cortical Reorganization Measurement via EEG

Based on the digital analysis of the EEG brain signals, the cerebral cortex around electrodes C3, C4, and Cz locations deal with sensory and motor functions since they are lying above motor cortex, as shown in Figure 2.3 [30]. In this figure, electrodes Fp1, Fpz, Fp2, F7, F3, Fz, F4, and F2 are to be placed above the frontal lobe of brain, T3, T4, T5 and T6 overlying temporal lobe, P3, Pz and P4 above parietal lobe, whereas O1, Oz and O2 are overlying the occipital lobe. As shown in Figure 2.4, Fast Fourier Transform (FFT) is then performed on sections of EEG data to determine the power content of the four main frequency bands. The bottom graph shown in the figure displays the power content against frequency. The resulting waveforms can also be displayed as a brain map which will show the scalp distribution of the power within each frequency band. Artefact removal will be done using ICA to preserve all the recorded trials, thus producing event-related potential (ERP) which is the measured brain response as a direct result of a specific sensory, cognitive or motor event.

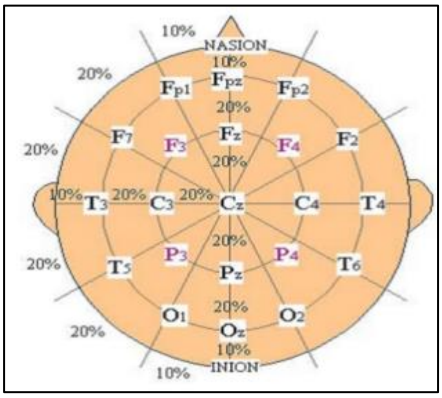


Figure 2.3: Scalp electrode locations [30]

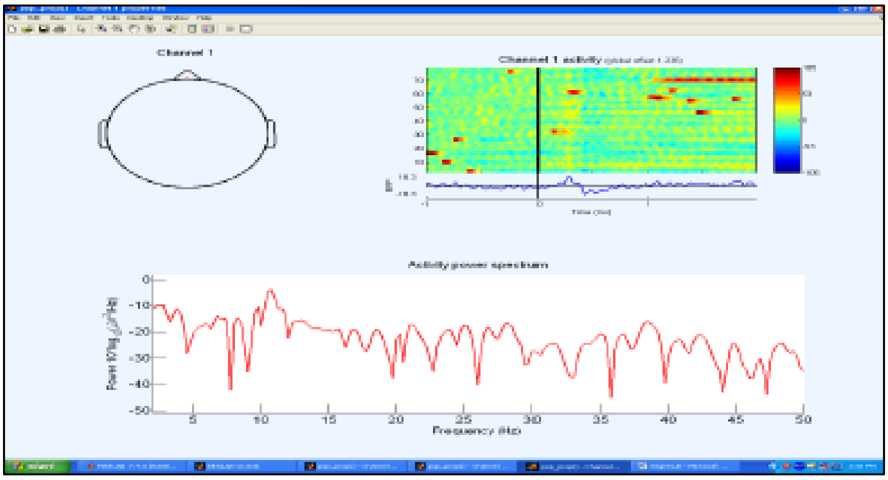


Figure 2.4: Example of power spectrum after FFT [30]

One technique of quantifying meaningful indices of connectivity as an indication of cortical reorganization is based on graph theory where the information processing and propagation is represented by a set of nodes and links between the nodes, as shown in Figure 2.5 below [31]. According to the number of local connections at each node and the path length between nodes, the characteristics of brain networks can be defined. It can be either regular, small world, or random. In general, a small world may be considered optimally efficient, due to the high clustering coefficient with some long-range connections. The degree of efficiency is one metric that has been used commonly to quantify brain networks. It is inversely proportional to the path length, while directly proportional to clustering coefficients [31].

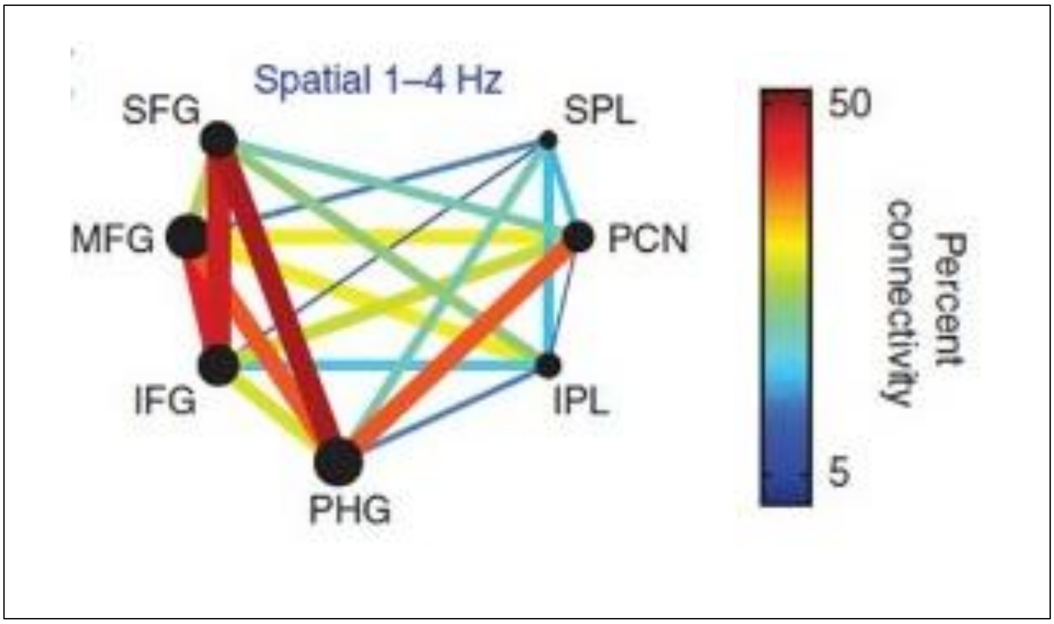


Figure 2.5: Graph theory analysis with brain nodes and links between nodes [31]

Philips, Daly and Principe have demonstrated that the Topographical measurement of functional connectivity can be used as a measure of post-stroke motor recovery where they utilized the generalized measure of association (GMA) and concept of graph theories, to come out with indices including global and local efficiency, as well as hemispheric interdensity and intradensity [32]. These topological measures are actually functional connectivity values which offer potential application in biofeedback. In a subset of 17 subjects possessing lesions of the cerebral cortex, reductions of global and local efficiency, as well as the intradensity of the unaffected hemisphere are found to be associated with functional improvement. Figure 2.6 below shows the overall EEG data processing flow, starting from the acquisition of EEG data, categorization of EEG into different bands, quantification of connectivity using graph theories and eventually the correlation between functional connectivity and muscle improvement.

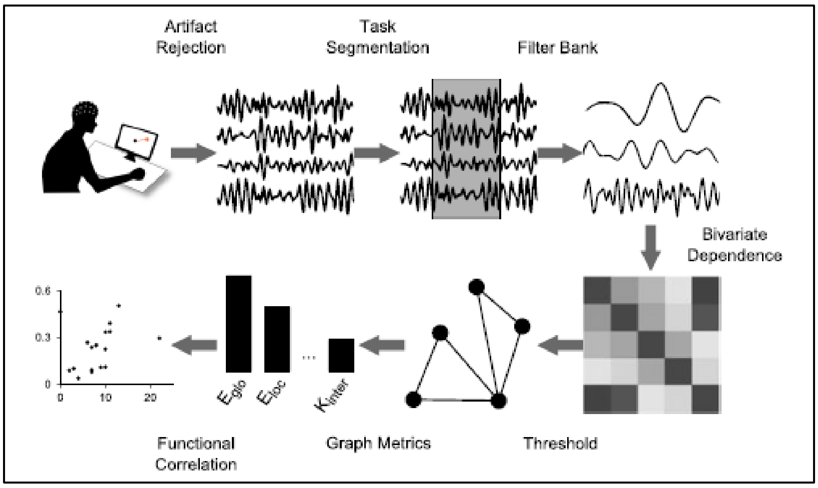


Figure 2.6: EEG data processing pipeline [32]

Besides that, there are two main concepts known as coherence and phase delay which are commonly used in indicating the cortical reorganization or sometimes is called brain functional connectivity. Coherence is the degree of association between frequency spectra by taking the amount of phase stability into account. In other words, it is also interpreted as the functional association between two brain regions [33]. When the amplitude and phase difference between two signals is constant then coherence = 1, whereas zero coherence happens when the amplitude and phase difference between signals is random. Meanwhile, phase delay is a measure of leading or lagging behind, between two simultaneously recorded EEG signals. It implies the directional flow of information between two EEG electrodes or brain regions [33].

Quinlan et al. have shown that coherence can be used to quantify the brain connectivity in indicating the cortical reorganization or brain functional recovery of stroke patients [34]. As shown in Figure 2.7 below, the brain recovery of patients was quantified by computing beta coherence index between ipsilesional primary motor (ipsilesional M1) electrode and premotor cortex (PM) electrode. Throughout their recovery process, the coherence index was strongly correlated with the Fugl Meyer (FM) score. This strong and positive correlation signifies that the recovery of muscle is associated with the functional recovery of brains.

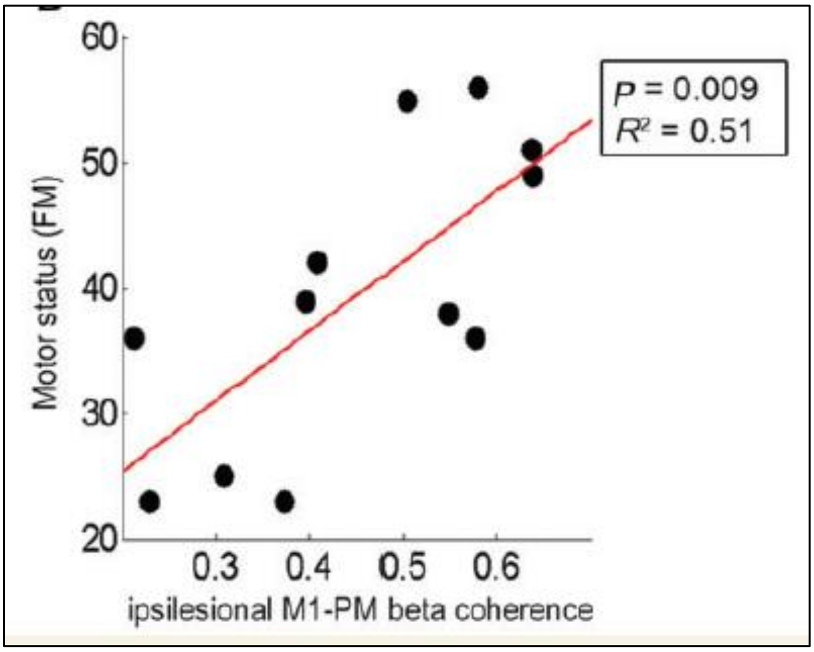


Figure 2.7: Strong positive correlation between motor status and beta coherence [34]

2.7 Cortical Reorganization Measurement via fMRI

The brain is a complex integrative network of a large number of different brain regions that each have their own task and function, and continuously conveying signals with each other. Thus, information is continuously processed and transported between structurally and functionally linked brain regions. This has made the exploration of functional connectivity in the human brain to be significant. In the past years, an increasing body of neuroimaging studies has started to explore functional connectivity by measuring the level of co-activation of resting-state fMRI time-series between brain regions.

Resting-state fMRI studies are similar with the conventional task-related fMRI with the focus in measuring the correlation between spontaneous activation of brain regions. Subjects will be placed into the fMRI scanner and told to close their eyes during a resting-state experiment. They need to keep their mind as calm as possible, without falling asleep. At the same time, the BOLD fMRI signals will be measured throughout the experiment. As shown in Figure 2.8 below, in order to examine the functional connectivity between the selected seed voxel and a second brain region, the resting-state time-series of the seed voxel is correlated with the resting-state time-series of the other region [35]. A high correlation between the time-series of these two voxels implies a high level of functional connectivity between these regions.

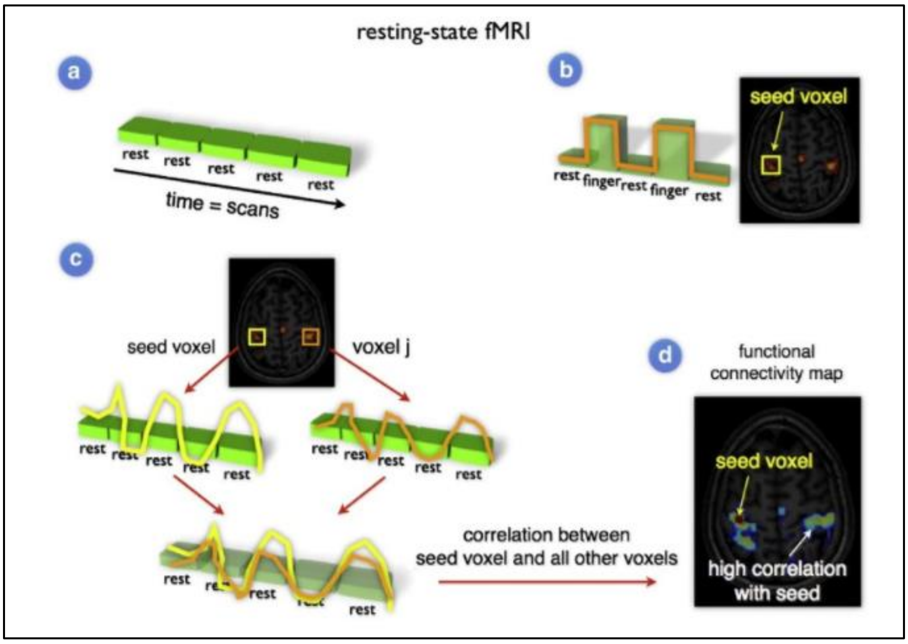


Figure 2.8: Pipeline for construction of functional connectivity map [35]

Primary motor cortex (M1) was also observed to be connected with the supplementary motor cortex (SMC), ventral premotor cortex (PMv), the dorsal premotor cortex (PMd), primary somatosensory cortex, and secondary somatosensory cortex by fibers, and these connections with M1 stopped to occur after about 5 months [36]. However, a new network was formed between PMv and the primary somatosensory cortex [36]. The results of these studies showed that a cortical somatotopic representation is a pervasive pattern covering a wider range of the cortex. Adoption of regions nearby damaged lesion is common during cortical reorganization.

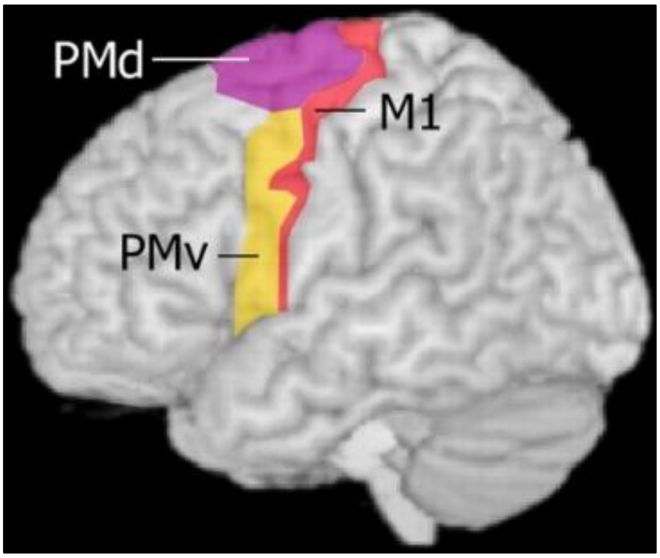


Figure 2.9: Location of PMv and PMd relative to M1 [36]

Volz discussed the use of seed-based analysis via BOLD signals to identify motor network connectivity between primary motor area (M1) voxel and other brain regions [37] via the application of intermittent theta-burst stimulation (iTBS) which resulted in higher functional connectivity of the stimulated M1 with a bihemispheric network as shown with the high level of activation as indicated by the colour scale in Figure 2.10 below. Bihemispheric network comprises of ipsilateral midcingulate cortex (MCC), bilateral supplementary motor area (SMA), contralesional dorsal premotor cortex (PMd) and contralesional M1 as depicted in the figure. This outcome signified the recovery of a brain network in which information is continuously conveyed and processed between structurally and functionally linked brain regions.

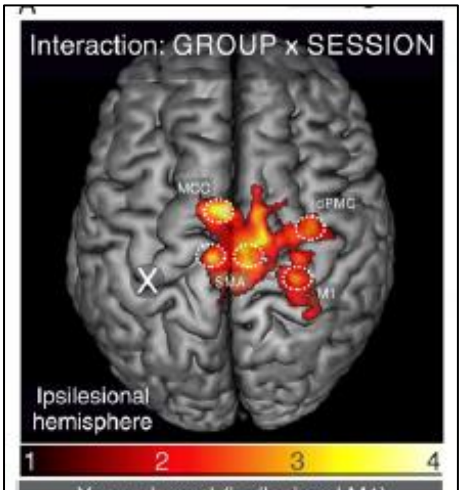


Figure 2.10: Functional connectivity and activation at bihemispheric network [37]

Subsequently, by investigating the influence of fMRI motor connectivity on the relative grip strength of patients, it was shown that the changes in connectivity significantly correlated with motor outcome for all the five regions as mentioned previously [37] and depicted in Figure 2.11 below. This trend was similar regardless of control group or stimulation group. In line with this observation, higher level of motor network connectivity is associated with better motor recovery. However, the relationship between increased levels of M1-connectivity and motor outcome is not specific to the iTBS intervention only but is also applicable to the stroke rehab for motor recovery.

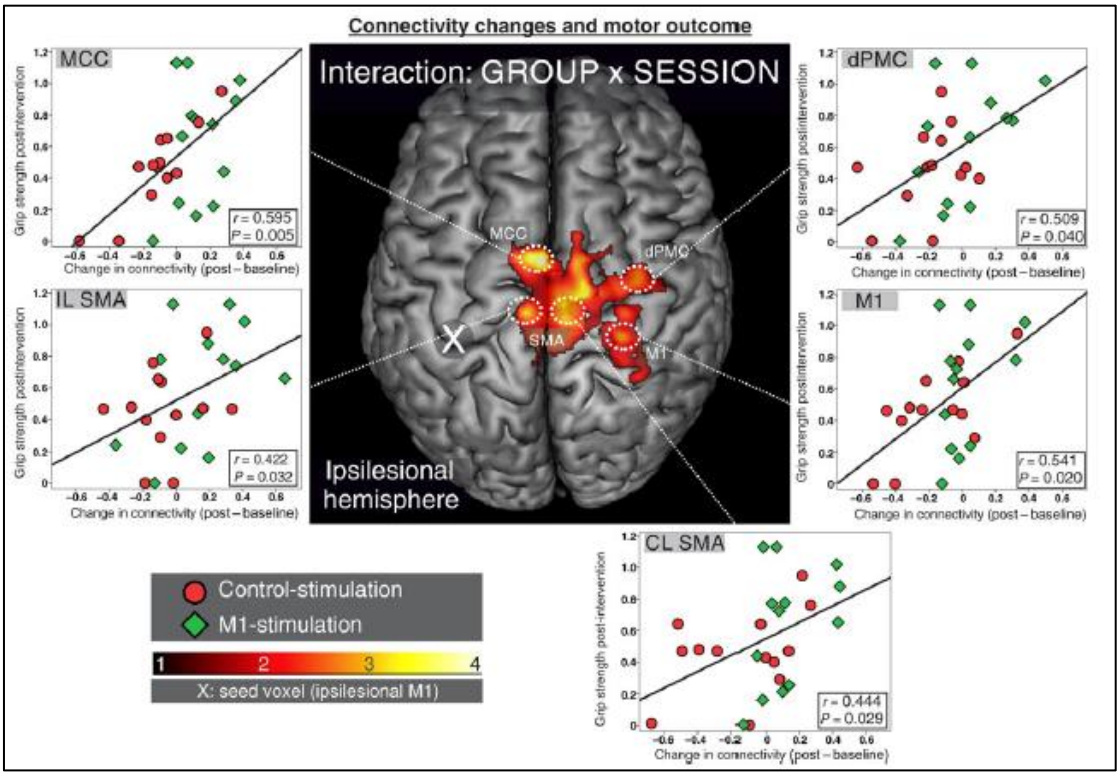


Figure 2.11: Correlation between brain functional connectivity and grip strength [37]

CHAPTER 3: RESEARCH METHODOLOGY

3.1 Introduction

This chapter describes the overall methodology of the work. The methodology covers the following sections:

i. Visual Feedback Setup
ii. Engagement Measurement using EEG
iii. EEG Beta Coherence Quantification
iv. Resting-state Functional Connectivity via fMRI

3.2 Visual Feedback Setup

The overall set-up of rehab system prototype with visual feedback display is as shown in Figure 3.1 below. In this iLLSRM machine, the visual feedback occurs when the range of motion is displayed on screen in real-time with the use of ultrasonic sensors by measuring the distance travelled by lower limbs on the foot plates.

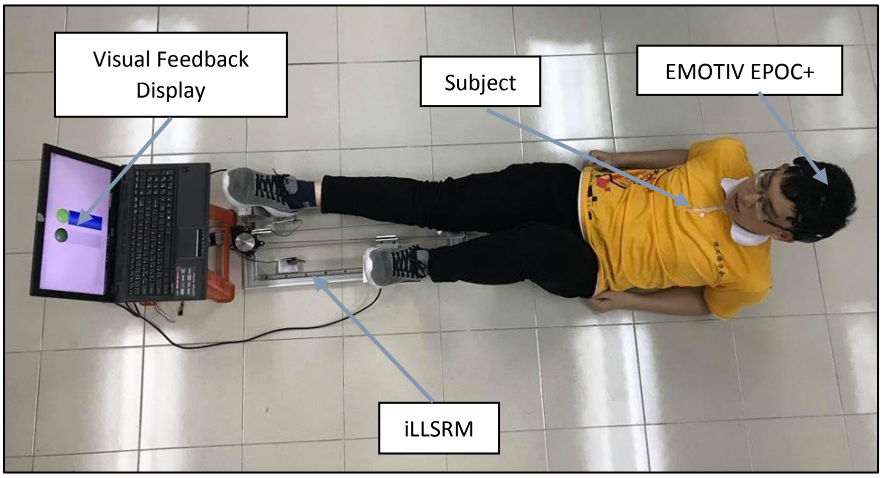


Figure 3.1: Set-up of iLLSRM system

Figure 3.2 below shows the goal-oriented visual feedback display with the two balls on top of the bars representing the goals for patients to reach to, in every cycle of their rehab. The left and right bar represent the range of motion of the left and right lower limb respectively. It is noted that the balls on the bars will only light up when the range of extension motion of limb reaches its maximum. The condition happened in Figure 3.2 was during the maximum extension of the right limb, while the left limb was at its maximum flexion.

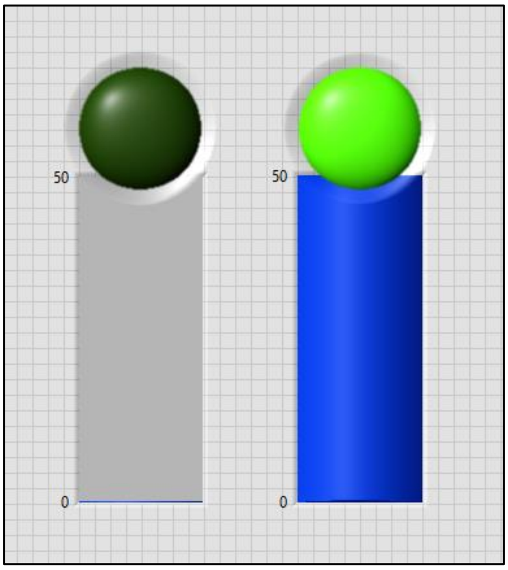


Figure 3.2: Goal-oriented visual feedback display

In this experiment to investigate whether the application of goal-oriented visual feedback will enhance the engagement of stroke patients in rehabilitation, there were initially five healthy subjects recruited, with age 21–24 (mean = 22.8 ± 1.3 years). They were using the iLLSRM machine in two different types of conditions, which were with and without the goal-oriented visual feedback display. At the same time, EMOTIV EPOC+ was worn by them and EMOTIV control panel can show the relative changes of engagement index. Then, the relationship between goal-oriented visual feedback and engagement was established by comparing the values of engagement indices in those two different conditions.

3.3 Engagement Measurement using EEG

Generally, the measurement and recording of engagement was done in real time while the subject was doing task. The collected raw EEG signals from all the fourteen channels were filtered through different band-pass filters to obtain β, α, and θ, with the combined power in the ranges of 12-30Hz, 8-12Hz and 4-7Hz frequency respectively. The engagement index was quantified using the following formula. As shown in Figure 3.3, the EMOTIV Control Panel shows the relative changes of engagement index while recording. Meanwhile, the generated report is as shown in Figure 3.4.

$$Engagement\ Index = \frac{\beta}{\alpha + \theta}$$

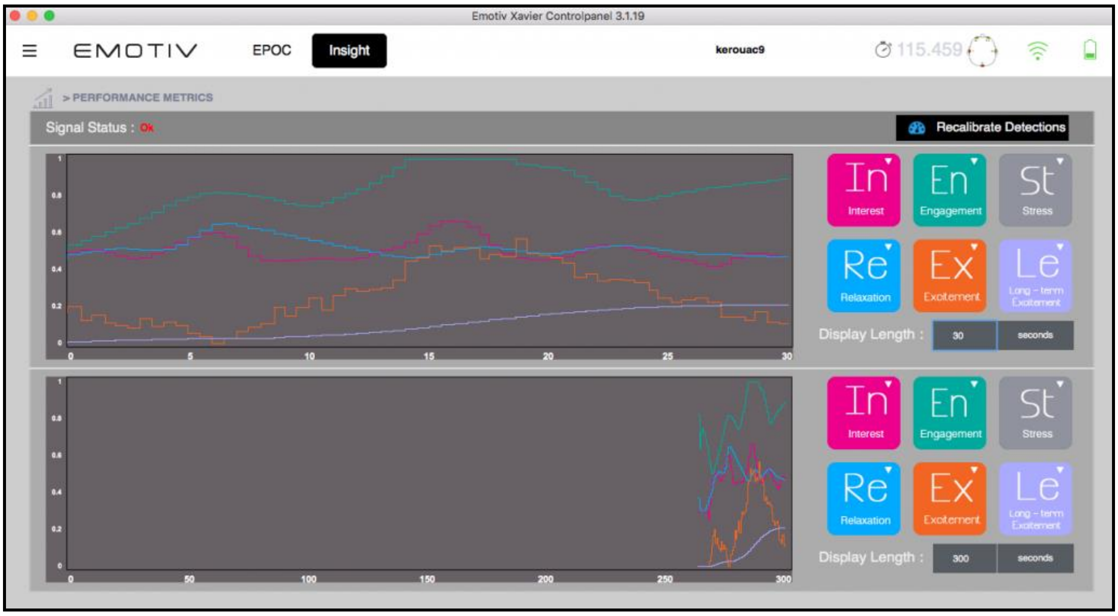


Figure 3.3: EMOTIV control panel with engagement index

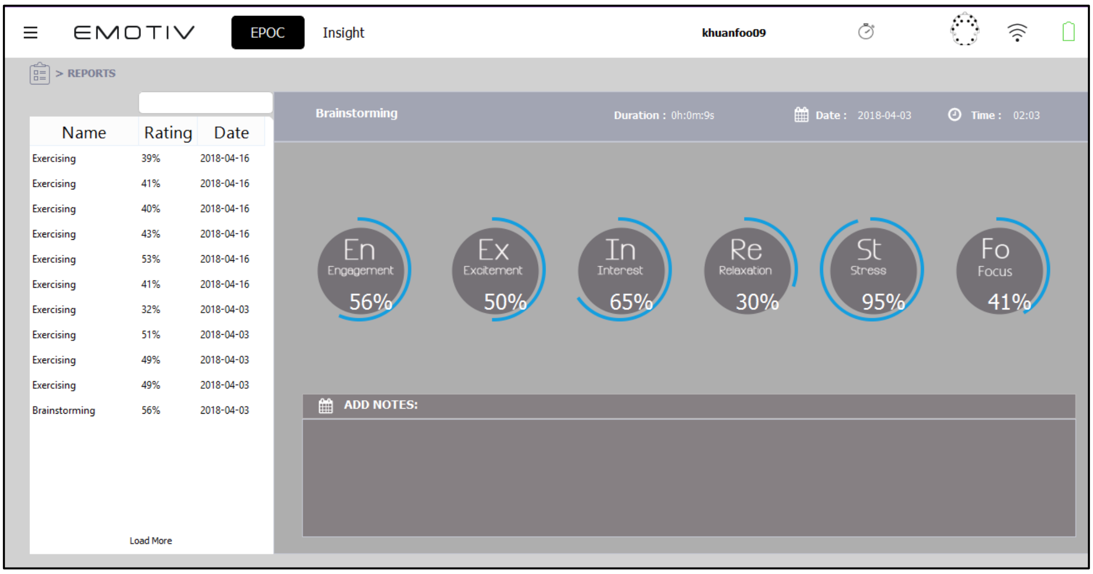


Figure 3.4: Generated report stated with average engagement index

3.4 EEG Beta Coherence Quantification

The second objective of this project is to design an EEG algorithm to quantify the cortical reorganization or brain functional recovery of stroke patients. Basically, the algorithm is designed by using MATLAB and it comprises of the following steps. EEG signal is first acquired by using EMOTIV EPOC+ device. The electrodes which are placed on the scalp can record the electrical activities which are sent out from the underlying cortex. The signals are then transmitted via Bluetooth to computer.

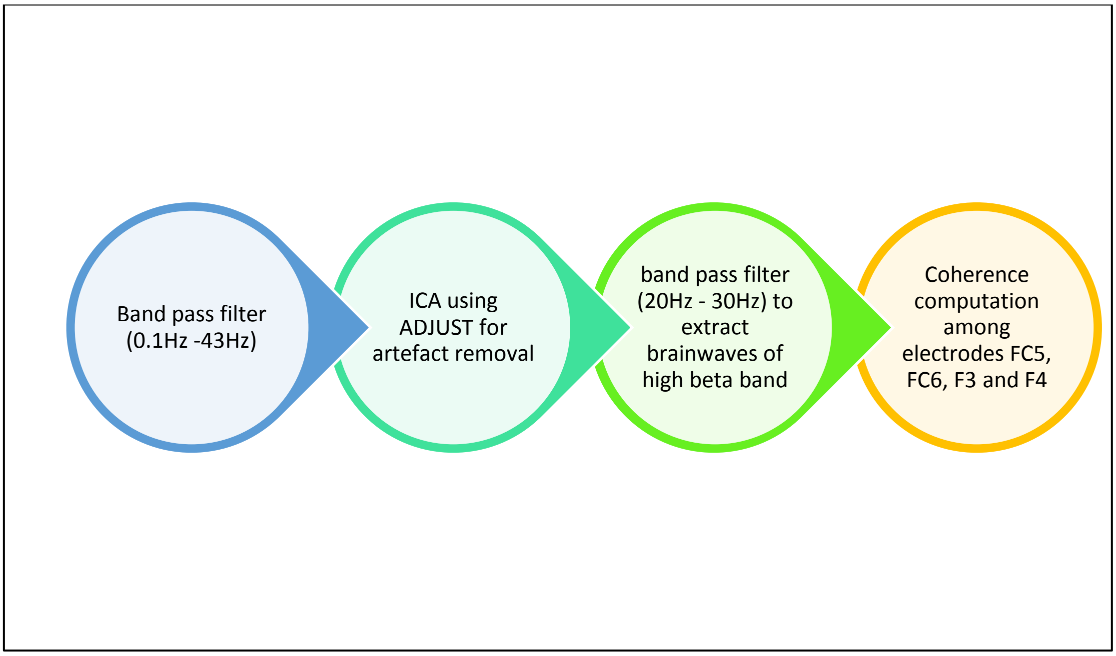


Figure 3.5: Flow chart of EEG processing steps

As shown in Figure 3.5 above, the EEG signals would undergo filtering to remove unwanted noise present in the brain signals. A band pass filter with a bandwidth between 0.1 to 43 Hz is implemented as this is the range of frequencies for brainwaves. Rejection via visual inspection can also be done whenever necessary. After that, independent component analysis (ICA) decomposition is done on the signals. This step is carried out with the plugin of EEGLAB toolbox available in MATLAB, called ADJUST. It is an automatic algorithm that identifies independent components (IC) containing artefacts by combining stereotyped artifact-specific spatial and temporal features [21]. Artifacts include eye vertical movements, horizontal movements, eye blinks, and generic discontinuities can be captured and removed from the data, thus leaving the clean signals for further processing steps. Vertical eye movements occur when their Spatial Average Difference (SAD) and Maximum Epoch Variance (MEV) exceed certain thresholds. SAD is related to higher amplitude in frontal areas compared to posterior areas, whereas MEV computes the maximum value over the epochs of temporal variance [21]. Meanwhile, horizontal eye movements happen when Spatial Eye Difference (SED) and MEV are more than certain limit. SED is related to anti-phase large amplitudes in frontal electrodes near to the eyes. Apart from that, eye blinking occurs when SAD and Temporal Kurtosis (TK) exceed threshold values. TK is sensitive to outliers in the amplitude distribution. General discontinuity artefacts occur when the Generic Discontinuities Spatial Feature (GDSF) and MEV features are more than the limits. GDSF is a feature sensitive to local spatial discontinuities [21].

Next, band pass filter with the range of 20Hz to 30Hz is then implemented to extract brainwaves of high beta band as high beta band is associated with the motor system [38]. Eventually, the functional connectivity between brain regions is estimated from EEG coherence among electrodes overlying the motor and premotor regions [39], namely electrodes FC5, FC6, F3 and F4 of EMOTIV EPOC+ as shown in Figure 3.6 below. Coherence ranges from zero to one, with a coherence value near one indicating EEG signals have almost similar phase and amplitude at all time points. In other words, coherence indicates the functional association between two brain regions. The higher the coherence index, the greater the brain functional recovery [40]. Figure 3.7 shows the final MATLAB Graphical User Interface comprising of all the stated processing steps. There are 4 respective coherence indices for the electrode pairs FC5-FC6, F3-F4, FC5-F4 and F3-FC6. The mean value of all these 4 indices is the desired EEG beta coherence index.

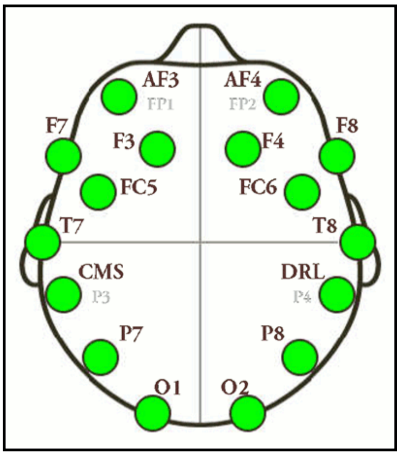


Figure 3.6: Electrodes' position of EMOTIV EPOC+ [14]

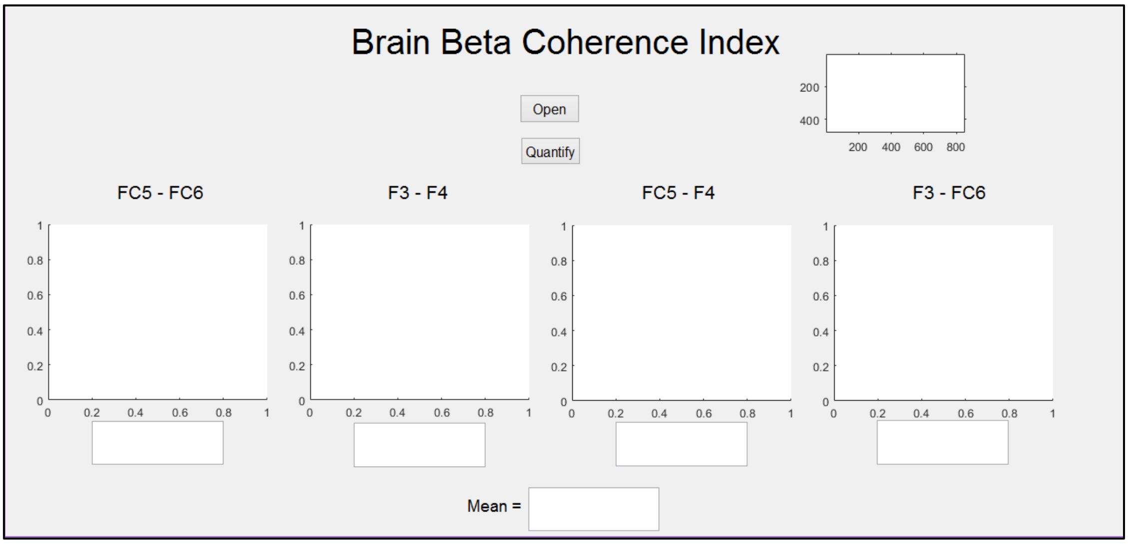


Figure 3.7: MATLAB graphical user interface designed for EEG beta coherence

After the algorithm design is done, a total of five healthy subjects were recruited with age 21–24 (mean = 22.8 ± 1.3 years). Then, the EMOTIV EPOC+ was worn and their respective EEG data was recorded in resting-state condition for a period of 2 minutes. They were instructed to be stationary to reduce undesirable movements which might lead to unwanted artefacts in the EEG raw signals. The EEG signals were then captured and processed using the designed MATLAB GUI and the brain beta coherence was computed.

3.5 Resting-state Functional Connectivity via fMRI

In this project, resting-state fMRI functional connectivity is used as a validation method for the results obtained from EEG brain beta coherence. In general, fMRI is a noninvasive test that uses a strong magnetic field and radio waves to create anatomical and functional images of the brains. Since the amount of oxygen carried in the blood affects the magnetic properties of blood, thus fMRI can detect and capture the blood-oxygen-level dependent (BOLD) contrast which is the changes in oxygen levels in the blood flow. It is able to indicate the property of cortical activity. When an area of the brain is in use, blood flow to that region also increases as the demand for oxygen increases. In order to compute the level of functional connectivity between a selected seed voxel and second brain region, the measured resting-state BOLD signal of the seed voxel was correlated with the time-series of the other correlated region [15]. The major brain regions to be analyzed are the left and right hemispheric motor cortices since the major concern is on the motor recovery of stroke patients.

The software used to compute the resting-state functional connectivity is called CONN Functional Connectivity toolbox, as shown in Figure 3.8 below. CONN is a MATLAB-based cross-platform open-source software for the computation, display and analysis of resting-state functional connectivity for fMRI [41]. Before functional connectivity is computed, there are few pre-processing steps of functional and anatomical volumes to be done, including realignment, slice-timing correction, outlier identification, coregistration, segmentation, normalization and smoothing [41]. After that, denoising step is run to increase the quality of functional connectivity measures, by addressing residual physiological and motion artifacts that are very salient even after all the previous steps. In short, all the pre-processing steps are shown in Figure 3.9.

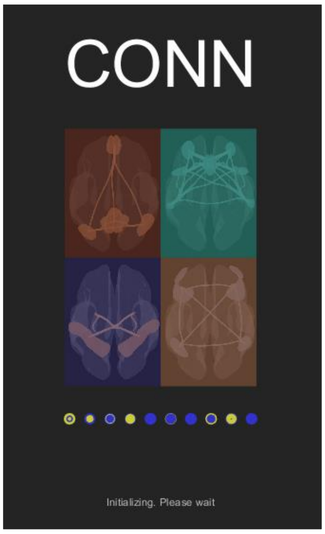


Figure 3.8: CONN toolbox

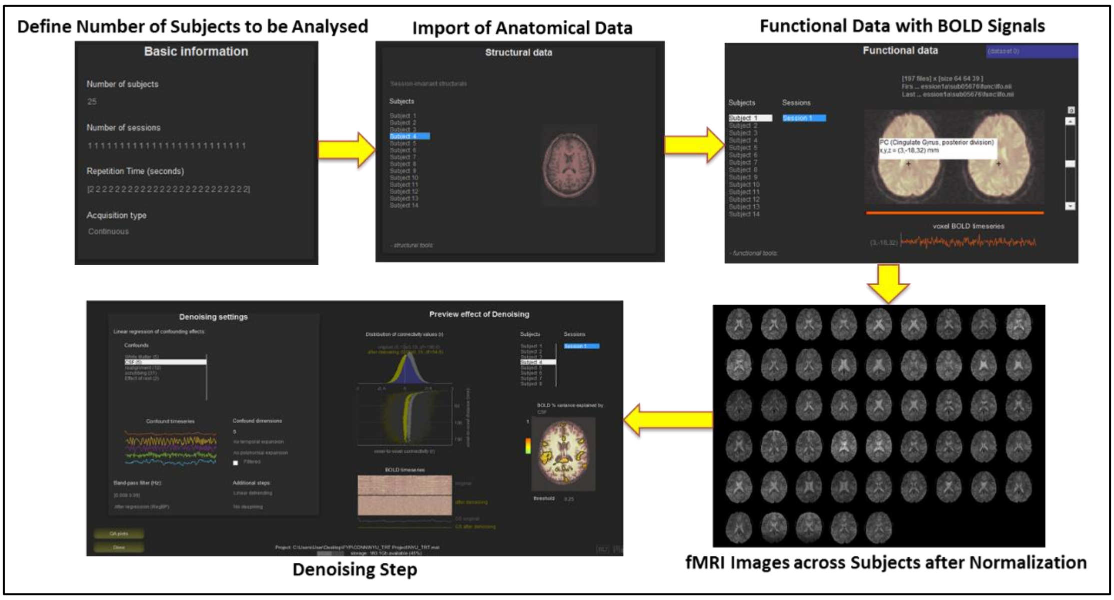


Figure 3.9: Pre-processing steps on fMRI images

Then, the fMRI images of five healthy participants gathered during rest as well as anonymized anatomical images of them were downloaded from the NYU CSC TestRetest website. The participants were part of the NewYork_a contribution to the 1000 Functional Connectomes Project [42]. The resting-state fMRI images were collected during the first resting-state scan in a scan session. The resting-state functional connectivity values are computed by using the CONN toolbox. These results are then compared with the results of EEG brain beta coherence indices computed for the other five healthy subjects as discussed in previous section.

In short, Figure 3.10 below summarize the overall methodology for the use of EEG in quantifying brain functional recovery as well as the adoption of fMRI as the validation tool.

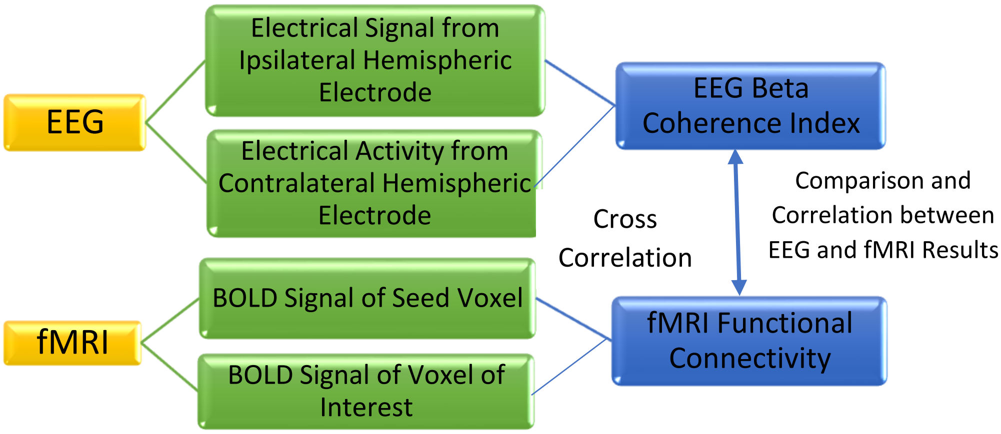


Figure 3.10: Flow chart of the overall methodology

CHAPTER 4: RESULTS AND DISCUSSION

4.1 Effect of Visual Feedback on Engagement

The results of the engagement measure of all the five healthy subjects with age 21–24 (mean = 22.8 ± 1.3 years), undergoing exercises with and without visual feedback were tabulated in the following Table 4.1.

Table 4.1: Engagement measure of healthy subjects

Subject	Engagement Measure (%)	
	Without Visual Feedback	**With Visual Feedback**
1	53	68
2	56	69
3	59	62
4	48	70
5	51	59
Mean	53	66
Percentage Increment (%)	**24.53**	

A box plot was then plotted as shown in Figure 4.1 below to compare the engagement measure before and after the goal-oriented visual feedback was introduced in the exercise.

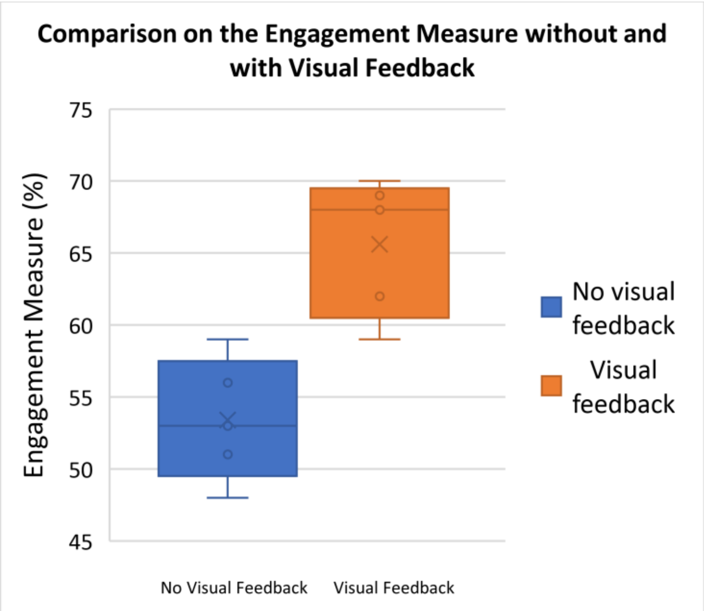


Figure 4.1: Engagement comparison for exercises without and with visual feedback