Detection of Neural Activity for Cerebrovascular Disease using MRI and EEG

By

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A thesis submitted in partial fulfillment of the requirement for the degree of
Master of Science in Biomedical Engineering

Khulna University of Engineering & Technology
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Declaration

This is to certify that the thesis work entitled "**Detection of Neural Activity for Cerebrovascular Disease using MRI and EEG**" has been carried out by **G. M. Mahmudur Rahman** in the Department of **Biomedical Engineering**, Khulna University of Engineering & Technology, Khulna, Bangladesh. The above thesis work or any part of this work has not been submitted anywhere for the award of any degree or diploma.

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August, 2016   **G. M. Mahmudur Rahman**

Abstract

Cerebrovascular disease (CVD) such as stroke is the leading cause of long-term disability and third most common reason of death in the world. Due to the neuronal deficiency occurred by impaired blood flow to the brain, half of the stroke patients survive a severe cognitive impairment such as impaired speech, numbness in limbs, immobilization of limbs, visual impairment and many other observable symptoms. In the recent days, due to the gradual increase of hypertensive and diabetic patient, the risk of developing stroke is growing tremendously. The evaluation of actual neuronal status in stroke patient is thus very important to determine the indication of neurosurgical treatment.

To diagnosis the type, source and location of stroke in the brain, generally, cerebral blood flow (CBF) test, neuroimaging, and electrical activity test are being used. Among all of these tests, electroencephalogram (EEG) is a useful tool for acute stroke detection and monitoring affected tissue owing to its relatively cheap and completely hazardless for quantitative and statistical analysis. Although a large number of studies have been performed on the ischemic stroke using EEG, no investigation has been carried out on the interplay between the infarcted cerebral hemisphere with other healthy part. Moreover, earlier studies are also limited only age-related changes in EEG activity or memory performance compared younger people between the ages of about 20 to 30 years with older participants between the ages of about 60 to 80 years. There is also no study at all for the child below the age of 20 years to show the change and compare the neuronal deterioration of the infarcted part of brain.

This work focused on the correlation between the extent of infarction and the clinical effect to monitor the degree of hypo-activity of the affected part through the EEG analysis. An indication for the assessment of neuronal activity and the degree of severity of stroke patient has been proposed. A parallel study has also been carried out on healthy volunteers of under fifteen years to find the comparison of neural activity between different age group. From the analysis it is found that delta activities of EEG are highly unique of brain pathophysiology, and preservation of alpha and beta frequencies following stroke is evidently indicative of neuronal survival and a good prognosis. In order to assess brain

pathophysiology in supratentorial brain lesion patients the delta/alpha ratio (DAR) and delta-plus-theta to alpha-plus-beta ratio (DTABR) have also been used. It is observed that the DAR and DTABR values of the left cerebral hemisphere of the patient are much higher than the right cerebral hemisphere. It is also higher in both cerebral hemispheres than the control. A threshold value of ~3.7 for DAR and ˜3.5 for DTABR has been obtained. It is observed that DAR and DTABR of left hemisphere of patient are greater than 3.7and 3.5 respectively for all the measurements indicating severe ischemic stroke in the fronto-temporal region of left hemisphere. The findings have been further confirmed by a neuroimaging technique such as magnetic resonance imaging (MRI).This study also show that DAR and DTABR of the healthier child is~1.It is also found that delta and DAR indices of the old age are two times more than the child indicating the diminishing of neuronal activity of old age is half of the child. These results could be important for stroke diagnosis, prognosis, re-habitation strategies, and proper neurosurgical treatment.

Dedicated

To

My Beloved Parents

&

Respected Teachers

Contents

LIST OF FIGURE

LIST OF ILLUSTRATION

ACA   Anterior cerebral artery

CF   Cerebral Blood Flow

CVD   Cerebrovascular Disease

CT   Computed tomography

DAR   Delta-Alpha ratio

DM   Diabetes mellitus

DTABR   (Delta+Theta)(Alpha+Beta)ratio

EEG   Electroencephalogram

FFT   Fast Fourier transformation

HTN   Hypertension

IS   Ischemic Stroke

MCA   Middle cerebral artery

MRI   Magnetic Resonance Imaging

PCA   Posterior cerebral artery

TIA   Transient Ischemic Attack

QEEG   Quantitative EEG

CHAPTER I

INTRODUCTION

1.1 Introduction

Cerebrovascular disease (CVD) is the leading cause of long-term disability and third most common cause of death in the world [1, 2]. There are a number of different types of cerebrovascular disease including stroke, transient ischemic attack (TIA), subarachnoid hemorrhage, and vascular dementia. World Health Organization data has revealed that world-wide 4.5 million people die each year due to CVD such as stroke [3]. Nearly 30% of patients die within one year after a stroke, and percentage increases among the older person. About 40% of stroke related deaths occur in males, and 60% in females. The leading causes of death in the world are shown in Fig. 1.1 and 1.2. The neuronal deficiency which occurs due to the impaired blood flow to the brain tissue brings miserable sufferings to the stroke patient. Depending on the damaged area in the brain, half of the stroke patients survive a severe cognitive impairment such as impaired speech, numbness in limbs, immobilization of limbs, visual impairment (partial or full loss of sight) and many other observable symptoms. The following characteristics are very common among stroke survivors over 65 years of age [4].

- 50% had some hemiparesis

- 30% were unable to walk without some assistance

- 26% were dependent in activities of daily living

- 19% had aphasia

- 35% had depressive symptoms

- 26% were institutionalized in a nursing home.

The 10 leading causes of death in the world by percentage

Legend		
Hypertensive heart disease	Road injury	Diarrhœal diseases
Trachea bronchus, lung cancers	Diabetes mellitus	HIV/AIDS
Ischaemic heart disease	Lower respiratory infections	COPD
	Other causes	Stroke
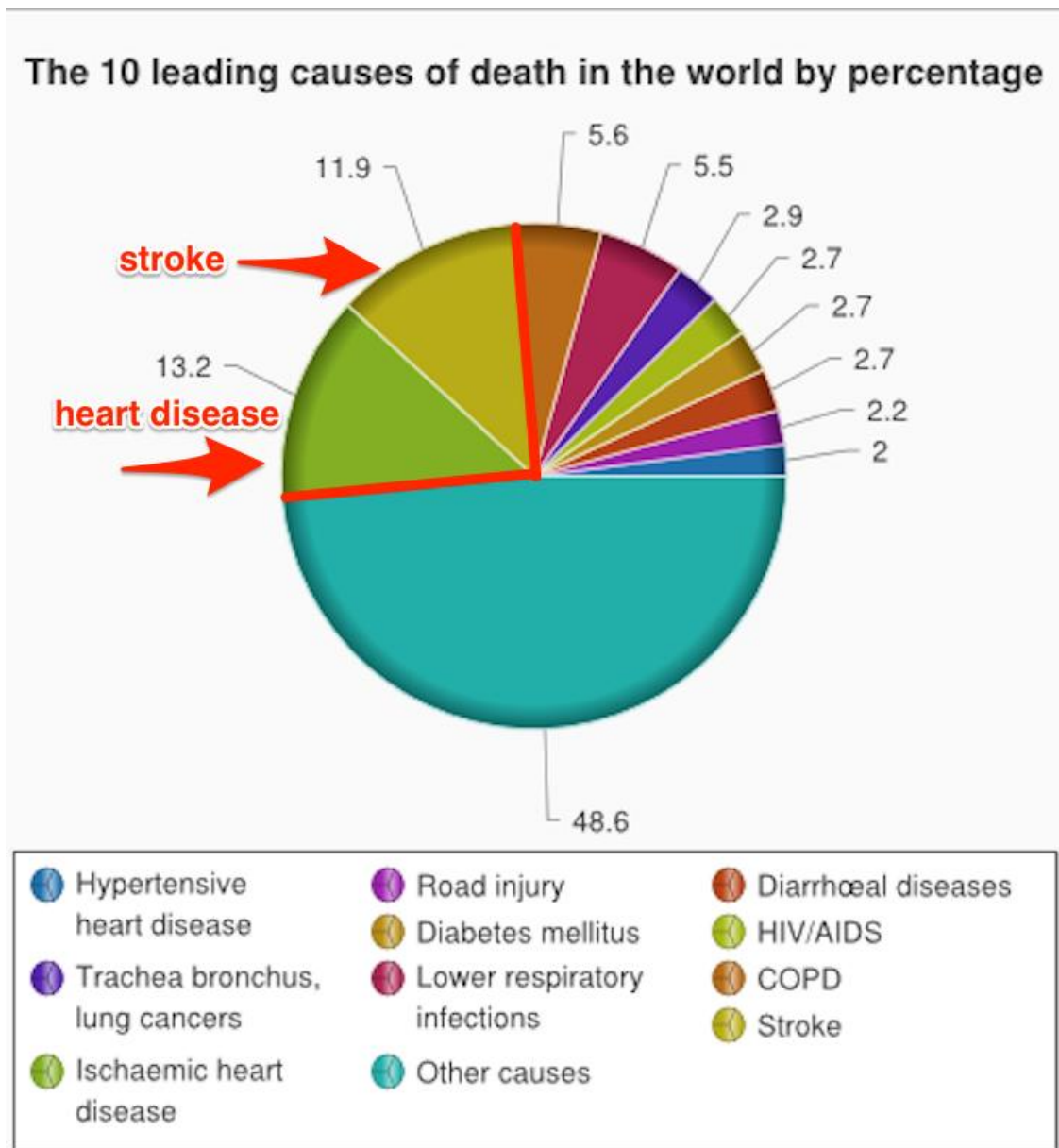
Figure 1.1: Mortality rate of different diseases.

In the recent days, due to the gradual increase of hypertensive and diabetic patient, the risk of developing stroke is growing tremendously. In Stroke patient, the cerebral blood flow (CBF) to the brain is reduced significantly. The delivery of oxygen and glucose to the brain is also reduced. As a consequence, cerebral infarction is developed and establishes a hypo-metabolic state in the infracted region. The evaluation of actual neuronal status in stroke patient is very important to determine the indication of neurosurgical treatment.
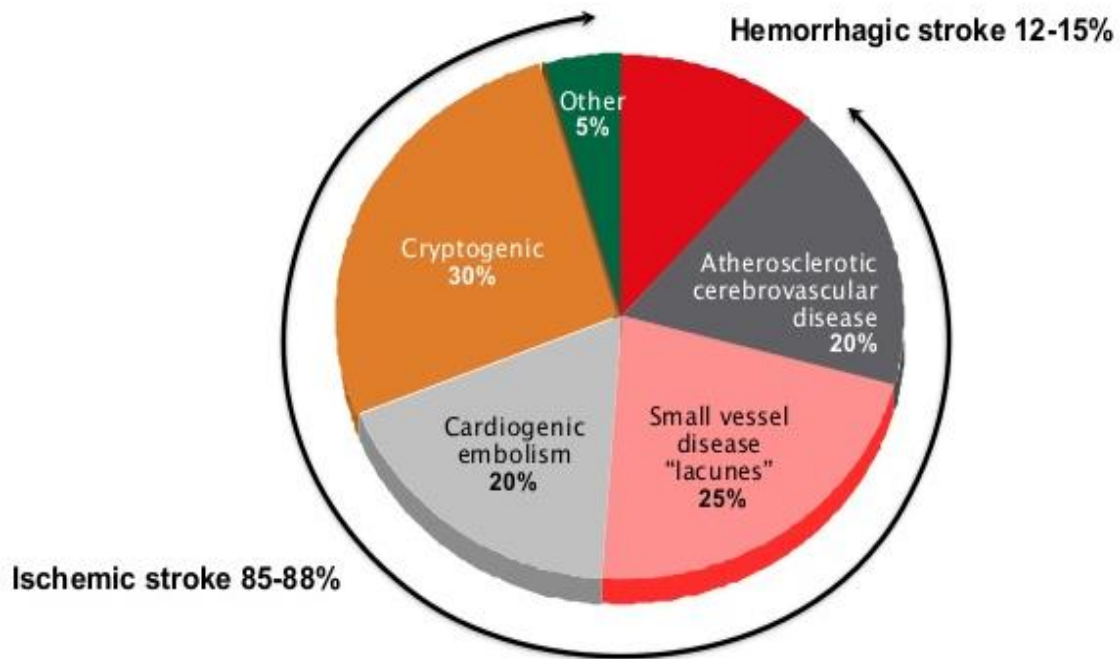
Figure 1.2: Comparison between different types of Stroke

To diagnosis the type, source and location of stroke in the brain, generally, cerebral blood flow (CBF) test, neuroimaging, and electrical activity test are being used. Cerebral blood flow test such as cerebral angiography can visualize the size and location of blockages in the blood vessel. Neuroimaging including magnetic resonance imaging (MRI) and computer tomography (CT) scan show the location and severity of stroke. The MRI scan is sharper and more detailed than the CT scan and so it can be used to diagnosis small deep injuries.[5] To measure the brain activity as well as abnormal functionality within the brain structure, electrical activity test such as electroencephalogram (EEG) has been used over the past few years. EEG offers a continuous, real-time, non-invasive measure of brain function. When cerebral blood flow (CBF) becomes compromised, changes occur in both the metabolic and electrical activity of cortical neurons, with associated EEG changes. Thus, EEG can be potentially a useful tool for acute stroke detection and monitoring affected tissue. The gradual deterioration from ischemia or stroke develops an infarct over a range of CBF. If diffusion weighted magnetic resonance imaging (DWI MRI) is able to distinguish the changes within 30 minutes [6], EEG can sense that changes within a second. Furthermore, when the CT is negative during the early stage of infarction or there is a mismatch between DWI MRI and the clinical examination, EEG can play a vital role in pathology detection.

Evaluation of cortical electrical activity using EEG is also a relatively cheap and completely hazardless for quantitative and statistical analysis. Thus, EEG can be used as the most appropriate tools of early, fast and accurate diagnosis of stroke [7, 8].

1.2 Motivation

A large number of studies have been performed on the ischemic stroke using EEG [9,10]. Generally, EEG reads scalp electrical activity generated by the brain structures. The basic brain waves obtained from EEG have been categorized into four basic groups - beta (>13 Hz), - alpha (8-13 Hz), - theta (4-8 Hz), and - delta (0.5-4 Hz). Most of those studies focus on the changes of the different EEG wave patterns (i.e. beta, alpha, theta, delta) due to the various types of strokes [11, 12]. Their works [13, 14] show that ischemic stroke (IS) produces abnormal, slow EEG activity – particularly in the delta frequency range (1–4 Hz) – and attenuation of normative, faster activity, particularly in the alpha frequency range (8–12 Hz) [15, 29] . Some of those studies have shown the aging effects on EEG activity [16-19]. Robust age effects on EEG power have been reported in the alpha frequency range (8-12 Hz). These studies consistently show that alpha power decreases with age in healthy people, especially during later parts of life span [16, 17]. Studies investigating the effects of age on slower EEG frequencies such as delta (< 4 Hz) and theta (4-8 Hz) reported heterogeneous results. Some studies found that the power of these slow EEG frequencies increased with age, which has been associated with an overall "slowing" of the EEG activity with age[20, 21] . In contrast, there are studies that found no changes in delta or theta power with age [22] or a decreased power in elderly compared to young adults [23, 24]. Gender differences on EEG activity as well as in memory functions are also shown in several works [25-28]. For instance, a few studies found higher delta and theta power in women compared to men during the performance of different cognitive tasks [25-28]. Gender differences in EEG activity were explained by underlying biological mechanisms, such as callosal size or interhemispheric transmission efficacy [30, 31] . Cultural and environmental influences, gender differences concerning cognitive processing in the brain [27,31] . In higher EEG frequencies such as the gamma frequency band, no gender differences could be observed [33]. There is also some evidence of gender differences in functional brain connectivity, showing higher EEG coherence in women than in men [34, 35]. However, no investigation has been carried out on the interplay between the infarcted cerebral hemisphere with other healthy part. Moreover, prior studies that found age-related changes in EEG activity or memory performance

compared younger people between the age of about 20 to 30 years with older participants between the age of about 60 to 80 years [22, 23, 36]. There is also no study at all for the child below the age of 20 years to show the change and compare the neuronal deterioration of the infarcted part of brain.

To achieve the real time detection of critical brain events, raw EEG would require continuous expert review. Although telemedicine has become a prominent tool for cerebrovascular diseases, centralized EEG monitoring with access to around-the-clock neurophysiology experts is not currently available and would be extremely expensive. By applying a Fourier transformation, EEG can be quantified which we called quantitative EEG (QEEG) in terms of its amplitude, power, frequency, and rhythmicity in order to generate numerical values, ratios, or percentages. Like raw EEG, QEEG is proficient of reflecting the changes in neuronal functional status as well as the metabolic condition [37]. The different quantitative parameters have also their own strength for a given clinical condition. Another limitation of EEG lies in the difficulty of resolving and spatially localizing its sources [38]. In order to overcome such limitations and clarify the relationship of EEG to normal and pathological brain function, researchers are increasingly using multi-modal measurements. The combined EEG with MRI as a multi-modal measuring tool is able to correlate neural activity with a sequence of highly space-resolved images. However, to monitor the degree of hypo-activity of the affected part in brain, it is very essential to correlate the extent of infarction and the clinical effect detected by MRI and the analysis of EEG waves. To investigate the changes of neuronal activity between the old person and the child below fifteen years old, a detailed study on the EEG activity is also indispensable.

1.3 Objectives

The present study focused on the correlation between the extent of infarction and the clinical effect detected by MRI and to monitor the degree of hypo-activity of the affected part through the EEG analysis. A detailed investigation of the changes of neuronal activity between an old person and a boy under fifteen years is also performed. In order to accomplish these, a patient of 60 years old suffering from right sided hemiplegia with motor aphasia and a healthy young boy below fifteen years old have been selected. In the course of this thesis the following objectives are fulfilled:

➢ To determine the neuronal activity of a stroke patient and detection of the degree of severity using signal analysis and imaging.

➢ Determination of neuronal signal difference between the affected and unaffected cerebral hemisphere of the patient.

➢ To find the comparison of neural signal between different age group specifically between child and old person.

➢ To compare the evolution of EEG signs with that of motor functions and activities of daily living.

➢ Continuous monitoring to inform about the efficacy of thrombolysis and decisions about intra-arterial intervention.

➢ To inform outcome prognostication and decision about rehabilitation strategies.

1.4 Synopsis

Chapter I: This chapter contains introductory information such as mortality rate in different diseases and the importance of cerebrovascular disease its impacts on the society as well as the objectives, contribution and applications of this thesis.

Chapter II: In this chapter basic information about cerebrovascular diseases, electroencephalogram, neuron and action potential, magnetic resonance imaging have been discussed.

Chapter III: The detail method of collection of the EEG signal and MRI image has been discussed in this chapter.

Chapter IV: This chapter deals with the final results of this research with elaborate discussions by analyzing different EEG signal and their corresponding parameters and MRI images.

Chapter VI: Finally this section deals with concluding talks and future works.

CHAPTER II

BACKGROUND KNOWLEDGE

2.1Introduction

This chapter deals with some basic information about cerebrovascular diseases, it's pathophysiology, clinical feature and management, electroencephalogram and the characteristics of it's different waves, neuronal structure with different parts and action potential, magnetic resonance imaging including mechanism of action with clinical application have been discussed briefly.

2.2 Cerebrovascular Disease

Cerebrovascular disease is the most common cause of disability and third most common cause of death after cancer and ischemic heart disease. Cerebrovascular includes two parts-"cerebro" which refers to the major part of the brain and "vascular" which means arteries and veins.Stroke is the most common clinical manifestation of cerebrovascular diseases with an annual incidence between 180 and 300 per 1000000.The incidence is rising with gradual increasing of diabetic and hypertensive patient. Acute Stroke is illustrated as the focal neurological function deficit most commonly a hemiplegia with or without signs of focal higher cerebral dysfunction (such as motor aphasia), hemisensory loss,visual field defect or brain stem deficit.

When ischemia occurs due to occlusion of the vessels it is known as the infarctive stroke and when the blood vessel is ruptured it is known as the hemorrhagic stroke,About 65% of all stroke are caused by arterial occlusion either with a thrombus which is formed locally at the site of atherosclerotic plaque or an embolic clot and 15% of stroke are caused by hemorrhage.Small arterial occlusion which is known as the lacunar infarct occupies the rest 20% of total stroke. During a stroke there is a core area where blood flow is almost absent and the cells die within five minutes. How much area of the brain is affected depends on exactly how far downstream in the artery the blockage occurs. However the physiological function of the body is regulated by
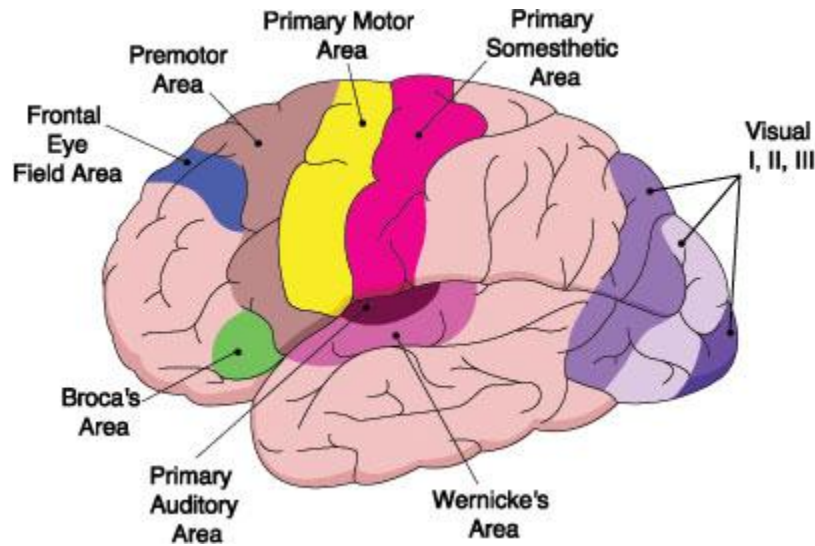
Figure 2.1:Different functional area of brain.

different lobe of the brain. Clinical manifestation due to impaired blood flow of a stroke patient is determined by the site of the lesion of the brain area as different parts of the brain performs the definite function of the brain.

2.3 Types of cerebrovascular disease

There are a number of different types of cerebrovascular disease. The four most common types are:

- **stroke** – a serious medical condition where one part of the brain is damaged by a lack of blood supply or bleeding into the brain from a burst blood vessel
- **transient ischemic attack (TIA)** – a temporary fall in the blood supply to one part of the brain, resulting in brief symptoms similar to stroke
- **subarachnoid hemorrhage** – a type of stroke where blood leaks out of the brain's blood vessels on to the surface of the brain
- **vascular dementia** – persistent impairment in mental ability resulting from stroke or other problems with blood circulation to the brain
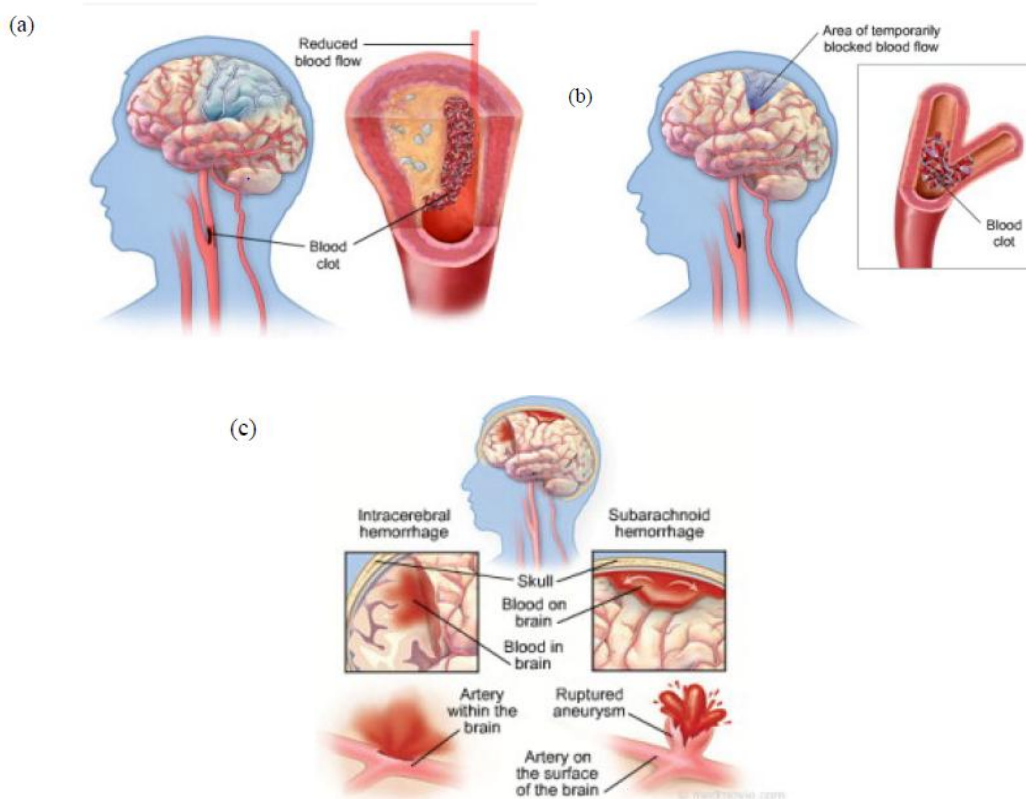
Figure 2.2: Stroke classification (a) Ischemic Stroke, (a) Transient ischemic Stroke, (c) Hemorrhagic Stroke

2.4 Types of Stroke

2.4.1 Ischemic Stroke

Ischemic stroke is by far the most common type of stroke, accounting for a large majority of strokes. There are two types of ischemic stroke: thrombotic and embolic. A thrombotic stroke occurs when a blood clot, called a thrombus, blocks an artery to the brain and stops blood flow. An embolic stroke occurs when a piece of plaque or thrombus travels from its original site and blocks an artery downstream. The material that has moved is called an embolus. How much of the brain is damaged or affected depends on exactly how far downstream in the artery the blockage occurs.
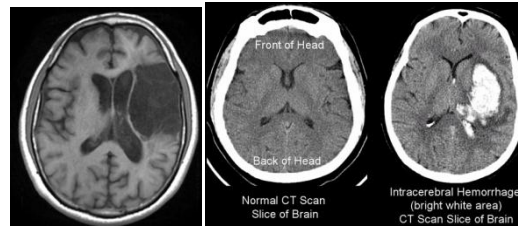
Figure 2.3:MRI image showing infarct and hemorrhage.

2.4.2 Hemorrhagic Stroke

A hemorrhagic stroke can be caused by hypertension, rupture of an aneurysm or vascular malformation, or as a complication of anticoagulation medications. An intracerebral hemorrhage occurs when there is bleeding directly into the brain tissue, which often forms a clot within the brain. Hemorrhagic stroke usually requires surgery to relieve intracranial (within the skull) pressure caused by bleeding

2.5 Pathophysiology of Stroke

Once a reduction in blood flow occurs, that lasts seconds the brain tissue suffers ischemia. If the interruption of blood flow is not restored in minutes, the tissue suffers infarction followed by tissue death. When the low cerebral blood flow persists for a longer duration, then overcomes an infarction in the border zones (areas of poor blood flow between the major cerebral artery distributions). In more severe instances, global hypoxia-ischemia causes widespread brain injury leading to a severe cognitive squeal call hypoxic-ischemic encephalopathy.

Strokes can also result from embolisms, furthermore, embolism blocks small arteries, causing damage to occur.Spontaneous rupture of a blood vessel in the brain causes a hemorrhagic stroke. Another form of cerebrovascular disease includes aneurysms.Cerebral aneurysms can be genetic in nature, due to a wall deformity of the artery. Such aneurysms are common in individuals with genetic diseases (connective tissue disorders, polycystic kidney disease, and arteriovenous malformations).

The process of neuronal ischaemia and infarction. (1) Reduction of blood flow reduces supply of oxygen and hence ATP. H^+ is produced by anaerobic metabolism of available glucose. (2) Energy-dependent membrane ionic pumps fail, leading to cytotoxic oedema and membrane depolarization, allowing calcium entry and releasing glutamate. (3) Calcium enters cells via glutamate-gated channels and (4) activates destructive intracellular enzymes, (5) destroying intracellular organelles and cell membrane, with release of free radicals. Free fatty acid release activates pro-coagulant pathways which exacerbate local ischemia. (6) Glial cells take up H^+, can no longer take up extracellular glutamate and also suffer cell death, leading to liquefactive necrosis of whole arterial territory.

2.6 Stroke risk factors

Fixed

- Age
- Gender (male > female, except in the very young and very old)
- Race (Afro-Caribbean > Asian > European)
- Heredity
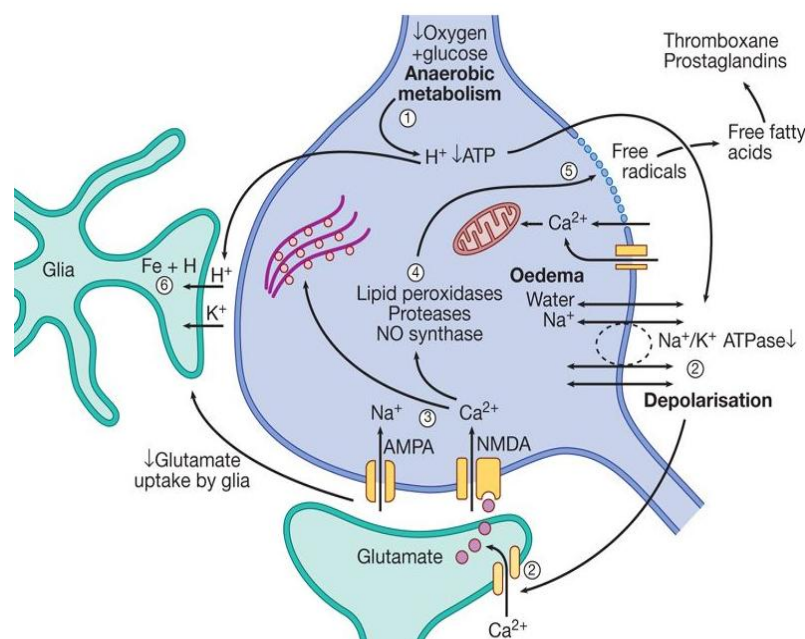
Figure 2.4: Mechanism of brain tissue damage due to ischemia

- Previous vascular event, e.g. myocardial infarction, stroke or peripheral embolism
- High fibrinogen

Modifiable

- High blood pressure
- Heart disease (atrial fibrillation, heart failure, endocarditis)
- Diabetes mellitus
- Hyperlipidemia
- Smoking
- Excess alcohol consumption
- Polycythemia
- Oral contraceptives
- Social deprivation

2.7 Clinical features

The clinical presentation of stroke depends upon which arterial territory is involved and the size of the lesion, both of which will have a bearing on management, such as suitability for carotid endarterectomy. The neurological deficit can be identified from the patient's history and, if the deficit is persistent, from the neurological examination. The presence of a unilateral motor deficit, a higher cerebral function deficit such as aphasia or neglect, or a visual field defect usually places the lesion in the cerebral hemisphere. Ataxia, diplopia, vertigo and/or bilateral weakness usually indicate a lesion in the brain stem or cerebellum. Different combinations of these deficits define several stroke syndromes which reflect the site and size of the lesion and may provide clues to underlying pathology.

Reduced conscious level usually indicates a large-volume lesion in the cerebral hemisphere but may result from a lesion in the brain stem or complications such as obstructive hydrocephalus, hypoxia or severe systemic infection.

Figure 2.5: Right sided hemiplegia affected by CVD.

2.8 Cerebrovascular Diagnostic Tests

The majority of cerebrovascular problems can be identified through diagnostic imaging tests. These tests allow neurosurgeons to view the arteries and vessels in and around the brain and the brain tissue itself.

Cerebral angiography. This procedure is monitored by a fluoroscope (a special x-ray that projects the images on a TV monitor). The contrast dye is injected into the neck area through the catheter, and x-ray pictures are taken.

Carotid duplex (also called carotid ultrasound): In this procedure, ultrasound is used to help detect plaque, blood clots, or other problems with blood flow in the carotid arteries.

Computed tomography (CT or CAT scan): A CT scan is a useful diagnostic test for hemorrhagic strokes because blood can easily be seen. However, damage from an ischemic stroke may not be revealed on a CT scan for several hours or days.

Doppler ultrasound:. There is a "swishing" sound on the Doppler if the venous system is normal. Both the superficial and deep venous systems are evaluated.

Electroencephalogram (EEG): A diagnostic test using small metal discs (electrodes) placed on a person's scalp to pick up electrical impulses. These electrical signals are printed out as brain waves.

Lumbar puncture (spinal tap): An invasive diagnostic test that uses a needle to remove a sample of cerebrospinal fluid from the space surrounding the spinal cord. This test can be helpful in detecting bleeding caused by a cerebral hemorrhage.

Magnetic Resonance Imaging (MRI): A diagnostic test that produces three-dimensional images of body structures using magnetic fields and computer technology. It can clearly show various types of nerve tissue and clear pictures of the brain stem and posterior brain. MRI of the brain can help determine whether there are signs of prior mini-strokes. This test is noninvasive, although some patients may experience claustrophobia in the imager.

Magnetic Resonance Angiogram (MRA): This is a noninvasive study which is conducted in a Magnetic Resonance Imager (MRI). The magnetic images are assembled by a computer to provide an image of the arteries in your head and neck. The MRA shows the actual blood vessels in the neck and brain and can help detect blockage and aneurysms.

2.9 Management
Management is aimed at minimizing the volume of brain that is irreversibly damaged, preventing complications, reducing the patient's disability and handicap through rehabilitation, and reducing the risk of recurrent episodes.

Early admission of patients to a specialized stroke unit facilitates coordinated care from a specialized multidisciplinary team and has been shown to reduce both mortality and residual disability amongst survivors. Consideration of a patient's rehabilitation needs should commence at the same time as acute medical management. Dysphagia is common after stroke and can be

detected by an early bedside test of swallowing. This allows hydration, feeding and medication to be given safely, if necessary by nasogastric tube or intravenously

2.10 Electro-Encephalogram

An EEG is the graphical presentation of neuronal electrical activity recorded from the surface of the scalp using a number of electrodes .Normally there are four type EEG wave-such as alpha, beta, theta and delta wave.The EEG data is analyzed by perceiving the signal from a set of frequency band.

The EEG data is analyzed by examining the signal in a set of frequency bands, These frequency sub bands are usually defined as delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz) and beta (>12 Hz) . Delta andTheta sub-bands are categorical as a slow wave with low frequency but high in amplitude. While Alpha and Beta sub-bands are categorical as a fast wave with high frequency and in low amplitude. Beta sub-band associated with a state of mental activity, in active thinking and concentration. Alpha sub-band associated with a state of relaxation and also in dominant close eyes condition**.** Theta sub-band represented a daydream, light sleep, emotional and stress and problems with attention, profound sleep whereas deep sleep are in delta sub-band in human activity.
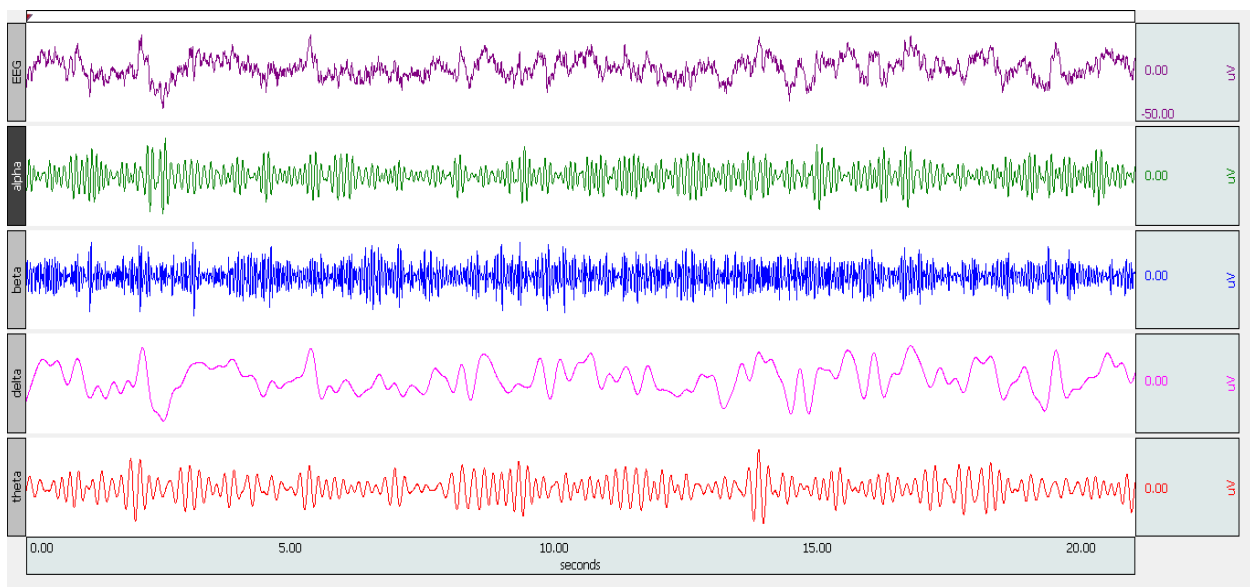

Figure 2.6:EEG with different waves.

2.10.1 Short History of EEG

German physiologist and psychiatrist Hans Berger (1873–1941) recorded the first human EEG in 1924.[7] Expanding on work previously conducted on animals by Richard Caton and others, Berger also invented the electroencephalogram (giving the device its name), an invention described "as one of the most surprising, remarkable, and momentous developments in the history of clinical neurology". His discoveries were first confirmed by British scientists EdgarDouglas Adrian and B. H. C. Matthews in 1934 and developed by them.

In 1934, Fisher and Lowenback first demonstrated epileptiform spikes. In 1935 Gibbs, Davis and Lennox described interictal spike waves and the three cycles/s pattern of clinical absence seizures, which began the field of clinical electroencephalography. Subsequently, in 1936 Gibbs and Jasper reported the interictal spike as the focal signature of epilepsy. The same year, the first EEG laboratory opened at Massachusetts General Hospital.FranklinOffner (1911–1999), professor of biophysics at Northwestern University developed a prototype of the EEG that incorporated a piezoelectric ink writer called a Crystograph (the whole device was typically known as the OffnerDynograph).In 1947, The American EEG Society was founded and the first International EEG congress was held. In 1953 Aserinsky and Kleitman described REM sleep.

In the 1950s, William Grey Walter developed an adjunct to EEG called EEG topography, which allowed for the mapping of electrical activity across the surface of the brain. This enjoyed a brief period of popularity in the 1980s and seemed especially promising for psychiatry. It was never accepted by neurologists and remains primarily a research tool.

The first human EEG recording obtained by Hans Berger in 1924.
The upper tracing is EEG, and the lower is a 10 Hz timing signal.
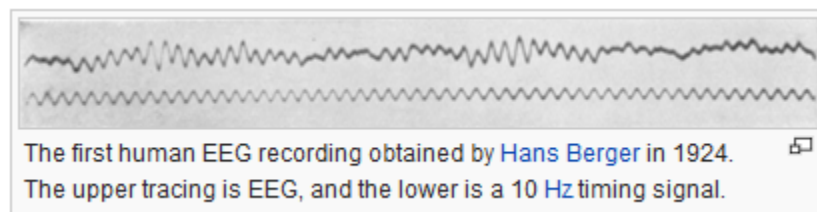
Figure 2.7:First EEG tracing by Hans Berger.

2.10.2 EEG changes in ischemia

EEG changes are closely tied to CBF [35]. When normal CBF declines to approximately 25-35 ml/100 g/min, the EEG first loses faster frequencies, then as the CBF decreases to approximately 17-18 ml/100 g/min, slower frequencies gradually increase. This represents a crucial ischemic threshold at which neurons begin to lose their transmembrane gradients, leading to cell death (infarction). In the setting of carotid clamping, CBF that decreases instantaneously to the ischemic threshold leads to rapid and reversible changes in the EEG (within 20 seconds) [35]. Infarction may not occur for hours at this degree of flow limitation [36] and some electrical activity (mostly delta frequencies) may be seen, but as the CBF continues to decrease toward the infarction threshold (10-12 ml/100 g/min and below), the EEG becomes silent and cellular damage becomes irreversible [35,36,37]

Figure 2.8:The relationship of cerebral blood flow to electroencephalogram (EEG) and pathophysiology. ATP, adenosine triphosphate (CBF). Data from [35,37]

Figure 2.9:Layer of Cerebral Cortex

2.10.3 Cortical layer and EEG wave generation-

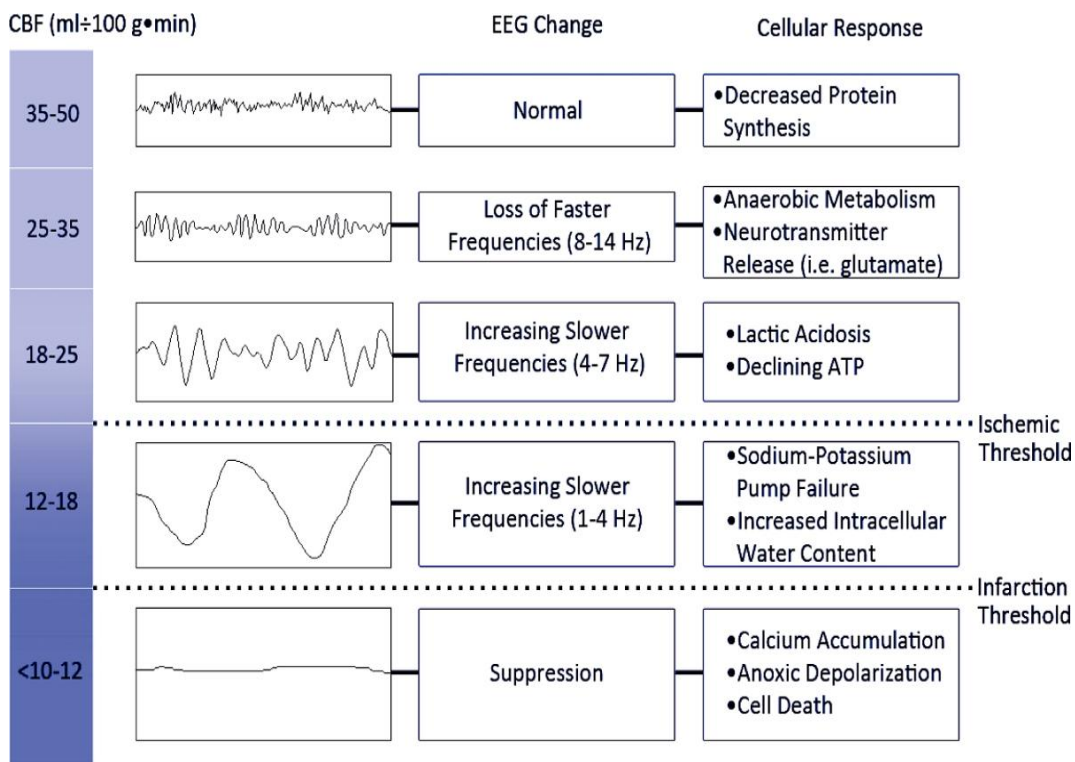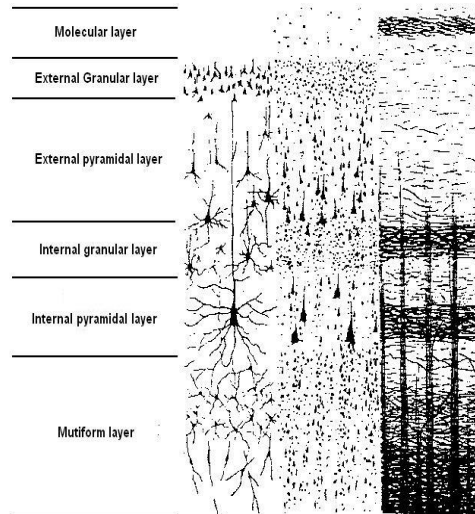Cerebral corte has six layers –(I) Plexiform layer ,(II)Outer granular layer,(III)Outer pyramidal cell layer, (IV)Inner granular layer,(V) Inner pyramidal cell layer,(VI) Multiform layer. Slower frequencies (typically delta [0.5-3 Hz] or theta [4-7 Hz]) are generated by the thalamus and by cells in layers II-VI of the cortex. Faster frequencies (or alpha, typically 8-12 Hz) derive from cells in layers IV and V of the cortex [39]. All frequencies are modulated by the reticular activating system, which corresponds to the observation of reactivity on the EEG [40]. Pyramidal neurons found in layers III, V, and VI are exquisitely sensitive to conditions of low oxygen, such as ischemia, thus leading to many of the abnormal changes in the patterns seen on EEG [12].

2.11 Neuronal Structure and Action Potential

The structural and functional unit of nervous system is called neuron. Most neurons consist of three parts : the **cell body,** or **perikaryon**, which is thesynthetic or trophic center for the entire nerve cell and is receptive to stimuli; the **dendrites,** many elongated processes specialized to receive stimuli from theenvironment, sensoryepithelial cells, or other neurons; and the **axon** (Gr. *axon*, axis), which is a single process specialized in generating and conducting nerve impulses to other cells (nerve, muscle, and gland cells). Axons may also receive information from other neurons, information that mainly modifies the transmission ofaction potentials to those neurons. The distal portion of the axon is usually branched as the **terminal arborization.** Each branch
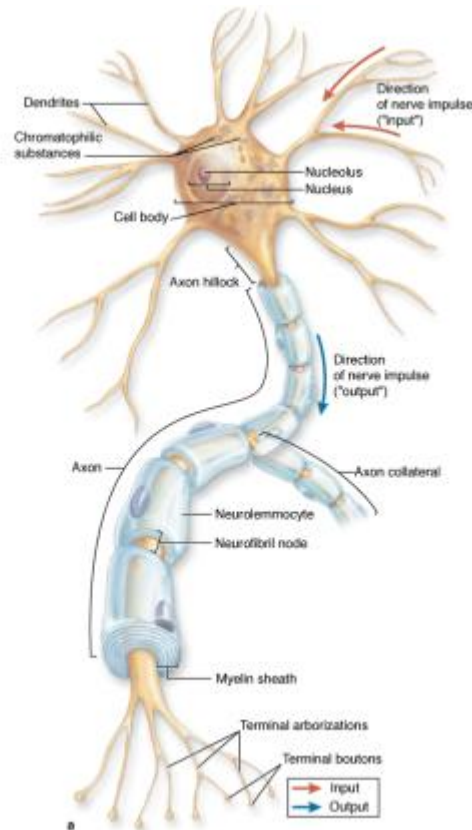
Figure 2.10: Structure of neuron.

terminates on the next cell in dilatations called **end bulbs** (**boutons**), which interact with other neurons or no nerve cells at structures called **synapses.** Synapses initiate impulses in the next cell of the circuit.

2.12 Action Potential

An EEG is the summation of action potentials from the nerve fibers under the electrodes placed on the scalp. In physiology, an action potential is a short-lasting event in which the electrical membrane potential of a cell rapidly rises and falls, following a consistent trajectory. Action potentials occur in several types of animal cells, called excitable cells, which include neurons, muscle cells, and endocrine cells, as well as in some plant cells. In neurons, they play a central role in cell-to-cell communication. In other types of cells, their main function is to activate intracellular processes.
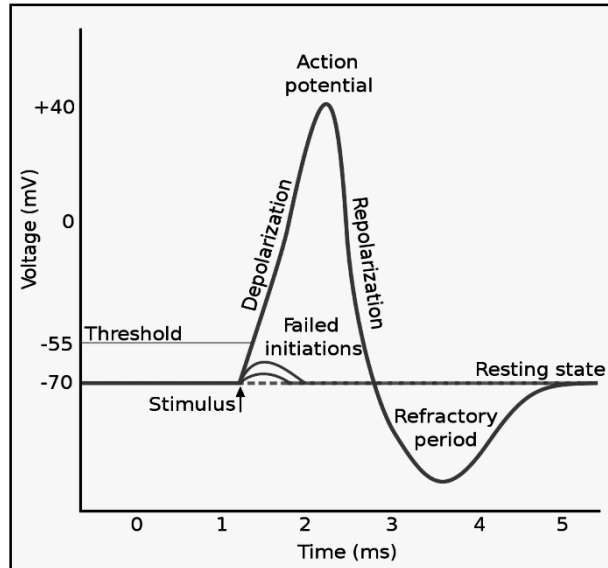
Figure 2.11: Voltage induction process in neuron by Action potential.

Approximate plot of a typical action potential in Figure 2.4 shows its various phases as the action potential passes a point on a cell membrane. The membrane potential starts out at -70 mV at time zero. A stimulus is applied at time = 1 ms, which raises the membrane potential above -55 mV (the threshold potential). After the stimulus is applied, the membrane potential rapidly rises to a peak potential of +40 mV at time = 2 ms. Just as quickly, the potential then drops and overshoots to -90 mV at time = 3 ms, and finally the resting potential of -70 mV is reestablished at time = 5 ms.

All cells in animal body tissues are electrically polarized. In other words, they maintain a voltage difference across the cell's plasma membrane, known as the membrane potential. This electrical polarization results from a complex interplay between protein structures embedded in the membrane called ion pumps and ion channels. In neurons, the types of ion channels in the membrane usually vary across different parts of the cell, giving the dendrites, axon, and cell body different electrical properties. As a result, some parts of the membrane of a neuron may be excitable (capable of generating action potentials), whereas others are not. Recent studies have shown that the most excitable part of a neuron is the part after the axon hillock (the point where the axon leaves the cell body), which is called the initial segment, but the axon and cell body are also excitable in most cases.

Each excitable patch of membrane has two important levels of membrane potential: the resting potential, which is the value the membrane potential maintains as long as nothing perturbs the cell, and a higher value called the threshold potential. At the axon hillock of a typical neuron, the resting potential is around –70 millivolts (mV) and the threshold potential is around –55 mV. Synaptic inputs to a neuron cause the membrane to depolarize or hyperpolarize; that is, they cause the membrane potential to rise or fall. Action potentials are triggered when enough depolarization accumulates to bring the membrane potential up to threshold. When an action potential is triggered, the membrane potential abruptly shoots upward; often reaching as high as +100 mV, then equally abruptly shoots back downward, often ending below the resting level, where it remains for some period of time. The shape of the action potential is stereotyped; that is, the rise and fall usually have approximately the same amplitude and time course for all action potentials in a given cell. In most neurons, the entire process takes place in about a thousandth of a second. Many types of neurons emit action potentials constantly at rates of up to 10–100 per second; some types, however, are much quieter, and may go for minutes or longer without emitting any action potentials.

2.13 Magnetic Resonance Imaging (MRI)

An MRI scan uses a large magnet, radio waves, and a computer to create a detailed cross-sectional image of the patient's internal organs and structures. The scanner itself typically resembles a large tube with a table in the middle, allowing the patient to slide into the tunnel.

The first full-body MRI scanner was created by Prof. Raymond Damadian in 1977 and took nearly 5 hours to produce the first ever full body scan of a human. Dr. Ramadan nicknamed the first MRI scanner the "Indomitable" and it is currently housed in the Smithsonian Institute.[2]

The idea for MRI was initially conceived by Damadian in 1971 after he recognized that under nuclear magnetic resonance certain mouse tumors would display elevated relaxation times compared with normal tissues in vitro.

Reflecting the fundamental importance and applicability of MRI in medicine, Paul Lauterbur of the University of Illinois at Urbana-Champaignand Sir Peter Mansfield of the University of Nottingham were awarded the 2003 Nobel Prize in Physiology or Medicine for their "discoveries

concerning magnetic resonance imaging".The actual research that won the prize was done almost 30 years before while Paul Lauterbur was a professor in the Department of Chemistry at Stony Brook UniversityinNew York[41].

2.13.1 Basic Principles of MRI

The basis of MRI is the directional magnetic field, or *moment*, associated with charged particles in motion. Nuclei containing an odd number of protons and/or neutrons have a characteristic motion or precession. Because nuclei are charged particles, this precession produces a small magnetic moment. When a human body is placed in a large magnetic field, many of the free hydrogen nuclei align themselves with the direction of the magnetic field. The nuclei precession about the magnetic field direction like gyroscopes. This behavior is termed Larmor precession.

The frequency of Larmor precession is proportional to the applied magnetic field strength as defined by the Larmor frequency ω_0

$$\omega_0 = \gamma B_0$$

Where γ is the gyromagnetic ratio and B_0 is the strength of the applied magnetic field. The gyromagnetic ratio is a nuclei specific constant. For hydrogen γ=42.6 MHz/Tesla.

To obtain an MR image of an object, the object is placed in a uniform magnetic field, B_0 of between 0.5 to 1.5 Tesla. As a result, the object's hydrogen nuclei align with the magnetic field and create a net magnetic moment, *M* parallel to B_0This behavior is illustrated in Figure 2.12.

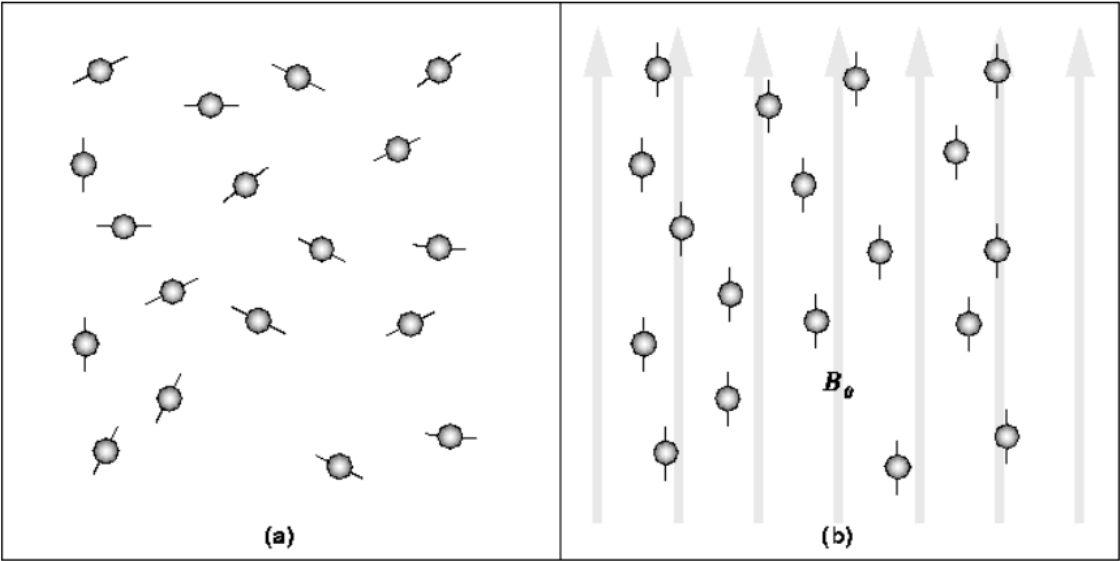**Figure 2.12:** In the absence of a strong magnetic field, hydrogen nuclei are randomly aligned as in (a). When the strong magnetic field B_0.is applied, the hydrogen nuclei precess about the direction of the field as in

Next, a radio-frequency (RF) pulse, B_{rf} is applied perpendicular to B_0 This pulse, with a frequency equal to the Larmor frequency, causes M to tilt away from B_0 as in Figure
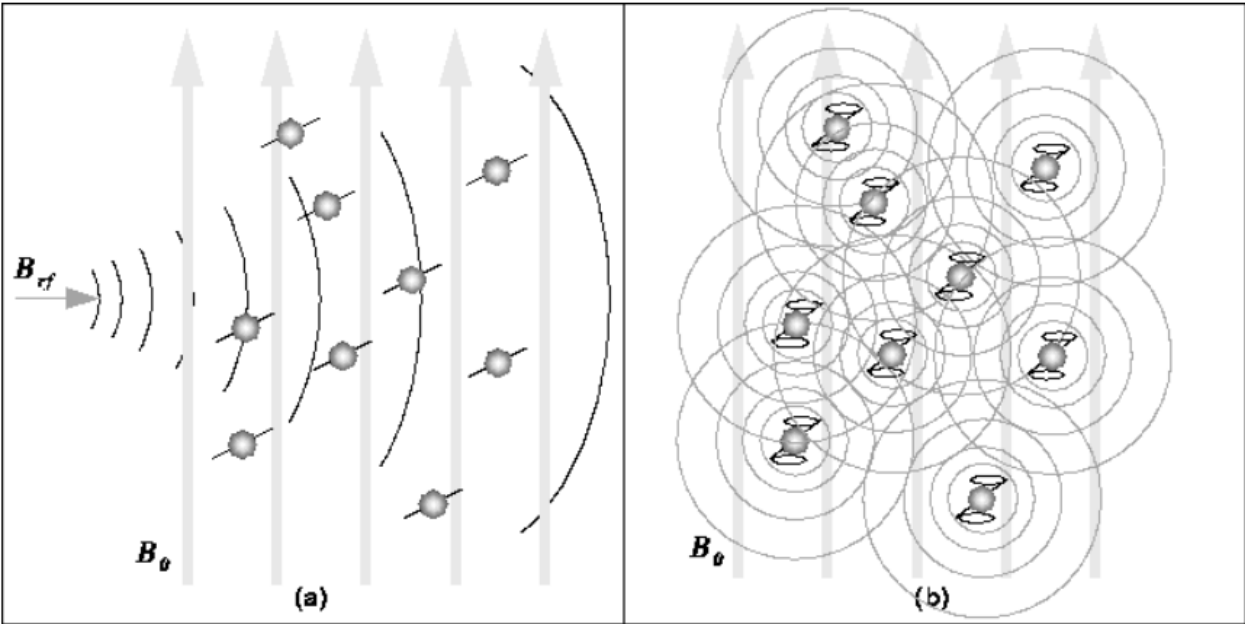
Figure 2.13: (a) The RF pulse, B_{rf} causes the net magnetic moment of the nuclei, M to tilt away from B_0 b) When the RF pulse stops, the nuclei return to equilibrium such that M is again parallel to B_0 During realignment, the nuclei lose energy and a measurable RF signal

Once the RF signal is removed, the nuclei realign themselves such that their net magnetic moment, M is again parallel with B_0. This return to equilibrium is referred to as *relaxation*. During relaxation, the nuclei lose energy by emitting their own RF signal . This signal is referred to as the free-induction decay (FID) response signal. The FID response signal is measured by a conductive field coil placed around the object being imaged. This measurement is processed or reconstructed to obtain 3D grey-scale MR images.

To produce a 3D image, the FID resonance signal must be encoded for each dimension. The encoding in the axial direction, the direction of B_0, is accomplished by adding a gradient magnetic field to B_0. This gradient causes the Larmor frequency to change linearly in the axial direction. Thus, an axial slice can be selected by choosing the frequency of B_{rf} to correspond to the Larmor frequency of that slice. The 2D spatial reconstruction in each axial slice is accomplished using frequency and phase encoding. A ``preparation'' gradient, G_y, is applied causing the resonant frequencies of the nuclei to vary according to their position in the y-direction. G_y is then removed and another gradient, G_x , is applied perpendicular to G_y As a result, the resonant frequencies of the nuclei vary in the x -direction due to G_x and have a phase variation in the y-direction due to the previously applied G_y. Thus, x-direction samples are encoded by frequency and y-direction samples are encoded by phase. A 2D Fourier Transform is then used to transform the encoded image to the spatial domain. The voxel intensity of a given tissue type (i.e. white matter vs grey matter) depends on the *proton density* of the tissue; the higher the proton density, the stronger the FID response signal. MR image contrast also depends on two other tissue-specific parameters:

1.The longitudinal relaxation time,*T1* and

2. the transverse relaxation time,*T2*

T1 measures the time required for the magnetic moment of the displaced nuclei to return to equilibrium (ie. realign itself with B_0). *T2* indicates the time required for the FID response signal from a given tissue type to decay.

When MR images are acquired, the RF pulse, B_{rf} is repeated at a predetermined rate. The period of the RF pulse sequence is the repetition time,TR. The FID response signals can be measured at various times within the TR interval. The time between which the RF pulse is applied and the response signal is measured is the echo delay time,TE. By adjusting TR and TE the acquired MR image can be made to contrast different tissue types.

The MR images used in this thesis were all acquired using a Multiple Echo Spin Echo pulse sequence in which two images are acquired simultaneously. TR and TE are adjusted such that tissues with a high proton density appear bright in the first image and tissues with a long *T2* appear bright in the second image. The two images are said to be proton density-weighted (PD-weighted) and T2-weighted respectively. Figure 2.14 shows 2D slices from the weighted MRI volumes.
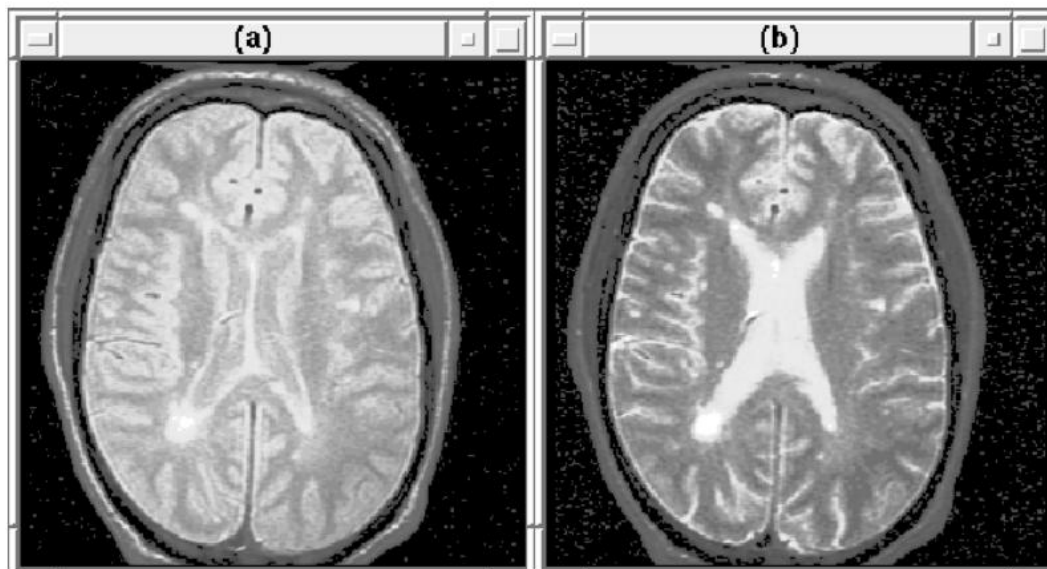
Figure 2.14: (a) A proton density (PD) weighted MR image slice. (b) The same T2-weighted slice.

2.13.2 Application of MRI in human body

The following are just some of the examples where an **MRI scan** is used:

- Abnormalities of the brain and spinal cord
- Tumors, cysts, and other abnormalities in various parts of the body
- Injuries or abnormalities of the joints, such as back pain
- Certain types of heart problems
- Diseases of the liver and other abdominal organs
- Causes of pelvic pain in women (e.g. fibroids, endometriosis)
- Suspected uterine abnormalities in women undergoing evaluation for infertility.

The extraordinary ability to allow an immediate diagnosisof stroke and to generate non-invasively such a range ofinformation about the status of blood vessels and the brain makes it an attractive imaging option forpatients presenting with stroke.The anatomical location of the area of ischaemiaand its viability (on diffusion-weighted imaging),together with arterial imaging (on magnetic resonanceangiography), are important pieces of information,which allow the clinician to establish the mechanism ofstroke. For example, lesions seen on diffusion-weightedimaging in

Figure 2.15:MRI machine

both hemispheres or in more than one arterial territory might suggest a cardiac source of embolism, border-zone lesions often indicate ipsilateral high-gradecarotid artery stenosis, or a lesion restricted to the territory of a single small penetrating vessel suggests in-situ small vessel thrombosis.

CHAPTER III

METHODOLOGY

3.1Introduction

The detail method of collection of the EEG signal and MRI image has been discussed in this chapter. Cerebral Hemisphere of the brain regulate the function of the contralateral side of the body. If the right side of the body is paralyzed then it should be assumed that the location of the lesion is in the left cerebral hemisphere. At the site of the lesion the neuronal activity will be diminished that will be reflected in the EEG waves and the image of MRI.

3.2 Subjects Specifications

A 60 years old patient suffering from right sided hemiplegia with motor aphasia due to cerebrovascular diseases and a healthy young child were enrolled for this study.The Subjects had not taken any medication during the week prior to the study.None of the Subjects were smokers and they refrained from alcohol and caffeine containing drinks.After being informed of the study design, they gave their written consent. The study was approved by the local Ethics Committee. Each participant had an initial visit to the experimental laboratory for a physical examination and a medical history assessment.

3.3 Necessary Tools Specifications

There are different types of tool and software required for data acquisition from subjects. Among them some important tools are listed in Table 3.1. It should be remember that we used other basic tools like personal computer, connecting cable, chair, table etc. Detail about these items is listed in Table 3.1. These tools are required for whole experimental period (during data/signal recording as well as signal analysis).

Table3.1:Tools required for data acquisition

Si. No.	Name of the tool	Model	Description	Used for
1	Cable	SS2LA (Biopac, USA)	Fully shielded, permits high-resolution recording	Collecting ECG signal from body through electrodes
2	Pulse Transducer	SS4LA (Biopac, USA)	Permits high-resolution sensing	Collecting pulse signal from skin

				and recording	
3	LDF Probe	TSD 140 (Biopac, USA)	Highly sensitive and calibrated	Blood flow measurement from human skin
4	Vinyl Electrode	EL503 (Biopac, USA)	Disposable	Connecting the body skin with data acquisition cable
5	Electrode Gel	GEL101 (Biopac, USA)	Formulated with 0.5% saline in a neutral base	Ensuring better conductivity between skin and the electrode
6	Data Acquisition Unit	MP36 (Biopac, USA)	Built-in universal amplifiers	Recording and conditioning electrical signals from the skin
8	LDF Amplifier	LDF100C (Biopac, USA)	Blood perfusion amplifiers	Recording and conditioning LDF signals from skin
9	Interfacing Cable	Biopac, USA	Reliable interfacing between computer and module	Connecting MP36 unit with computer
10	Computer System	Windows XP & Windows 7	Highly configured	Data recording and analysis throughout whole exp. Period
11	Biopac Student Lab Software	BSL Lessons 3.7.3 & BSL PRO 3.7.3 (Biopac, USA)	Complete guide for designed experiments	Data recording and analysis
12	Skin Cleanser	Biopac, USA	Active chemical	Clean the skin of subjects and remove dust, etc.
13	AcqKnowledge	AcqKnowledge	Data recording and	Data recording and

	Software	4.0 & 4.1 (Biopac, USA)	analyzing software	analysis

3.4 Experimental Setup

The study was performed in a quiet room with the temperature kept constant at 25°C (24-26). Initially, we verified all connections and power supply of computer before turning it on. We also verified the connection of power supply for each module of MP36 data acquisition unit as well as their individual interfacing cable between computer and MP36 unit. We turned only the computer on after ensuring that all connections associated with hardware were ok for our experiment. Biopac student lab (BSL 3.7.3 and BSL PRO 3.7.3) software and AcqKnowledge software (AcqKnowledge 4.0 or AcqKnowledge 4.1) were installed in our computer before.

3.4.1 Hardware Setup

In this thesis, I used single modules of MP36 data acquisition unit. At first, the BIOPAC MP36 data acquisition units were turned off. Then electrode lead set (SS2LA) was plugged into channel 1 of MP36 (Biopac, USA) data acquisition unit for the purpose of EEG recordings as showed in Figure. Plugs into Channel 1

3.4.2 Database - Subject Preparation

For EEG recordings, three electrodes (EL503) were placed on the Subject body as showed in Figure3.1.It is important that I followed the electrode procedure below to obtain an optimal EEG recording:

- The surface of the skin was abraded at the point of electrode placement in about a 2"diameter.
- Alcohol was not used to clean the skin because alcohol dries the skin and prevent good electrical contact with the electrode.
- An electrode was peeled off using the tab without touching the adhesive.
- A drop of GEL electrode gel was placed on to the small sponge of the electrode.
- The electrodes were attached to the skin in the positions shown (over the previously abraded areas).
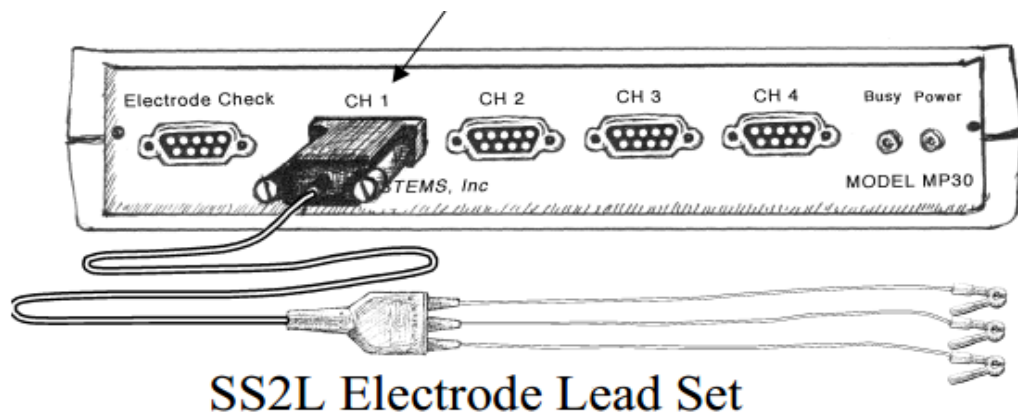
Figure 3.1: Hardware setup of MP36 module 1 for EEG recordings
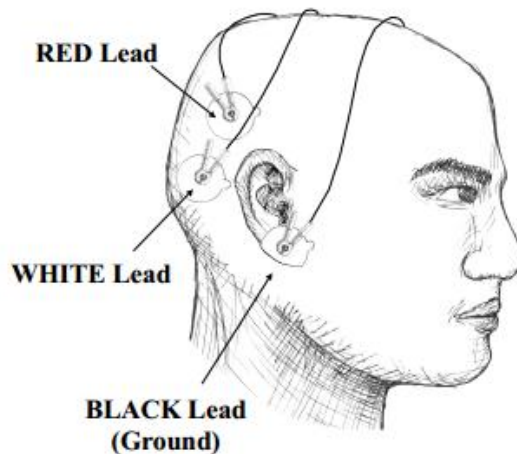
Figure 3.2: Subject setup for EEG recordings

After placing three electrodes, the Subjects were rested in chair in sitting position. For optimal electrode adhesion, the electrodes were placed on the Subject's skin at least 5minutes before the start of the calibration procedure.

3.4.3 End-Connection Setup

The electrode lead set (SS2LA) was attached to the electrodes (EL503) placed on the Subject, following the color code as showed in Figure 4.3(a). Each of the pinch connectors on the end of the electrode cable were attached to a specific electrode. The electrode cables connected each cable to the proper electrode. The pinch connectors work like a small clothespin, but will only latch into the nipple of the electrode from the one side of the connector. Electrode cables were positioned such that they were not pulling on the electrodes or the transducer.

The electrode cable clip (where the cable meets the three individual colored wires) was attached to a convenient location (cab be on the subject's clothes). This had relieved cable strain. The subject was not in contact with nearby metal objects (faucets, pipes, etc.), and any wrist or ankle bracelets were removed. The subject was relaxed in sitting position.

3.4.4 Software and Calibration Setup

Biopac Student Lab software was started in computer with which MP36 module 1 was connected and specific lesson for EEG were chosen. Experimental setup was finished with typing a filename where recorded data will be saved. The calibration procedure establishes the hardware's internal parameters (such as gain, offset, and scaling) and is critical for optimum performance. Close attention was being used to the calibration process. To calibrate MP36 module 1, electrode connections were checked again and the subject was relaxed. After starting calibration, we waited for calibration procedure to stop. The Subject was remained relaxed throughout calibration and the calibration procedure was stopped automatically after 8 seconds. At the end of the 8-sec calibration recording, the screen resembled Figure .

3.5 EEG Signals Recording

- The Subjects were relaxed in the sitting position throughout the whole experimental period.

- The recording was suspended before the Subject prepares for the next recording segment
- It was also made sure that the electrodes do not "peel up".
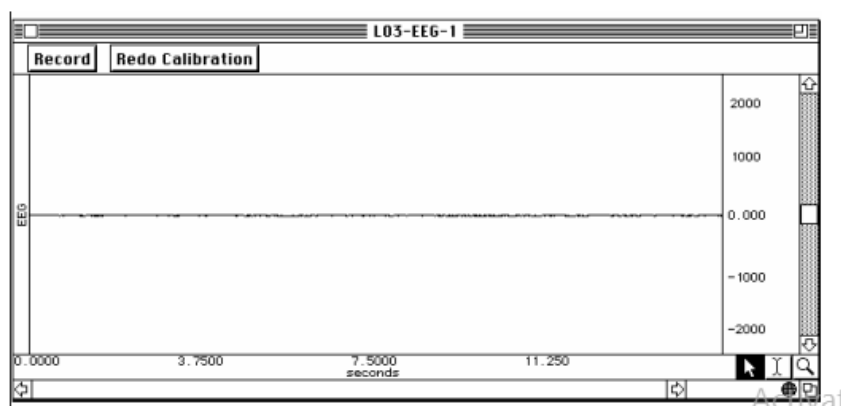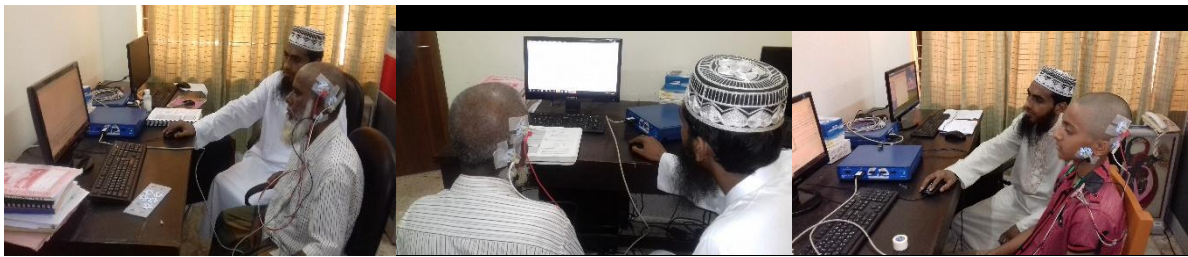- The whole data recording procedure is showed in Figure 3.3

Figure 3.3: Calibration procedure for EEG

| (a) | (b) | (c) |

Figure 3.4 :(a)EEG signal collection from left side of the patient (b)From the right side of the patient   and (c) From the boy in KUET lab.

3.6 Quantitative analysis of EEG

EEG data were recorded for several test conditions including ischemic stroke patient and a healthier child. Neuronal activities were determined using the acknowledge software healthier young. These data were then filtered through a band pass filter of frequency 0.5–40 from the recorded EEG. Figure 4.1 shows the raw EEG spectra taken from the stroke patient and the Hz and gain of 12 dB/octave. As a result, the EEG data were re-referenced to the common average reference. Digital EEG can be transformed into power spectra by fast Fourier transformation (FFT), compressing long periods of raw EEG into quantitative EEG (QEEG) parameters. These can be displayed as graphs and may reveal subtle changes in the EEG earlier than any other monitoring technique. These graphs can be used to monitor depth of sedation, intraoperative brain function (effects of sedation or brain injury), and detect seizures.

3.6.1 Spectrum Analysis of Neuronal Signals – Fourier Transform

Spectrum analysis is referred to as frequency domain analysis or spectrum density estimation, is the technical process of decomposing a complex signal into simpler parts. Many physical processes are best described as a sum of many individual frequency components. Any process that quantifies the various amounts (e.g. amplitudes, powers,

intensities, or phases), versus frequency can be called spectrum analysis. Spectrum analysis can be performed on the entire signal. Alternatively, a signal can be broken into short segments (sometimes called frames), and spectrum analysis may be applied to these individual segments. Periodic functions are particularly well-suited for this sub-division. General mathematical techniques for analyzing non-periodic functions fall into the category of Fourier analysis.

The Fourier transform of a function produces a frequency spectrum which contains all of the information about the original signal, but in a different form. This means that the original function can be completely reconstructed (synthesized) by an inverse Fourier transform. For perfect reconstruction, the spectrum analyzer must preserve both the amplitude and phase of each frequency component. These two pieces of information can be represented as a 2-dimensional vector, as a complex number, or as magnitude (amplitude) and phase in polar coordinates. A common technique in signal processing is to consider the squared amplitude, or power; in this case the resulting plot is referred to as a power spectrum.

In practice, nearly all software and electronic devices that generate frequency spectra apply a fast Fourier transform (FFT), which is a specific mathematical approximation to the full integral solution. Formally stated, the FFT is a method for computing the discrete Fourier transform of a sampled signal. Because of reversibility, the Fourier transform is called a representation of the function, in terms of frequency instead of time; thus, it is a frequency domain representation. Linear operations that could be performed in the time domain have counterparts that can often be performed more easily in the frequency domain. Frequency analysis also simplifies the understanding and interpretation of the effects of various time-domain operations, both linear and non-linear. For instance, only non-linear or time-variant operations can create new frequencies in the frequency spectrum.

3.6.2 Frequency Spectrum

The frequency spectrum of a time-domain signal is a representation of that signal in the frequency domain as shown in Figure 3.5. The frequency spectrum can be generated via a Fourier transform of the signal, and the resulting values are usually presented as amplitude and phase, both plotted versus frequency [60]. Any signal that can be represented as

amplitude that varies with time has a corresponding frequency spectrum. This includes familiar concepts such as visible light (color), musical notes, radio/TV channels, and even the regular rotation of the earth. When these physical phenomena are represented in the form of a frequency spectrum, certain physical descriptions of their internal processes become much simpler. Often, the frequency spectrum clearly shows harmonics, visible as distinct spikes or lines at particular frequencies that provide insight into the mechanisms that generate the entire signal.

A fast Fourier transform (FFT) is an algorithm to compute the discrete Fourier transform (DFT) and it's inverse. A Fourier transform converts time (or space) to frequency and vice versa; an FFT rapidly computes such transformations. As a result, fast Fourier transforms are widely used for many applications in engineering, science, and mathematics. The basic ideas were popularized in 1965, but some FFTs had been previously known as early as 1805. Fast Fourier transforms have been described as "the most important numerical algorithm of our lifetime" [61].
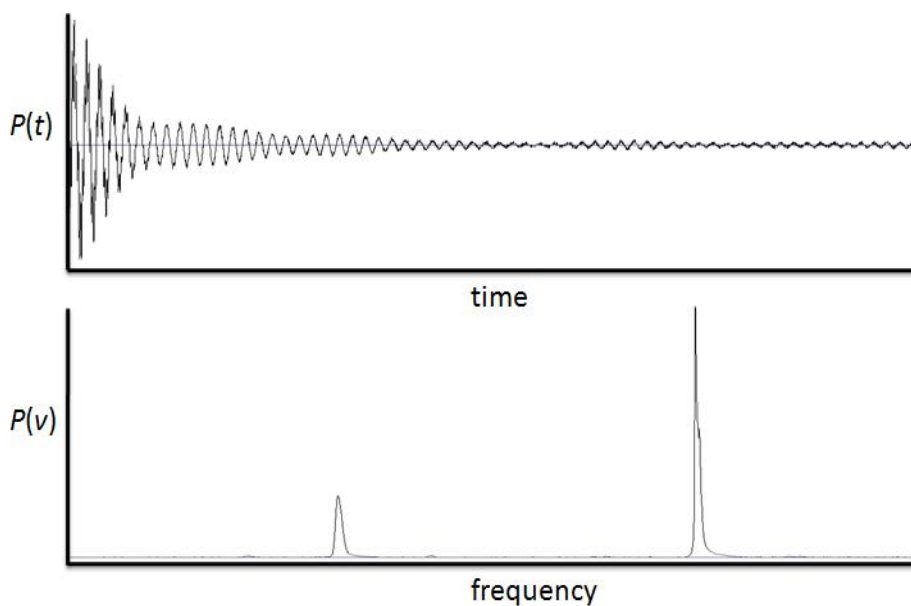
Figure 3.5: Frequency and time domain for the same signal

An FFT computes the DFT and produces exactly the same result as evaluating the DFT definition directly; the only difference is that an FFT is much faster. (In the presence of round-off error, many FFT algorithms are also much more accurate than evaluating the DFT definition directly, as discussed below.)

Let $x_0, x_1, \ldots\ldots, x_{N-1}$ be complex numbers. The DFT is defined by the formula-

$$X_k = \sum_{n=0}^{N-1} x_n\, e^{-j\frac{2\pi nk}{N}} \qquad k = 0,1,\cdots,N-1$$

Evaluating this definition directly requires $O(N^2)$ operations: there are N outputs X_k, and each output requires a sum of N terms. An FFT is any method to compute the same results in $O(N \log N)$ operations. More precisely, all known FFT algorithms require $O(N \log N)$ operations. To illustrate the savings of an FFT, consider the count of complex multiplications and additions. Evaluating the DFT's sums directly involves N^2 complex multiplications and $N(N-1)$ complex additions [of which $O(N)$ operations can be saved by eliminating trivial operations such as multiplications by 1].

3.7 Video EEG Signal Collection

For video EEG signal collection electrode were placed according to 10/20 system.The system is based on the relationship between the location of an electrode and the underlying area of cerebral cortex. The numbers '10' and '20' refer to the fact that the distances between adjacent electrodes are either 10% or 20% of the total front-back or right-left distance of the skull. Each site has a letter to identify the lobe and a number to identify the hemisphere location..Four anatomical landmarks are used for the essential positioning of the electrodes: first, the nasion which is the point between the forehead and the nose; second, the inion which is the lowest point of the skull from the back of the head and is normally indicated by a prominent bump; the pre auricular points anterior to the ear. No central lobe exists, the 'C' letter is used for identification purposes only. The 'z' (zero) refers to an electrode placed on the mid line. Even numbers (2,4,6,8) refer to electrode positions on the right hemisphere.Odd numbers (1,3,5,7) refer to electrode positions .

Electrode	Lobe
F	Frontal
T	Temporal
C	Central *
P	Parietal
O	Occipital
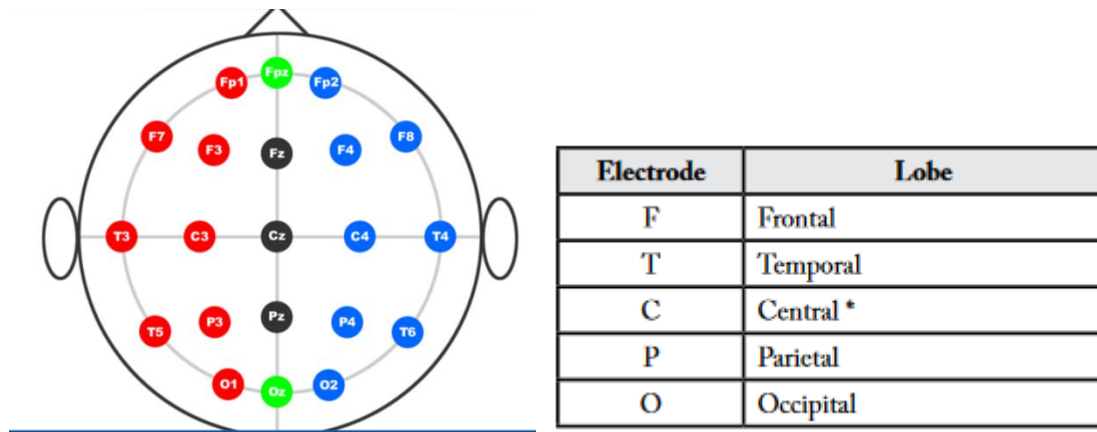
Figure 3.6:Position of the electrode in 10/20 system.
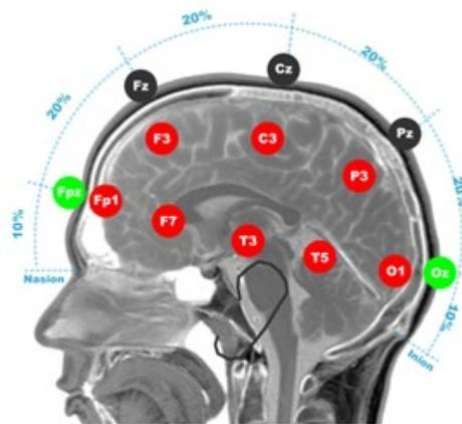
Figure 3.7:Electrode position shown in sagital section of brain.

3.8 Magnetic Resonance Image Collection

For MRI we used 1.5 T HITACHI scanner in Gazi Medical College Hospital Khulna which is a private medical college in Bangladesh which yielded 20 contiguous slices that were 5 mm thick repetition time (TR) 500 ms, echo time (TE) 10 ms.The whole image collection procedure is showed in Figure:

(a)

(b)

(c)

(d)

Figure 3.8:Video EEG signal collection(a)Electrode placement (b)Fixation of electrode (c)EEG recording (d)Monitoring of EEG.

(a)   (b)

(c)   (d)

Figure 3.9:MRI image collection (a+b)Patient sitting on MRI machine,(c+d) Taking the image of the patient
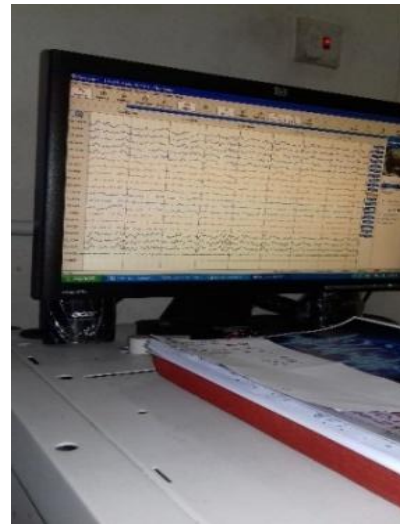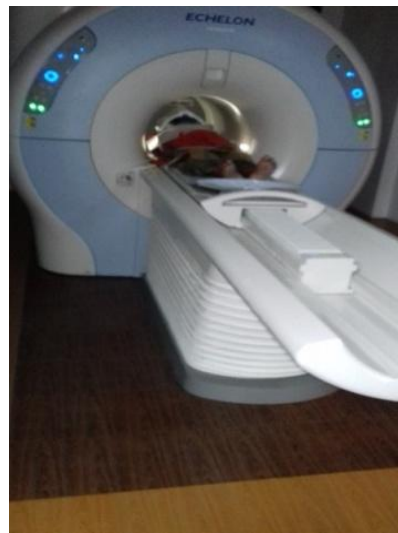
```
                    ┌──────────────────┐
                    │   Patient and    │
                    │ control selection│
                    └──────────────────┘
         ┌──────────────────┐        ┌──────────────────┐
         │   EEG signal     │        │    MRI image     │
         │collection from both│      │ collection of the│
         │patient and control│       │     patient      │
         └──────────────────┘        └──────────────────┘

         ┌──────────────────┐        ┌──────────────────┐
         │   Quantitative   │        │Detection the difference│
         │  analysis of EEG │        │between normal and│
         │      signal      │        │  abnormal part   │
         └──────────────────┘        └──────────────────┘

         ┌──────────────────┐        ┌──────────────────┐
         │    Comparison    │        │ Comparison with  │
         │ between the injured│      │  healthy part of │
         │and uninjured part │       │      brain       │
         └──────────────────┘        └──────────────────┘

         ┌──────────────────┐        ┌──────────────────┐
         │Relative comparison│       │   Detection of   │
         │ with the control in│      │pathological lesion│
         │  respect of age  │        │                  │
         └──────────────────┘        └──────────────────┘
                    ┌──────────────────┐
                    │   Detection of   │
                    │  neuronal status │
                    └──────────────────┘
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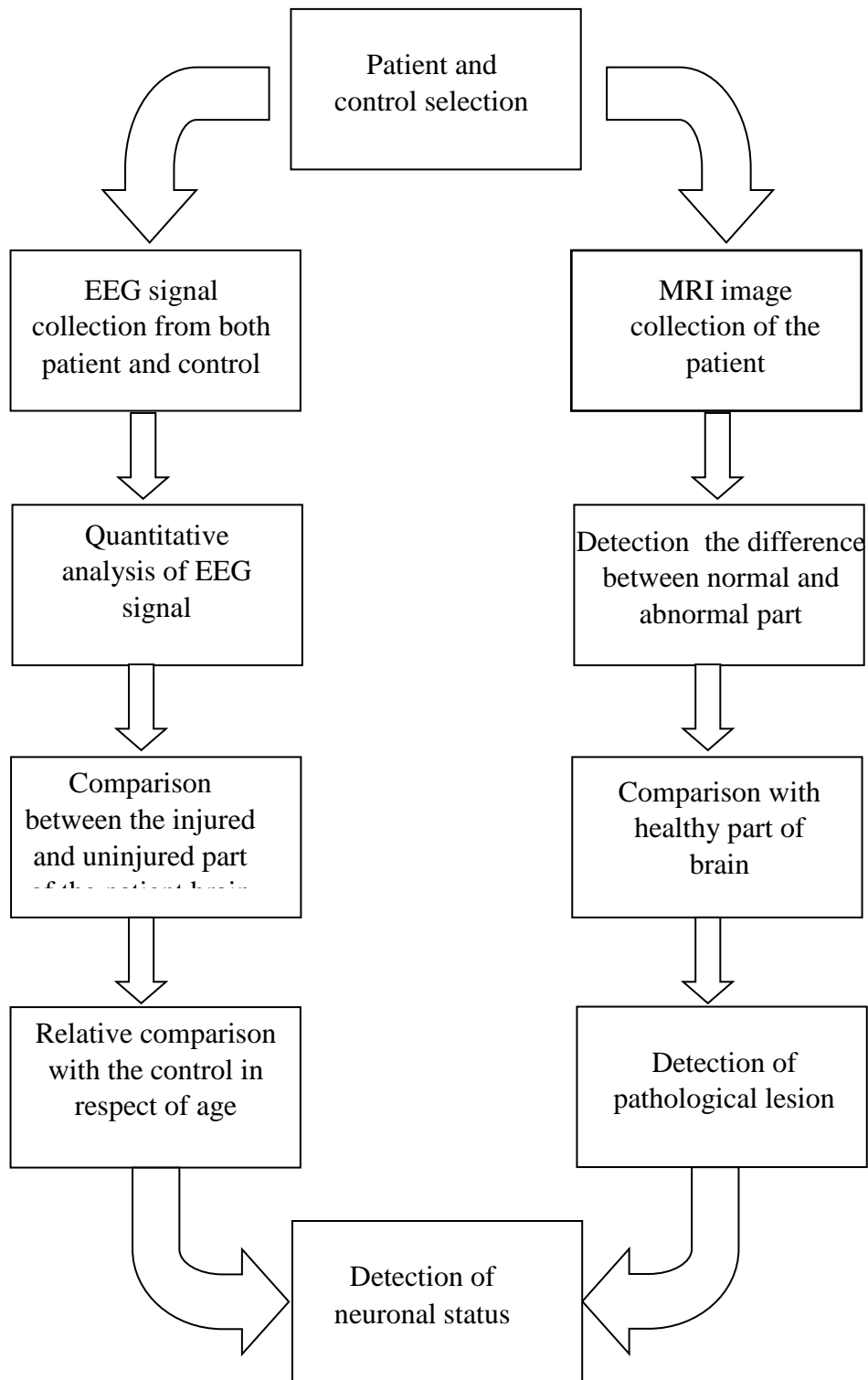Fig3.10:Flow chart showing the method of detection the neuronal status.

<p style="text-align:center">CHAPTER IV</p>
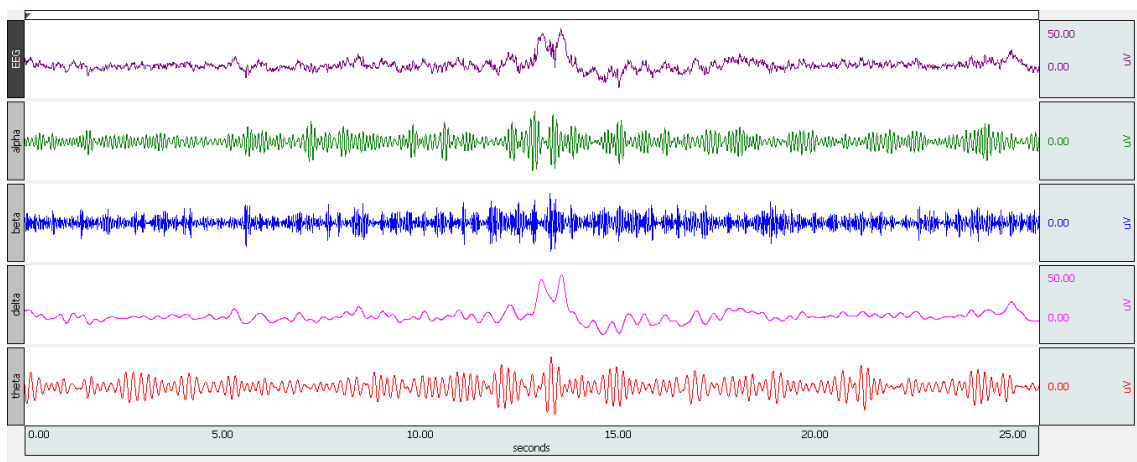
<p style="text-align:center">RESULTS AND DISCUSSION</p>
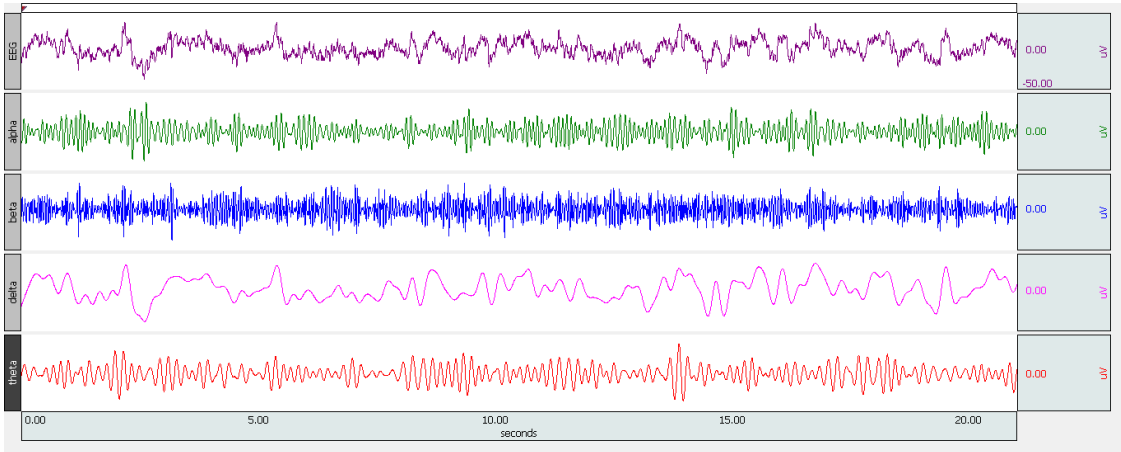
4.1 Introduction

In this chapter the delta activity of the of the both right and left cerebral hemisphere has been compared. Then the DAR and DTABR value was detected of both the control and the patient.The DAR and DTABR was compared between the healthy and injured part of the patient as well as with the control. Finally MRI image of the patient was correlated with the quantitative EEG analysis.
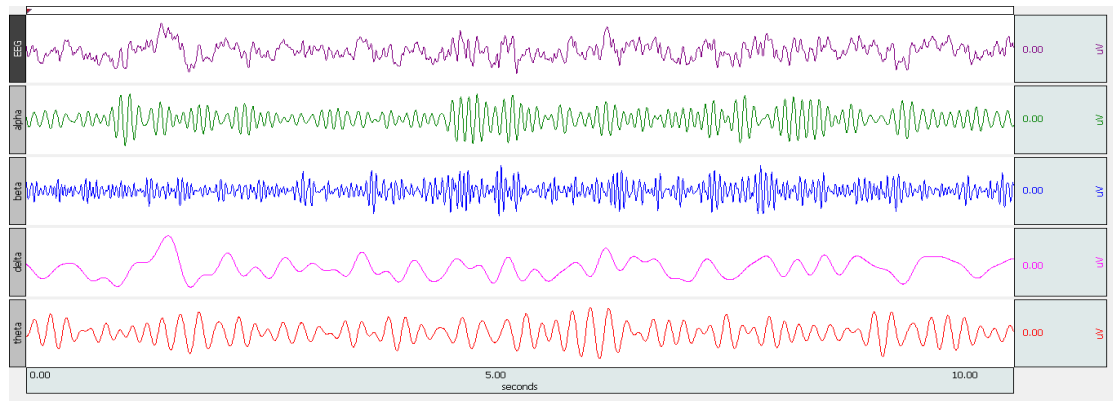
4.2 Analysis of EEG waves

EEG data were recorded for several test conditions including ischemic stroke patient and a healthier child. Neuronal activities were determined using the acknowledge software healthier young. These data were then filtered through a band pass filter of frequency 0.5–40 from the recorded EEG. Figure 4.1 shows the raw EEG spectra taken from the stroke patient and the Hz and gain of 12 dB/octave. As a result, the EEG data were re-referenced to the common average reference. Digital EEG can be transformed into power spectra by fast Fourier transformation (FFT), compressing long periods of raw EEG into quantitative EEG (QEEG) parameters. These can be displayed as graphs and may reveal subtle changes in the EEG earlier than any other monitoring technique. These graphs can be used to monitor depth of sedation, intraoperative brain function (effects of sedation or brain injury), and detect seizures.

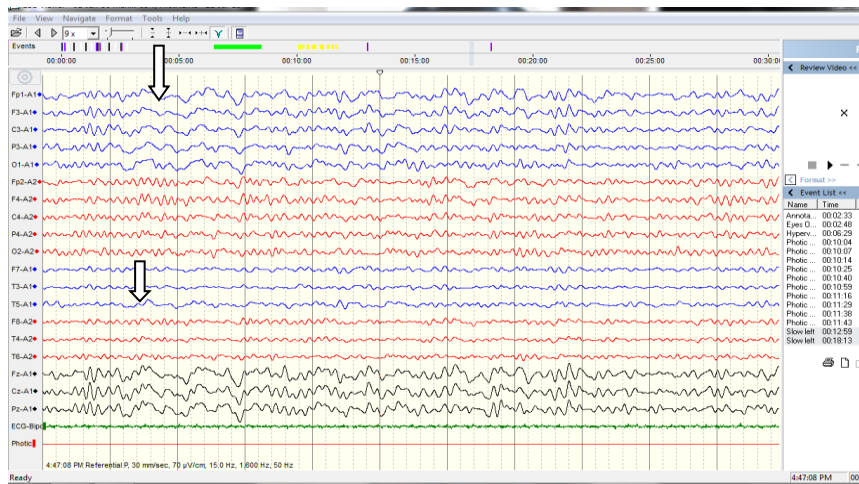
<p style="text-align:center">(a)</p>

(b)

(c)

(d)

Figure 4.1: EEG with its different waves. (a) Right Hemisphere (b) Left Hemisphere (c) EEG of the control (d) EEG (10/20 system) of the patient showing increased delta activity in fronto- temporal region

The brain function is represented on EEG by oscillations of certain frequencies. Slower frequencies (typically delta [0.5-3 Hz] or theta [4-7 Hz]) are generated by the thalamus and by cells in layers II-VI of the cortex. Faster frequencies (or alpha, typically 8-12 Hz) derive from cells in layers IV and V of the cortex. From the FFT analysis the value of such bands are defined in this work as delta (.56-3.90 Hz), theta (3.51-7.51Hz), alpha (7.08-12.89Hz), and beta (12.20-29.79 Hz).

Early studies suggest that alpha activity disturbances (e.g., amplitude attenuation; slowing) are generally indicative of cortical injury whereas abnormal delta activity reflects cortical differentiation due to subcortical and/or white matter injury [38]. However, this is speculative and more evidence is required to definitively assess these possibilities. Of 20 QEEG measures computed using Fourier- derived or other analyses, delta power measures had the strongest correlation with relative CBF (a negative correlation, and alpha power had a relatively strong positive correlation with the latter [39]. Other evidence indicates that delta activity may reflect pathophysiological processes such as oxidative stress [40]. It is well established in the literature that delta band would be significantly greater in the acute stroke sample, whereas relative alpha power would be significantly greater in the control sample.

4.2.1 **Analysis of Delta wave**

Generally, delta activity demonstrates the degree of IS monitoring and prognostication [41,42,43,44,45]. The relative delta percentage appears to provide the most robust correlation with CBF and metabolism during focal ischemia. Figure 4.2a, 4.2b, and 4.2c show the delta frequencies of the left cerebral hemisphere, right cerebral hemisphere of the stroke patient and the healthier child. Delta waves were analyzed between the frequency ranges of 0.56-3.90Hz. The values of delta activity for left and right cerebral hemisphere are summarized in Table 4.1. A relative comparison of delta activities between the left and right cerebral hemisphere are also shown in Fig. 4.4. From the Fig. 4.4, it is seen that the delta activity of the left cerebral hemisphere is much higher than the right cerebral hemisphere. The delta activity of both cerebral hemisphere are also higher than the control. It is also clear from the Fig. that delta activity in the left side show the much more higher value.

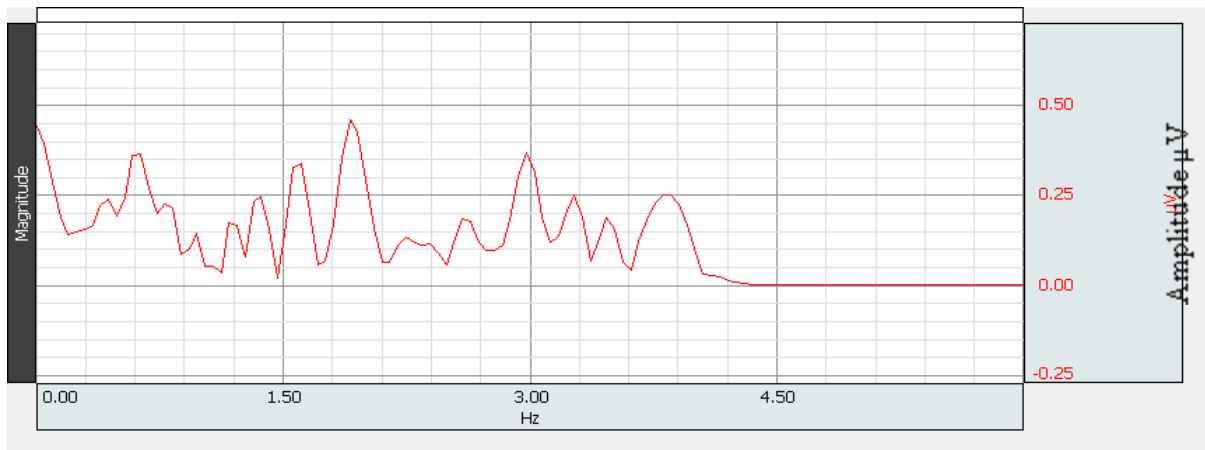Table 4.1: Delta value of the Right and left cerebral hemisphere of the patient:

Delta Wave	
Right Hemisphere(μV)	Left Hemisphere(μV)
0.10309	0.18462
0.10408	0.2478
0.10697	0.40445
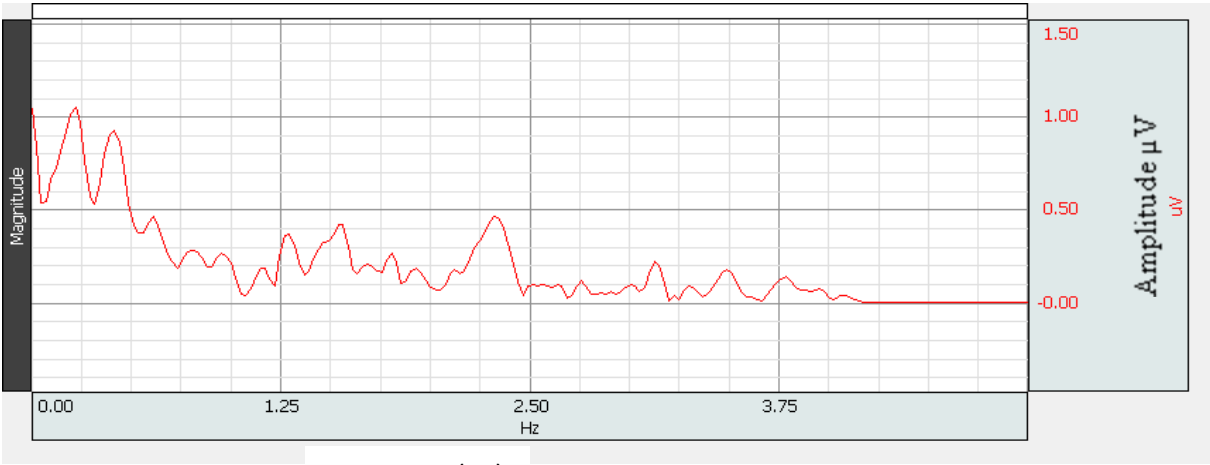
Frequency (Hz)   (a)
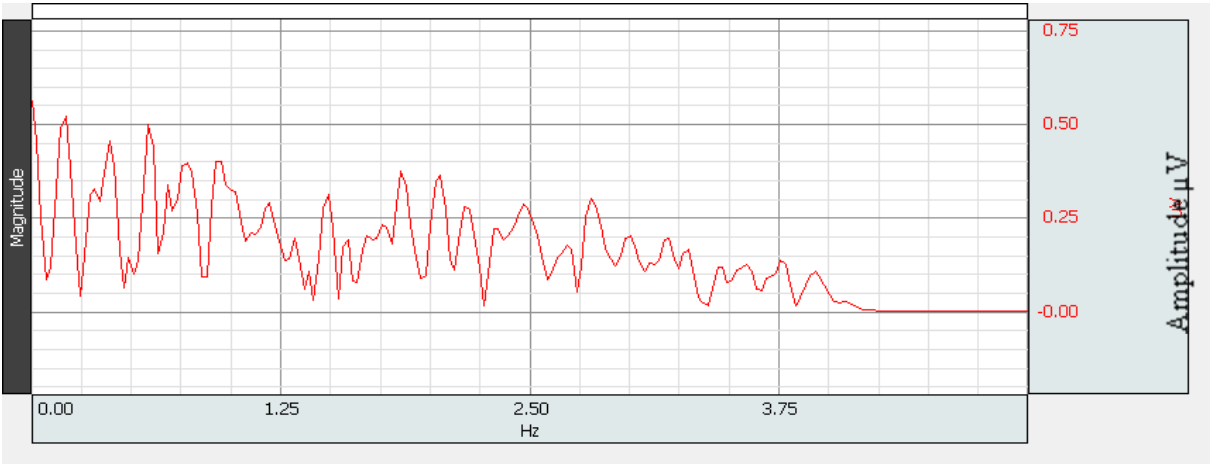
Frequency (Hz)   (b)

Frequency (Hz)

(c)

Figure 4.2: Horizontal axis indicate frequency(Hz) and vertical axis indicate amplitude (µV) (a) Right sided delta activity of the patient (b) Left sided delta activity of the patient (c) Delta activity of the control
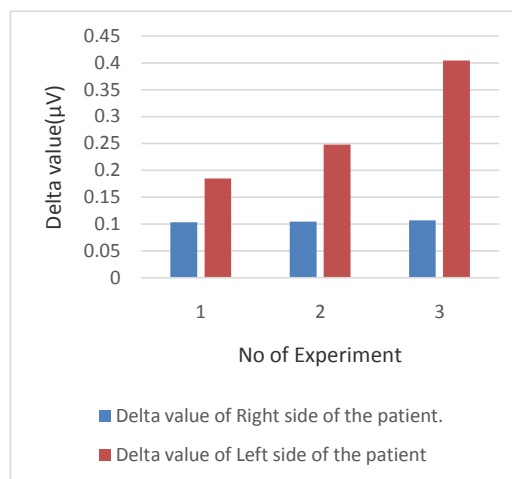

Figure 4.3 : Comparison of delta activity between the right and left cerebral hemisphere of the patient.

4.2.2 **Analysis of Alpha wave**

EEG changes are closely tied to CBF. When normal CBF declines to approximately 25-35 ml/100 g/min, the EEG first loses faster frequencies, then as the CBF decreases to approximately 17-18 ml/100 g/min, slower frequencies gradually increase. This represents a crucial ischemic threshold at which neurons begin to lose their transmembrane gradients, leading to cell death (infarction). Figure 4.3a, 4.3b, and 4.3c show the faster frequency i.e. alpha activities for the same subjects. These waves were analyzed between the frequency ranges of 7.08-12.89Hz. The alpha activity of EEG signal shows the highly significant correlations with functional outcome measures [43, 45].
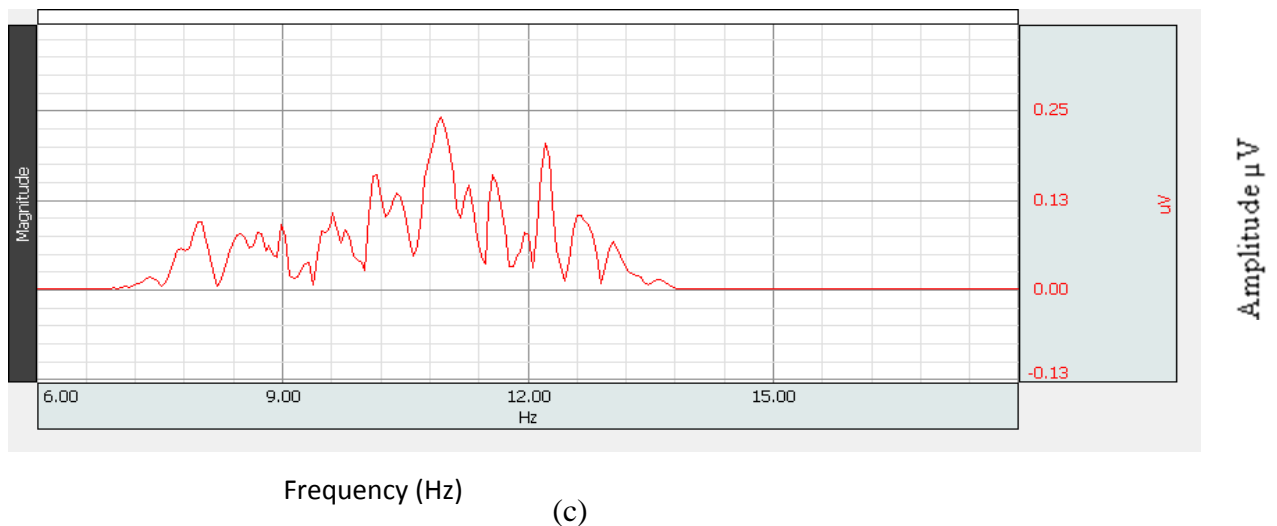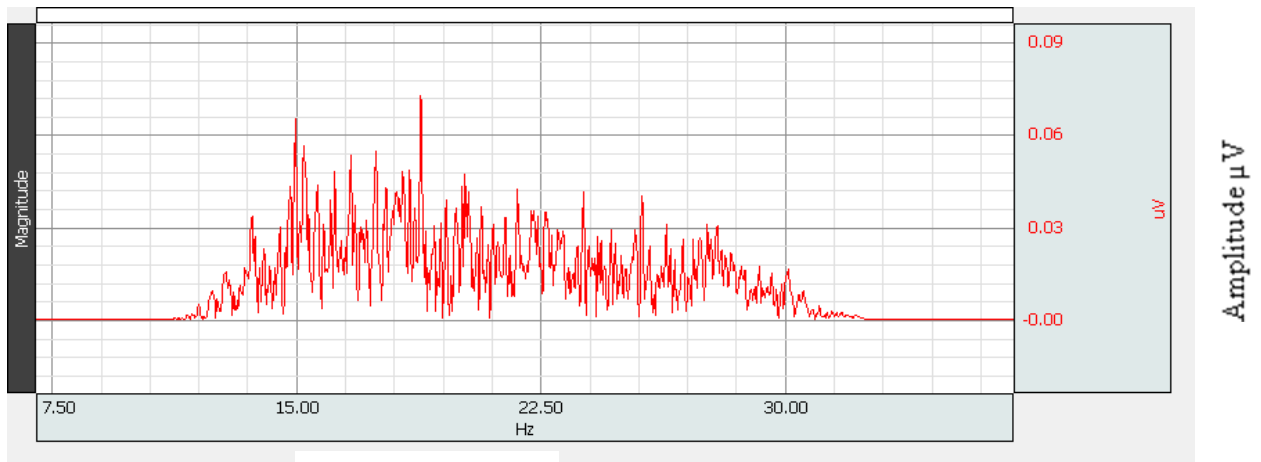

Frequency (Hz)   (a)

Frequency (Hz)   (b)

Frequency (Hz)

(c)
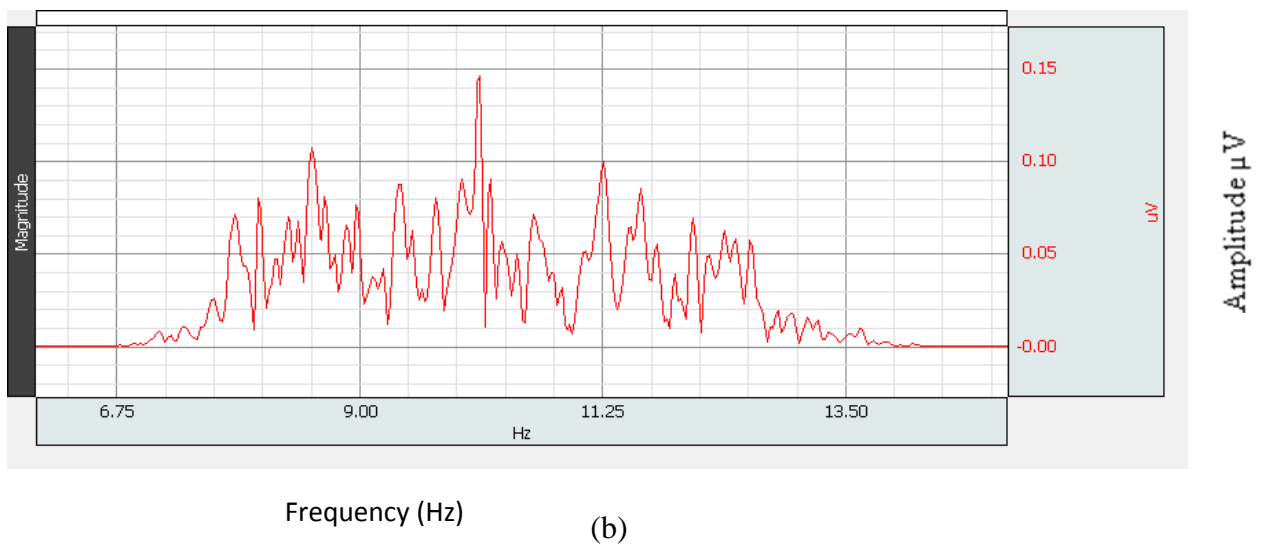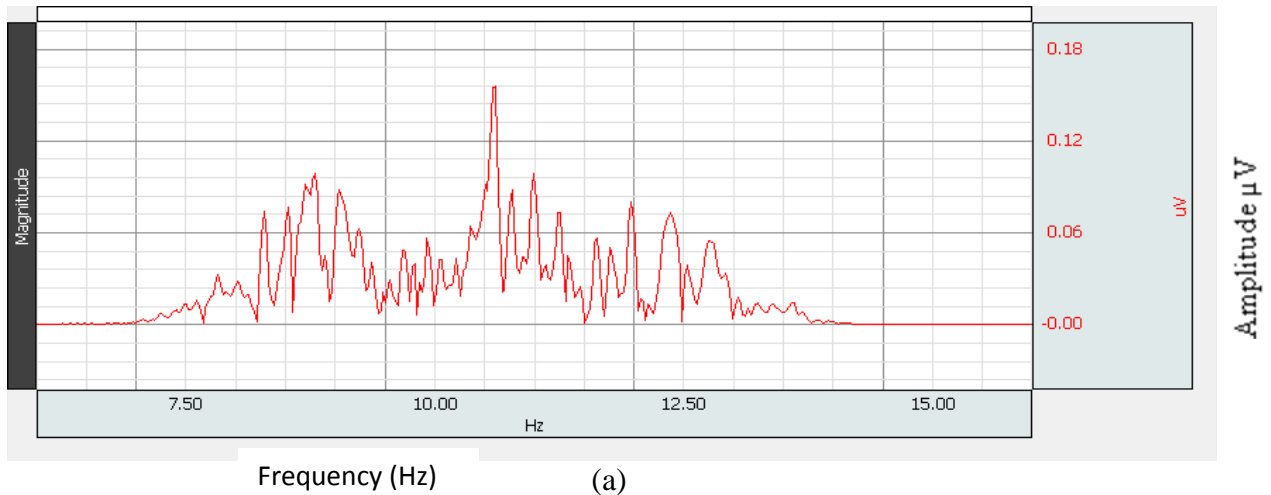
Figure 4.4:Horizontal axis indicate frequency(Hz) and vertical axis indicate amplitude(μV) (a) Alpha activity in Right hemisphere of the patient (b) Alpha activity in Left hemisphere of the patient(c) Alpha activity of the control

In IS studies wherein EEG was recorded at 48 h or later post-stroke, relative alpha power has demonstrated highly significant correlations with functional outcome measures [43, 45]. As shown in Fig. 4.4a, b and 4.4c, the frequency of the left cerebral hemisphere diminishes compared to healthier child.

4.2.3 Analysis of Beta and Theta wave

Fig 4.5 and 4.6 show the beta and theta activity of right and left side of the patient and the control. Beta waves were analyzed between the frequency range of 12.20-29.83Hz and the theta waves were analyzed between the frequency ranges of 3.51-7.51Hz. The mean values of theta relative power were higher on the injured hemisphere than on the non-injured hemisphere. The opposite pattern was observed for beta relative power. The difference was highly significant. Poor outcomes were predicted by delta activity and depression of faster alpha or beta activity in the ischemic hemisphere, whereas good outcomes were predicted by absence of these phenomena.
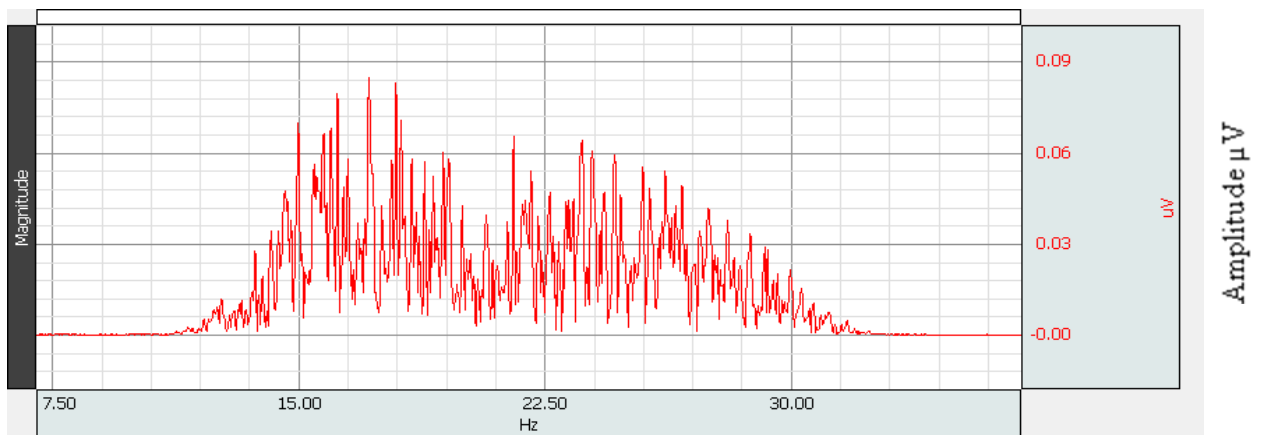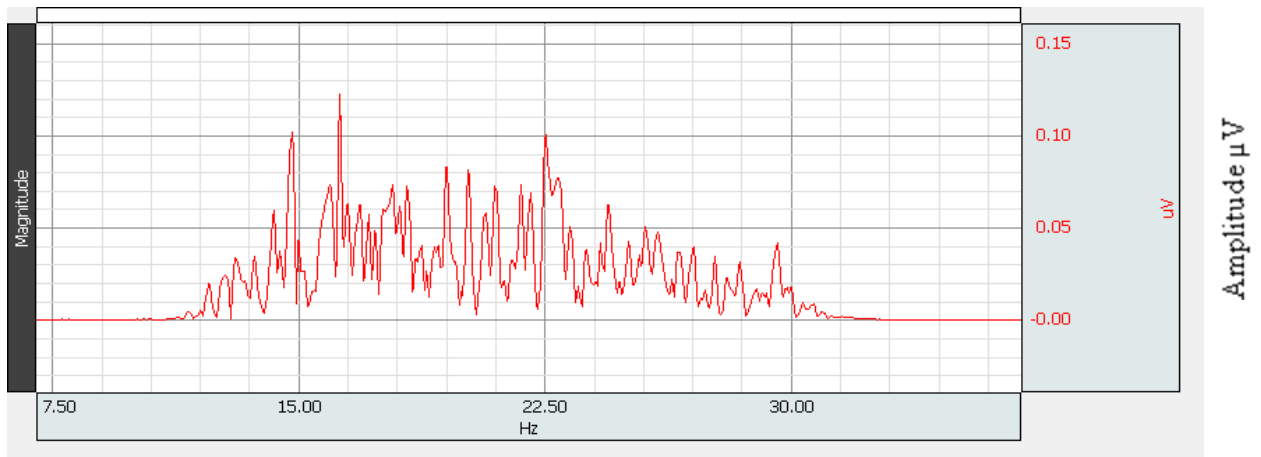
Figure 4.5: Horizontal axis indicate frequency(Hz) and vertical axis indicate amplitude (µV)

(a) Beta activity of the right side of the patient (b) Beta activity of the left side of the patient

(c)) Beta activity of the control

Frequency (Hz)　(a)

Frequency (Hz)　(b)

Frequency (Hz)　(c)

Figure 4.6: Horizontal axis indicate frequency(Hz) and vertical axis indicate amplitude (µV) (a) Theta activity in the patient right cerebral hemisphere (b) Theta activity in the patient left cerebral hemisphere (c) Theta activity of the control.
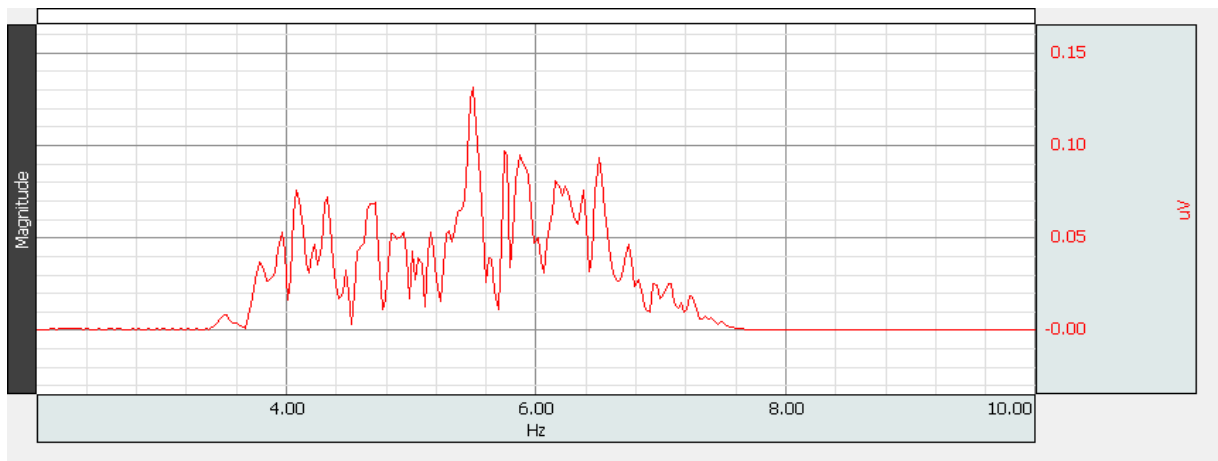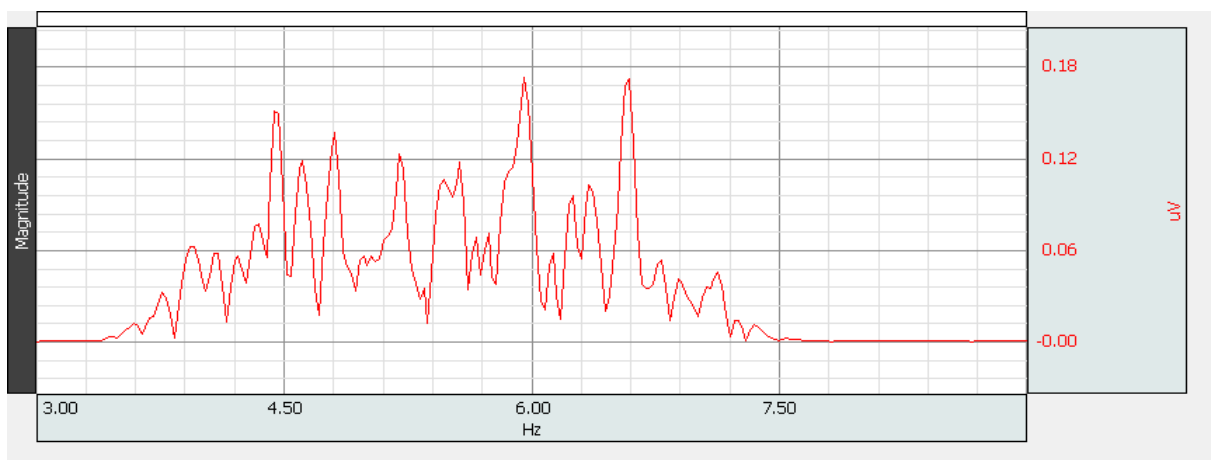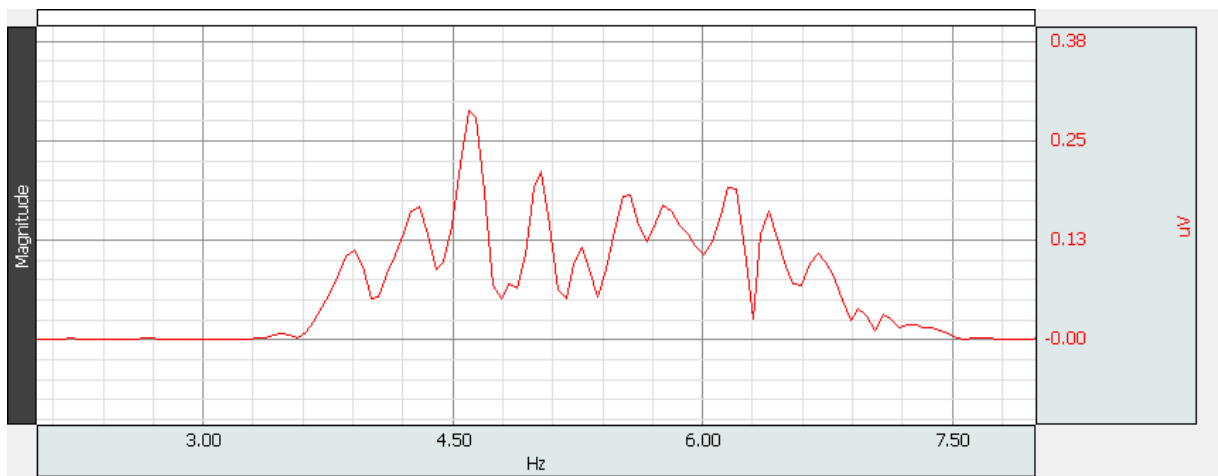
4.3 Analysis of delta/alpha ratio (DAR)

Delta frequencies are known to be highly characteristic of brain pathophysiology, and preservation of alpha and beta frequencies following stroke is evidently indicative of neuronal survival and a good prognosis [46], hence greater prognostic ability may be afforded by QEEG measure(s) which are specifically sensitive to such frequencies. Although large number of evidence showing an increase in delta and a decrease in alpha frequencies in patients during the acute phase of suffering a stroke [46], it is not clear which QEEG parameters are most sensitive to detect ischemia in patients with severe diffuse brain injury leading to coma. It was reported in earlier studies that delta/alpha ratio (DAR) to be the most effective of QEEG parameters investigated for detection of delayed cerebral ischemia in subarachnoid hemorrhage patients [47]. This is consistent with the large increases in delta activity and decreases in alpha activity in sub-acute stroke patients, reported by [48], and with other reports (e.g., [49-51]). Hence, the DAR warrants further investigation as a potential QEEG measure to aid monitoring and prediction of evolution of cerebral ischemia.

Recent studies [44-45] also show that DAR is the most accurate index for discriminating between radio logically-confirmed, acute IS and age-matched controls. Table 4.2 depicts the DAR of the right and left cerebral hemisphere of the patient and control. A relative comparison of DAR between patient right hemisphere and left hemisphere with the control are also shown in Fig. 4.6. The DAR values of the left cerebral hemisphere is high than the right cerebral hemisphere. It is also higher in both cerebral hemisphere than the control. The current outcomes update the scenario by indicating that DAR is a more accurate classifier index; DAR <3.7 is 100% specific for the absence, and >3.7 is 100% sensitive for the presence, of a recent, radio logically-confirmed IS lesion. The sample of middle cerebral artery IS patients included several cases with relatively small ischemic lesions on imaging and mild symptoms
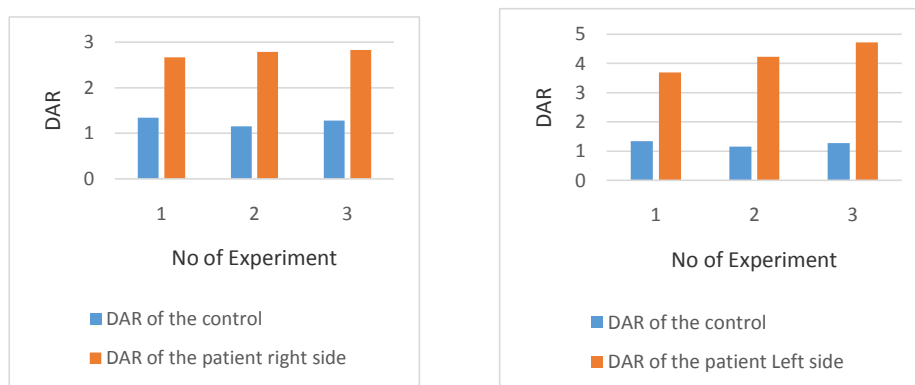
Figure 4.7: Comparison of DAR between patient right hemisphere and left hemisphere with the control.

DAR		
Right hemisphere	Left hemisphere	Control
2.671417	3.700358	1.347111
2.789601	4.232462	1.155598
2.834476	4.727645	1.283364

Table 4.2: DAR of the Right and Left cerebral hemisphere of the patient:

as well as a subcortical lesion suggesting this threshold may apply to all such cases. Three measures are taken from the patient and control. From the table 4.2 and bar chart 4.7, it is seen that DAR of left hemisphere of patient are greater than 3.7 for all the measurements indicating severe ischemic stroke in the fronto-temporal region of left hemisphere.

Some current clinical systems automatically compute and instantly display QEEG indices (as well as conventional EEG), hence the proposed abnormality assessment employing a DAR threshold can readily be applied at the bedside. This procedure may prove valuable for promptly detecting cerebral ischemia after subarachnoid hemorrhage ([47]), in other acute brain injury or ICU patients (e.g., [52-54]) or during carotid end arterectomy. Pending the outcomes of future studies, it may prove useful in other clinical contexts or neurological patient groups, such as distinguishing IS versus stroke mimic or medically unexplained symptoms. DAR indices can also be used in potential clinical application for continuous monitoring to inform decisions regarding reperfusion therapies in acute IS.

Table 4.3: DTABR of the Right and Left cerebral hemisphere:

DTABR		
Right hemisphere	Left hemisphere	Control
2.448613928	3.650358	0.985970005
2.851664985	3.862462	1.296204988
2.553791887	3.727645	1.164080989

4.4 Analysis of delta-plus-theta to alpha-plus beta power ratio (DTABR)

The delta-plus-theta to alpha-plus beta power ratio (DTABR) index [55] is another QEEG measure, which has been used to assess brain pathophysiology in supratentorial brain lesion [56], brain tumor [55], and Alzheimer's disease [57] patients. In comparison to the DAR, the DTABR is additionally sensitive to theta and beta activity, both of which may be significant in monitoring post-stroke brain pathophysiology [48, 51]. Figure 4.8 and the Table 4.4 shows the comparison of DTABR between the left and right cerebral hemisphere and between the healthy part of the patient and the control. Here, also the left sided value is higher than the right side and the value of the control.

DTABR has overall the second most accurate index as a classifier [58] proposed that DTABR <1 was 100% specific for the absence, and >3.5 was 100% sensitive for the presence, of a recent, radio logically-confirmed ischemic stroke lesion. From the table 4.2 and bar chart 4.7, it is seen that DTABR of left hemisphere of patient are greater than 3.7 for all the measurements indicating severe ischemic stroke in the fronto-temporal region of left hemisphere. From all of the discussion stated above, it is observed that among QEEG indices delta value was twice as high in the IS whereas mean relative alpha value was more than in controls.
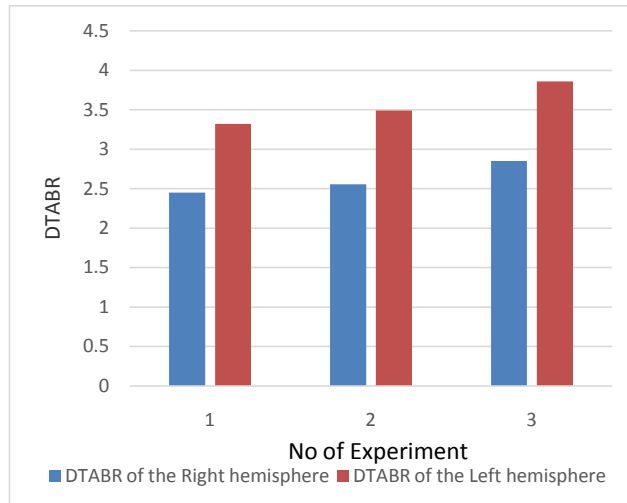
Figure 4.8: Comparison of DTABR between the right and left cerebral hemisphere of the patient
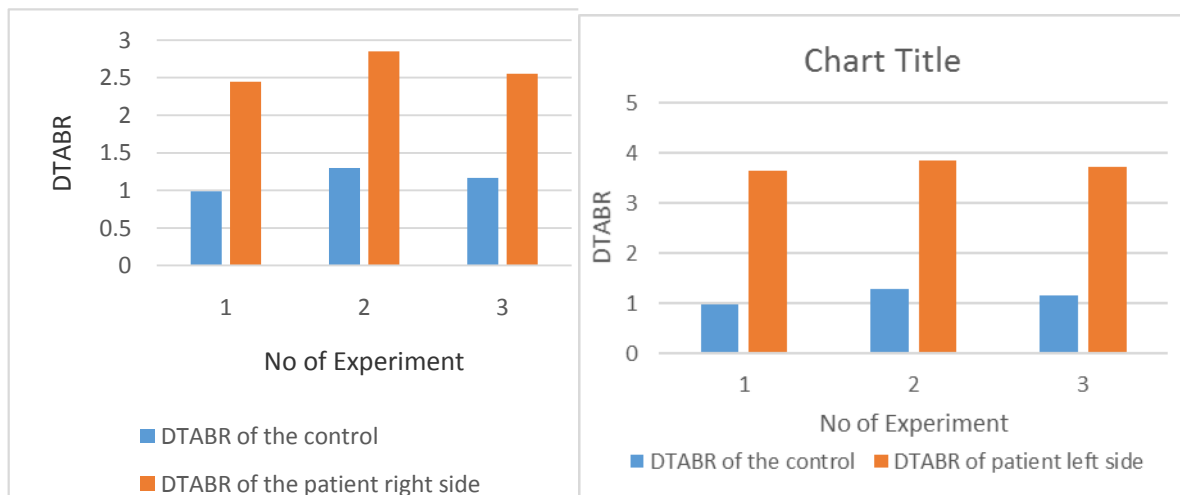
Figure 4.9: Comparison of DTABR between patient right hemisphere and left hemisphere with the control

DAR and DTABR was much higher in IS. Descriptive statistics of the control and stroke samples, and the outcomes of comparisons between them are Shown in Table 4.4. From the above discussion and QEEG analysis we can say that the neuronal activity of the left cerebral hemisphere has been diminished to a greater extent.

Table 4 : QEEG relative band value and their ratio, DAR: delta/alpha ratio; DTABR: (delta + theta)/(alpha + beta) power ratio; SD: standard deviation.

	Delta	Theta	Alpha	Beta	DAR	DTABR
Control						
Mean	0.17623	0.09652	0.07718	0.03377	2.283364	2.458315
SD	0.10035	0.06425	0.05431	0.02175	1.847726	2.164081
Patient						
Mean	0.278973	0.09106	0.065383	0.037277	4.220155	3.558126
SD	0.197713	0.06251	0.13511	0.07121	4.616312	3.882273

From the result of the research work it is evident that the DAR and DTABR value of the patient affected part is 4.220155 and 3.558126, respectively which are above the threshold level which indicate the reduced neural activity in left cerebral hemisphere .

4.3 **Analysis of the MRI image**

To generate non-invasively such a range of information about the status of blood vessels and the brain makes it an attractive imaging option for patients presenting with stroke.The anatomical location of the area of ischaemia and its viability (on diffusion-weighted imaging),together with arterial imaging (on magnetic resonanceangiography), are important
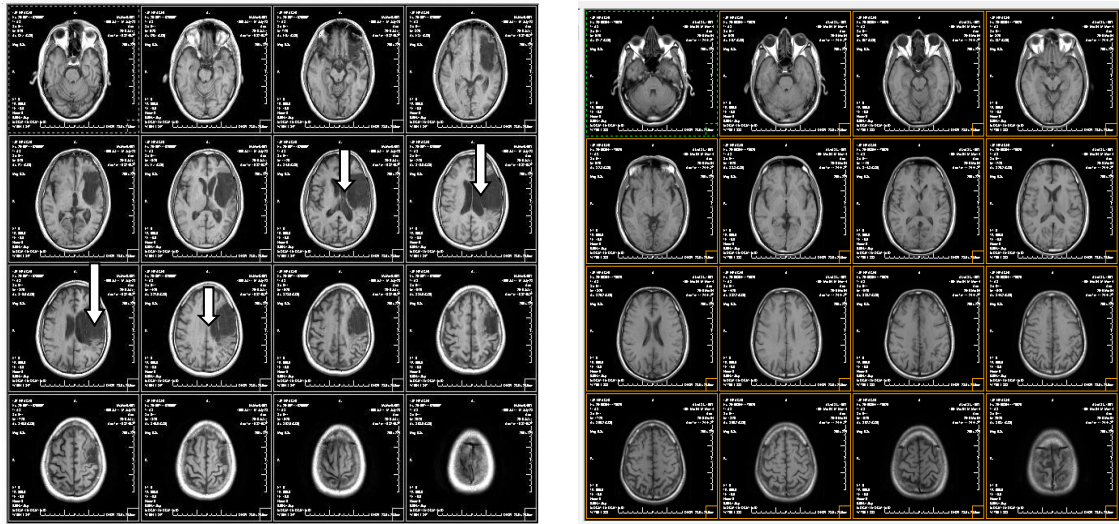
Fig 4.10: a) MRI findings of the patient showing an infarcted region b) MRI findings of the normal adult people c)Sagittal section of injured (left) hemisphere with a large infarct(d)Sagittal section of unaffected (right) hemisphere of the patient showing no pathology

pieces of information which allow the clinician to establish the mechanism of stroke. For example, lesions seen on diffusion-weighted imaging in both hemispheres or in more than one arterial territory might suggest a cardiac source of embolism, border-zone lesions often indicate ipsilateral high-grade carotid artery stenosis, or a lesion restricted to the territory of a single small penetrating vessel suggests in-situ small vessel thrombosis. On the MRI, the infarct is reflected by a black area in T_1weighted image. The MRI image clearly shows a large infarct in the fronto-temporal region both in sagittal and axial plane which reflect the result of the quantitative analysis of EEG and also the clinical findings of the patient as the patient is suffering from right sided hemiplegia with motor aphasia. The result also gives the important information about the diminished neuronal activity in the older people by comparing the brain wave signals between the normal hemispheres of the patient with that of the under 15 control participant.

It is not suggested that QEEG could replace neuroimaging techniques in clinical management of IS, however while imaging can indicate reperfusion it does not directly inform about potential response of ischemic, neural tissue to same. Whereas EEG directly measures neural (dyes) function and the latter, and DAR may constitute a reliable, bedside indicator of success of reperfusion therapy.

CHAPTER -V

CONCLUSION AND FUTURE WORK

5.1CONCLUSION:

This work investigated the neuronal status between the healthy people and the patient suffering from cerebrovascular disease.This study revealed a significant correlation of neural activity between the old and a younger group below fifteen years. A comparative scenario of the injured and uninjured part of cerebral hemisphere has also been presented.

In the earlier part of this thesis work,thequantitative value of different brain waves were analyzed and a comparative study was established between the injured and uninjured hemisphere of the patient.We have also compared cerebral brain waves of the patient with that of the healthy young boy.This work focused on the correlation between the extent of infarction and the clinical effect to monitor the degree of hypo-activity of the affected part through the EEG analysis. An indicationfor theassessment of neuronal activity and the degree of severityof stroke patient has been proposed. A parallel study has also beencarried out on healthy volunteers of under fifteen years to find the comparison of neural activity between different age group.From the analysisit is found that delta activities of EEG are highly unique of brain pathophysiology, and preservation of alpha and beta frequencies following stroke is evidently indicative of neuronal survival and a good prognosis. In order to assess brain pathophysiology in supratentorial brain lesion patientsthe delta/alpha (DAR) and delta-plus-theta to alpha-plus-beta ratio (DTABR) have also been used.It is observed that the DAR and DTABR values of the left cerebral hemisphere of the patient are much higher than the right cerebral hemisphere.It is also higher in both cerebral hemisphere than the control.A threshold value of ~3.7 of DAR and DTABR have been obtained. It is observed that DAR and DTABR of left hemisphere of patient are greater than 3.7 for all the measurements indicating severe ischemic stroke in the fronto-temporal region of left hemisphere.This study also show that DAR and DTABR of the healthier child is~1.It is also found that delta and DAR indicesof the old age are two times more than the child indicating the diminishing of neuronal activity of old age is half of the child.

On the next part of this research work, a video EEG was done for about thirty minutes for the clear detection of EEG wave abnormalities according to the site of the lesion of the brain .The clinical investigation confirms us that the delta activity is higher in the fronto-temporal region which is situated in the left cerebral hemisphere of the patientand the delta activity of both cerebral hemisphere are also higher than the control.The DAR and DTABR values of the left cerebral hemisphere is high than the right cerebral hemisphere.It is also higher in both cerebral hemisphere than the control

At the final part, a neuroimaging technique, Magnetic Resonance Imaging(MRI) was done for the final confirmation of the above findings.This modern technical investigation confirms us that there is a large infarctive lesion in the fronto-temporal region occupying a part of frontal,temporal and parietal area including brocas area (area 44, 45) and the pre and post central gyrus of left cerebral hemisphere.Overall, the results indicate thatthe neuronal activity grossly diminishes in old age not only in comparison to the adult but also it isreducedfrom the early childhood.

In conclusions, although neuroimaging can indicate reperfusion it does not directly inform about potential response of ischemicneural tissue. Whereas, EEG directly measures neural function, and DAR may constitute a reliable, bedside indicator of success of reperfusion therapy.These results could be important for detection the degree of neuronal impairment between old people and young age group specially under fifteen years and also it will reflect the actual scenario of neural activity in an old brain ischaemia due to cerebrovascular disease as well as in stroke diagnosis, prognosis, re-habitation strategies, and proper neurosurgical treatment.

5.2 Future Works

Neuronal status have been evaluated by EEG signal analysis and MRI image in old stroke patient.In future,

> ➢ stroke induced neuronal status of different age group can be observed which can help to a greater extent in case of medication and rehabilitation strategies.
> ➢ Aneuronal scale can also be established for observation the neuronal status of different people by comparing the brain waves of different age group in five years interval.
> ➢ The effect of continuing the thrombolytic effect on the infarction in a stroke patient can be observed.
> ➢ Effect of physiotherapy on the limb with associated improvement as well as the neuronal status can also be monitored.
> ➢ Assessment of behavioral risk factor of stroke by regular monitoring of different brain waves in different group of people can also be performed.

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