RESTING-STATE EEG FUNCTIONAL CONNECTIVITY ANALYSIS: SCHIZOPHRENIA PATIENTS

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Tajuk Projek : **RESTING-STATE EEG FUNCTIONAL CONNECTIVITY ANALYSIS: SCHIZOPHRENIA PATIENTS**

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ABSTRACT

Schizophrenia (SZ) is a mental disorder that involved a breakdown in the relation between behaviour, emotion and thoughts. It is a lifelong disorder and affects how a person feels, thinks and acts. Until now, there is no definitive standard in the diagnosis of schizophrenia, which is mainly based on patient interviews and symptom history. Furthermore, disorders of altered brain connectivity such as Schizophrenia calls for effective connectivity investigation. An alternative approach to this problem is the study of distributions or networks in the brain by using Resting-State Analysis. The general purpose of the project is to detect abnormalities in resting state EEG functional connectivity in Schizophrenia patients, in comparison to healthy controls. It was hypothesized that the default mode network (DMN) would show abnormal connectivity in patients with schizophrenia. 64 channel resting state EEG were recorded in 15 SZ subjects and 15 matched HC subjects. The software used in this project are EEGLAB, MATLAB and LORETA. First, pre-processing will be done on filtering which include high pass filter cut-off of 30 Hz and low pass filter cut-off of 0.3 Hz. The low pass filter is used to get rid of baseline drift while the high pass filter is to get rid of noise. For high pass filter, sodium chloride (electrolyte) from sweating reacting with metals of the electrodes may produce a slow baseline drift. After that, we down sample from 1000 to 250 Hz. Then, continued with manual rejection for muscle artifact and proceed using ICA in EEGLab to reject continuous data for eye/ocular artifacts. Next, the pre-processed data will be exported and analyzed using Loreta. Schizophrenia displayed increase lagged coherence and lagged phase synchronization between DMN networks, most notably in the left inferior parietal lobe, post cingulate gyrus and right inferior parietal lobe in the alpha and beta bands.

Keywords Independent Component Analysis. Lagged Phase Synchronization. Lagged Coherence. Schizophrenia. LORETA. Electroencephalogram. Resting-state. Default Mode Network.

ABSTRAK

Skizofrenia (SZ) adalah gangguan mental yang melibatkan pecahan dalam hubungan antara tingkah laku, emosi dan pemikiran. Ia adalah gangguan sepanjang hayat dan memberi kesan kepada bagaimana seseorang merasa, berfikir dan bertindak. Sehingga kini, tidak ada standard muktamad dalam diagnosis skizofrenia, yang sebahagian besarnya berdasarkan wawancara pesakit dan sejarah simptom. Tambahan pula, gangguan sambungan otak diubah seperti Skizofrenia panggilan untuk siasatan sambungan berkesan. Satu pendekatan alternatif kepada masalah ini ialah kajian pengagihan atau rangkaian di dalam otak dengan menggunakan *Resting-State Analisis*. Tujuan umum projek ini adalah untuk mengesan keabnormalan dalam keadaan berehat EEG sambungan berfungsi dalam Skizofrenia pesakit, berbanding dengan kawalan sihat. Ia telah hipotesis bahawa *Default Mode Network (DMN)* akan menunjukkan sambungan yang tidak normal dalam pesakit dengan skizofrenia. 64 saluran negeri berehat EEG telah direkodkan dalam 15 mata pelajaran SZ dan 15 mata pelajaran HC dipadankan. Perisian yang digunakan dalam projek ini adalah EEGLAB, MATLAB dan Loreta. Pertama, pra-pemprosesan akan dilakukan pada penapisan termasuk lulus tinggi penapis 30 Hz dan rendah penapis lulus potong 0.3 Hz. Penapis lulus rendah digunakan untuk menghilangkan *drift* asas manakala penapis lulus tinggi adalah untuk menghilangkan bunyi bising. Untuk penapis lulus tinggi, natrium klorida (elektrolit) dari berpeluh bertindak balas dengan logam elektrod boleh menghasilkan *drift* asas perlahan. Selepas itu, kami sampel 1000-250 Hz ke bawah. Kemudian, diteruskan dengan penolakan manual untuk artifak otot dan teruskan menggunakan ICA dalam EEGLab untuk menolak data berterusan untuk mata / artifak okular. Seterusnya, data pra-diproses akan dieksport dan dianalisis menggunakan Loreta. Skizofrenia dipaparkan peningkatan tertinggal kepaduan dan tertinggal penyegerakan fasa antara rangkaian DMN, terutamanya dalam lobus kiri lebih rendah parietal, *post gyrus cingulate* dan kanan lebih rendah parietal dalam alfa dan beta *band.*

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CHAPTER 1

INTRODUCTION

1.1 Background of Study

Resting state is a method of functional brain imaging that can be used to evaluate regional interactions that occur when a subject is not performing certain task. The word REST means Random Episodic Spontaneous Thoughts. Resting state is the dynamic substrate of the “present”, momentary state of the brain, and determines the fate of incoming information. Basically, the brain goes through all working modes such as sensory, attention, executive control, language and so on during rest. Although we are not doing any activities or movements, but our brain still function and work as usual. For example, when we are sleeping, our body is static but our brain is working and doing the normal brain activity. In this study, resting state is shown when the subjects are instructed to sit and close their eyes, relax but stay awake.

Electroencephalography (EEG) is the measurement of electrical activity produced by the brain as recorded from electrodes placed on the scalp. So-called scalp EEG is collected from electrodes positioned on different locations at the surface of the head. Every activity of the human is creating the brain signal. The signal form is based on the activities that human do. These brain signals can be captured using the Electroencephalogram machine. This machine is formally captured the different part of human machine. The signals (in the range of milli-volts) are amplified and digitalized for

later processing. EEG used to be a first-line method of diagnosis for stroke, tumour and other brain disorders. It also can diagnose coma, sleep disorders, brain death and epilepsy which causes abnormalities in EEG readings.

Schizophrenia is a mental disorder that involved a breakdown in the relation between behaviour, emotion and thoughts. It is a lifelong disorder and affects how a person feels, thinks and acts. Schizophrenia patient is having difficulty analysing between what is actual and what is imaginary. The causes of this disorder are still ambiguous but some theories said it comes from genetic, biology and possible viral infections and immune disorders. There are two syndromes that a person might have which are positive and negative syndrome. Positive syndrome is an additional feeling that contrast from a normal human feel for example, delusions and hallucinations, or in other words a person is imagining something that are not real and does not exist. The negative syndrome is a feeling that lack from a normal human feel, for example, lack of interest, social withdrawal, lack of drive and emotional flatness.

1.2 Problem Statement

Schizophrenia is the most chronic and disabling of the severe mental disorders [1]. Until now, there is no definitive standard in the diagnosis of schizophrenia, which is mainly based on patient interviews and symptom history [2]. Besides that, classical neuroimaging experimental methods give very limited information. Most studies focus on one or several brain regions. Furthermore, disorders of altered brain connectivity such as Schizophrenia calls for effective connectivity investigation [3]. An alternative approach to this problem is the study of distributions or networks in the brain by using Resting-State Analysis.

1.3 Objectives

The objectives of this study are:

1. To determine significant abnormal patterns of resting-state linear (lagged coherence) functional connectivity within the Default Mode Network (DMN) between schizophrenia (SZ) subjects and healthy control (HC) subjects.
2. To determine significant abnormal patterns of resting-state nonlinear (lagged phase synchronization) functional connectivity within the Default Mode Network (DMN) between schizophrenia (SZ) subjects and healthy control (HC) subjects.

1.4 Significance of Study

This study is essential to get know about the Schizophrenia patients better. Being an abnormal sometimes is very difficult because not everyone can feel and understand what is the real situation that they are go through. We are wondering, what is in their brain that make us so different because we cannot think, feel and imagine like what they did. Some of us might underestimate them and make the patients isolate themselves from us. This is not a good attitude. We as a human being must help each other and make them happy by approaching and playing with them. By doing so, we are given them spirit to live and make them know that we are indeed equivalent to each other. Just some thoughts that make us difference. Furthermore, by learning and knowing about this disorder we can slowly heal them and make the world a better place for them to live.

Schizophrenia is a psychotic disorder that alters patients' attitude, thought process and behaviour as evidenced by hallucinations, delusions, disorganised speech or behaviour, social withdrawal, and varied cognitive deficits [4]. Additionally, episodic memory and attention are significantly impaired in schizophrenia [5]. Disturbed integration of activity across multiple brain regions or dysfunctional connectivity between fronto-temporal brain regions is a central feature of schizophrenia [6,7]. Symptoms of schizophrenia have been attributed to a failure of functional integration or aberrant connectivity among regions or systems of the brain [7].

Because the mental processes involved in the default mode are relevant to schizophrenia, it was hypothesized that the default mode network would be abnormal in these patients. Since the default mode network is involved in many aspects of brain function, its healthy functional connectivity is imperative to normal mental function; impaired connectivity or activation, as seen in other brain networks in schizophrenia, might influence positive and negative symptoms of the disorder.

1.5 Scope of Study

To achieve the objective of the project, there are several scopes had been outlined:

1. Literature study

Do a lot of research on past studies by summarising 15 papers of journal which are related to my study to get more knowledge and understand better about this project.

2. Pre-processing EEG Data
   I. Filtering
   II. Down sampling
   III. Muscle artifact rejection and eye blink rejection with Independent components analysis (ICA)
   IV. Re-referencing
   V. Baseline correction
3. Analysis (functional connectivity)
4. Obtain result
5. Discussion regarding the current results and previous findings

The tools used are EEGLab, Matlab and LORETA software

1.6 Thesis Organisation

This thesis is organised into five chapters.

Chapter 1 will present the introduction of the project, objectives, problem

statements and scope of project which is brief information as the summary of works.

Chapter 2 contains theories and literature review. It is also briefed some of the MATLAB and Loreta application that involved in the Electroenchapolagraphy (EEG) signal analysis.

Chapter 3 discusses briefly on the methodology of the project. This chapter reveals about some theories and the algorithm procedures.

Chapter 4 is for results and discussion part. This cover the result for the Matlab and Loreta analysis.

Chapter 5 gives the conclusion of work done in this project. This chapter also stated the recommendation for future works.

CHAPTER 2

THEORY AND LITERATURE REVIEW

2.1 Introduction

Literature review is a very important part of research process. The general purpose of the literature review is to gain understanding of the current state of knowledge about the selected of research topics.

To proceed this study, first I need to understand the principle and the basic of Electroencephalography (EEG), EEG artifacts, Default Mode Network (DMN), and the analysis techniques such as Independent Component Analysis (ICA) and the tools used such as MATLAB, EEGlab and Loreta software.

2.2 The Brain

The brain is the most complex biological structure known, and comparing the brains of different species based on appearance is often difficult. Nevertheless, there are common principles of brain architecture that apply across a wide range of species. These are revealed mainly by three approaches.

The evolutionary approach means comparing brain structures of different species, and using the principle that features found in all branches that have descended from a given ancient form were probably present in the ancestor as well. The developmental approach means examining how the form of the brain changes during the progression from embryonic to adult stages. The genetic approach means analysing gene expression in

various parts of the brain across a range of species. Each approach complements and informs the other two.

The nervous system is your body's decision and communication centre. The central nervous system (CNS) is made of the brain and the spinal cord and the peripheral nervous system (PNS) is made of nerves. Together they control every part of our daily life, from breathing and blinking to helping you memorise facts for a test.

Nerves reach from our brain to our face, ears, eyes, nose, and spinal cord then reverse back from the spinal cord to the rest of our body. Sensory nerves gather information from the environment, send that information to the spinal cord, which then speed the message to the brain.

The brain then makes sense of that message and fires off a response. Motor neurones deliver the instructions from the brain to the rest of our body. The spinal cord, made of a bundle of nerves running up and down the spine, is like a superhighway, speeding messages to and from the brain at every second.

The brain is made of three main parts: the forebrain, midbrain, and hindbrain. The forebrain consists of the cerebrum, thalamus, and hypothalamus (part of the limbic system). The midbrain consists of the tectum and tegmentum. The hindbrain is made of the cerebellum, pons and medulla. Often the midbrain, pons, and medulla are referred to together as the brainstem.

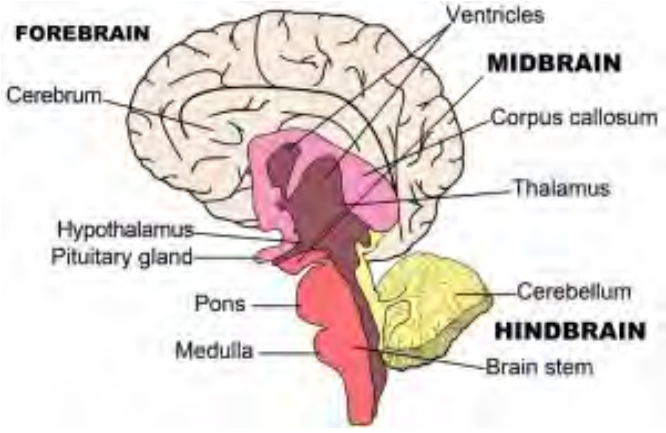

Figure 2.1 The Brain Structure [8]

2.3 The Electroencephalogram (EEG)

An electroencephalogram (EEG) is a test that measures and records the electrical activity of your brain. Special sensors (electrodes) are attached to your head and hooked by wires to a computer. The computer records your brain's electrical activity on the screen or on paper as wavy lines. Certain conditions, such as seizures, can be seen by the changes in the normal pattern of the brain's electrical activity.

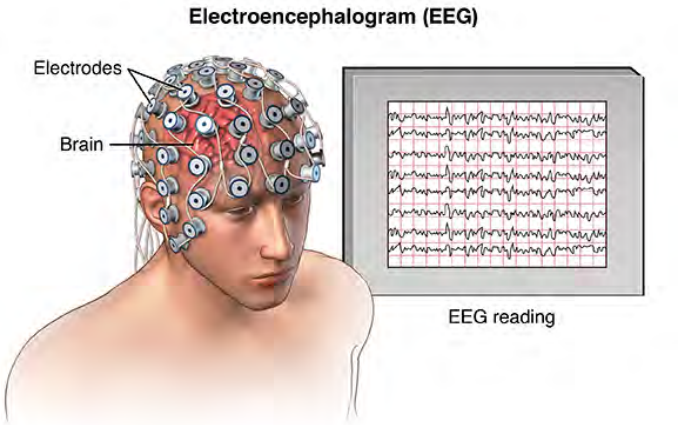

Figure 2.2 The EEG Test [9]

2.3.1 The History of Electroencephalogram (EEG)

Although the spontaneous electrical activity of the brain or the electroencephalogram (EEG) was discovered in rabbits and monkeys more than a century ago by Caton in 1875 and the first report concerning the human EEG appeared more than 60 years ago, much remains to be clarified about the nature and the origin of the EEG. Nonetheless, very soon after its discovery in humans, EEG became an important diagnostic tool and it has remained so. From 1924 to 1938, Berger laid the groundwork of our present applications of EEG.

2.3.2 Electroencephalogram Signal

Electroencephalogram (EEG), is a measure of brain activity. The word comes from