Study of Metrics that Could be Considered as Inputs to an Intelligent System for Diagnosing Schizophrenia based on an Electroencephalogram (EEG)

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Résumé—Intelligent systems are now part of human daily life. This justifies its application in various fields. However, the field of psychiatry still seems to be at a disadvantage. In this paper, we are interested in measures that can be used as input to an intelligent system for detecting brain diseases using an electroencephalogram (EEG). Indeed, spectral analysis and the study of brain connectivity are two methods of EEG analysis that can be used to characterize schizophrenia. The spectral analysis allows to calculate the power (absolute and relative), the frequency peak among others. Concerning the study of cerebral connectivity, the Phase Lag Index (PLI), which is an adjacency matrix; which is an adjacency matrix used to assess brain connectivity. Once the PLI is obtained, units such as degree, density and strength on each channel are calculated. These units are evaluated on twenty (28) EEGs, fourteen (14) of people suffering from schizophrenia and fourteen (14) of healthy people. On the other hand, the value of strength is always lower in sick people compared to healthy people. This is true regardless of the frequency band or channel used. This study shows that values such as degree, density, strength of a predefined adjacency matrix, then power, peak frequency band can be used as input values of an intelligent system for diagnosing psychiatric or brain diseases such as schizophrenia.

Index Terms—EEG, Schizophrenia, PLI, Strength, Degree, Density, ANOVA.

I. INTRODUCTION

Smoking, alcoholism, sedatives and drugs can be some of the causes of some mental or psychiatric illnesses such as depression, dementia and schizophrenia [1]. According to the Mental Health Atlas 2017, published by WHO in 2018 [2], about 30% of countries don’t have a dedicated mental health policy. On the other hand, the median number of mental health professionals is 9 per 100,000 inhabitants, but wide variations exist (from less than 1 per 100,000 inhabitants in low-income countries to more than 70 in high-income countries). Also, the biennial report (2016-2017) of WHO in the African region concludes that the region suffers from a serious shortage of mental health specialists, as well as the appropriate health establishments [3]. Schizophrenia is one of the most common serious mental disorders, affecting approximately 21 million people worldwide. It is characterized by a distortion of thought, perceptions, emotions, language, sense of self and behavior [4]. Schizophrenia can also be defined as a disorder of cerebral disconnection, characterized by a disruption of large-scale pre-temporal interactions [5]. Schizophrenia is often characterized as a prototypical disorder of integrated brain function involving almost all intrinsic connectivity networks [6]. The branch of medicine that deals mainly with brain disorders is called neurology. To diagnose brain abnormalities, neurologists often use neuroimaging and neurophysiology, also known as brain imaging. Brain imaging refers to the set of techniques for acquiring and rendering images of the brain from different physical phenomena, particularly when an individual is performing a cognitive task. There are several brain imaging techniques, including Positron Emission Tomography (PET), Functional Magnetic Resonance Imaging (fMRI), Magnetoencephalography (MEG) and Electroencephalography (EEG). Several works deal with applied brain imaging in psychiatry. A. Muselle and M. Desseilles [7] show that brain imaging is playing an increasingly important role in psychiatry. David E. and J. Linden [8] discuss diagnostic markers of disease and neurophysiological treatments to ensure psychiatrists are aware of the clinical relevance of the abnormalities reported. Ali Amad, Aïda Cancel and Thomas Fovet describe the current use of brain imaging in clinical psychiatric practice, particularly in the search for a differential diagnosis. Jean-Luc Martinot and Stéphanie Mana [9] suggest that brain imagery of psychiatric conditions has made it possible to explore the anatopmorphology of mental illnesses by emphasizing the involvement of the brain as a target organ of psychopathological phenomena, therapeutics and addictions, which have effects on its growth or plasticity. The high spatial resolution of the EEG, its very affordable cost and the fact that it can play an important role in psychiatry [7], in particular in the classification between psychiatric illnesses and organic illnesses, among others, make the EEG one of the main diagnostic tools of clinical neurology [9]. Hence the choice of the EEG for this work. Electroencephalography is a technique for recording and interpreting the electrical activity of the brain (calculating the potential difference between two electrodes) [10]. To record brain activity, several electrodes are placed on the patient’s hair cure. This recording produces a pattern called an electroencephalogram (EEG). Each potential

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difference in this trace is made up of several waves or rhythms or bands, including delta, theta, alpha, beta, gamma, and more. Figure 1 presents the process of acquiring an electroencephalogram. Electrodes are placed on the patient’s scalp and these electrodes are connected to an amplifier, which in turn is connected to a computer containing a program that will allow the drawing of traces displayed on the screen. However, there is no formal medical examination to diag-

![Figure 1. Processus d’acquisition d’un EEG.](image)

nose schizophrenia and other mental illnesses. Screening is usually done through symptoms and signs. Symptoms are the information given by the patient and his relatives and signs are what the doctor sees [8]. The goal of this long-term work is to be able to set up an artificial intelligence allowing to diagnose these pathologies. For this, a study of schizophrenia linked to the EEG made it possible to identify two methods of analysis of the EEG allowing to characterize schizophrenia: spectral analysis and the study of cerebral connectivity [9]. Spectral analysis is often called quantification of the EEG (QEEG). Indeed, the emergence of QEEG has enabled researchers to extract a multitude of variables that can be quantitatively measured. What made studies on EEG and psychiatric disorders more objective [11]. The power (absolute and relative), the coherence, the frequency of the peaks of the different waves (alpha, delta, beta, theta, gamma, etc.) are some factors to characterize during a spectral analysis [10], [12]. Figure 2 presents a spectral analysis made on the alpha band of an EEG, considering Very Low Frequency (VLF), Low Frequency (LF) and High Frequency (HF). Brain connectivity is the interaction between regions of the brain [13]. The study of brain connectivity is one of the major issues in neuroscience, with the aim of better understanding the organization and functioning of the brain, whether in healthy or pathological individuals. Brain Connectivity Analysis uses Phase Locking Value (PLV), Phase Lag Index (PLI) and Directed Transfer Function (DTF) among other measures [5], [11], [14]. This paper presents the first phase of the work. It consists in starting from the study of cerebral connectivity to identify the elements which could be considered as inputs of the intelligent system for diagnosing schizophrenia which will have to be set up. Many works are in progress on cerebral connectivity and schizophrenia. In general, the current state of knowledge regarding cerebral connectivity has suggested that changes in functional connectivity are mainly observed in schizophrenic patients, and that significant differences in theta frequency activity are also evident [15]. Tianyi Yan and Wenhui Wang [16] study the event phase synchronization, represented by the phase Lag Index (PLI), and suggest that patients with schizophrenia present specific alterations, indicated by an increased local connectivity in the gamma oscillations during facial treatment. This same paper shows that the sick people had a reduced functional connectivity of the beta band through the frontal regions and of the gamma band through the scalp compared to the control subjects. In the schizophrenic group, the severity of symptoms did not seem to be associated with functional connectivity. PLI can be a useful measure for the characterization and understanding of the intrinsic pathophysiological mechanisms of schizophrenia and a reliable biological marker for this disease [12]. Jonathan K. Wynn and Brian J. Roach [17] suggest that the pattern of results under visual processing conditions is similar in patients and controls. However, patients have neural synchronization deficits in the gamma band during basic treatment of illusory contours when attentional demand is limited. Elzbieta Olejarczyk and Jernajczyk [5] suggest that a comparison of different connectivity measures using graph-based indices for each frequency band, separately, could be a useful tool in the study of connectivity disorders such as schizophrenia. It shows that the analysis of the resting EEG showed an increase in delta, theta and beta activity, as well as a decrease in alpha frequency activity in the frontal cortex (“hypofrontality”) in patients versus controls. In this work it will be a question of evaluating, then analyzing the density, the degree and the strength on each channel of each PLI, calculated on different frequency bands, in order to compare the patients compared to healthy. This through a 3-ways ANOVA (Analysis of Variance). Elzbieta Olejarczyk and Jernajczyk [5] had already done a similar study, but using tools such as CSD Toolbox, REST Toolbox, HERMES Toolbox, etc. However, as part of this work, a code in python language was written. This allows greater flexibility in the configuration of the collected EEGs. Indeed, it is very important in future work to collaborate with doctors to have the exact frequencies, to remove the appropriate artifacts according to the disease and the conditions of acquisition of EEGs. Because the final goal is to set up an Artificial Intelligence allowing the diagnosis of schizophrenia.
II. MATERIAL AND METHOD

The PLI is an assessment of the functional connectivity of a multichannel EEG with reduced bias from common sources. It makes it possible to obtain reliable estimates of the phase synchronization which are invariant with respect to the presence of common sources \[13\]. The synchronization of oscillatory activity in the experience of characteristic symptoms such as verbal auditory hallucinations and thinking blocks have been studied in patients with schizophrenia \[15\]. To assess the connectivity between two nodes or factors of an adjacency matrix, some measures such as density, degree and strength can be used. The degree of a node or a channel is the number of edges (connections) attached to this node. The density of a node is an important factor influencing connectivity in an ad hoc network. Node strength is the sum of weights of links connected to the node. The strength of a node is the sum of the weights of the links connected to this node.

A. Description du problème

Most of the articles cited use tools to manipulate EEGs, but in this work, this was done via source code in python language written for the occasion. This made it possible to master the manipulation of EEGs from reading to results. Setting up artificial intelligence involves supplying a large amount of consistent, well-structured data as input to the system so that learning can be done quickly and efficiently. The challenge in this work is to evaluate, then analyze the density, degree and strength on each channel, of each PLI, calculated on different frequency bands, in order to compare people suffering from schizophrenia compared to healthy.

B. Participants

As describe in \[5\], The study comprised of 14 patients (7 males : 27.9 ± 3.3 years, 7 females : 28.3 ± 4.1 years) with paranoid schizophrenia, who were hospitalized at the Institute of Psychiatry and Neurology in Warsaw, Poland, and 14 healthy controls (7 males : 26.8 ± 2.9, 7 females : 28.7 ± 3.4 years). The patients met International Classification of Diseases ICD–10 criteria for paranoid schizophrenia (category F20.0). Study protocol was approved by the Ethics Committee of the Institute of Psychiatry and Neurology in Warsaw. All participants received a written description of the protocol and provided written consent to take part in this study. Inclusion criteria were : a minimum age of 18, ICD-10 diagnosis F20.0, and medication washout period of a minimum of seven days. Exclusion criteria were : pregnancy, organic brain pathology, severe neurological diseases (e.g. epilepsy, Alzheimer’s, or Parkinson disease), presence of a general medical condition, and very early stage of schizophrenia, i.e., first episode of schizophrenia. The control group was matched in gender and age to the 14 patients completing the study.

C. EEG Recording and analysis

According to \[5\], Fifteen minutes of EEG data were recorded in all subjects during an eyes-closed resting state condition. Data were acquired with the sampling frequency of 250 Hz using the standard 10–20 EEG montage with 19 EEG channels : Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2. The EEG analyzes were done using the python language, through the MNE library, which made it possible to write custom code.

D. Preprocessing

EEG analysis has been performed using thirty second segments without artefacts (i.e. eye movements, cardiac activity, muscle contractions). Then, the signals of each EEG channel were filtered using a Butterworth filter of order 2 in the following physiological frequency bands : 2–4 Hz (delta), 4.5–7.5 Hz (theta), 8–12.5 Hz (alpha), 13–30 Hz (beta), 30–45 Hz (gamma).

E. Statistical Analysis

To assess the connectivity between the two groups (i.e. healthy people and schizophrenia patients), a three-way ANOVA model was separately applied to the following indices for each metric : degree and strength. The ANOVA had the following factors : Group, Band (delta; theta; alpha; beta; gamma), and EEG channels (system of 19 channels : Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2). The statistical threshold was set at p<0.05.

F. Method and Description

The chosen method does not take into account the reference electrode. Indeed, in cases where no electrode is specifically designated as a reference, the EEG recording material will always treat one of the electrodes of the scalp as a reference \[15\]. In addition, several studies of functional EEG connectivity of the scalp, mainly clinical, seem to ignore the impact of the reference electrode \[19\]. The first four steps make up what is called "pretreatment". This is generally the procedure for transforming raw data into a format more suitable for in-depth analysis and interpretable by the user. The method is described as follows :

- **Reading the EEG (EDF).** It was done using the python MNE library especially the function `mne.io.read_raw_edf`;
- **Filter on each frequency band.** When looking at the frequencies of a digital signal, like the EEG, or whatever, an essential thing to do is to filter certain frequencies (delta, theta, alpha, beta and gamma), so that certain frequencies that will eventually be unused be deleted. Also, so that the capacities of the machine used are minimized, because the work will be carried out in turn on each frequency band;
- **Removal of artifacts.** Artifacts are signals that are picked up by the EEG system but do not actually come from the brain. There are many different sources of EEG data artifacts, which manifest themselves differently. EEG artifacts can be broadly classified as biological (some of the most common biological artifacts are blinking, eye movement, head movement, heartbeat, and muscle noise) or environmental (for example, the electrodes lose
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...their contact or other people’s movements during the experience; • EEG segmentation obtained in thirty-second segments. This step is particularly practical because it allows automatic rejection of corrupted time segments using the rejection mechanisms (epoch); • Calculation of the PLI on each frequency band. Function mne.connectivity.spectral_connectivity has been used. It returns a connectivity matrix which is the PLI;

- Calculation and recording in an Excel file of the degree, density and strength of each PLI, on each frequency band (Figure 3). In the group column, “A” means the healthy group and “B” the sick group. This piece of file shows only the gamma and delta frequency bands.;
- Analysis of the Excel file using SPSS statistics 25.

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Figure 3. Excel file obtained after calculation, via a python code of degree, density and strength.

III. RESULTS

An analysis using a 3-way ANOVA revealed, among other things, that there is a significant difference between the degree of patients and that of healthy control (significance = 0.032). Taking into account the three factors band, group and channel, the value of the degree as well as the density are always higher in the patients compared to the healthy controls, whatever the calculation channel and the frequency band used. However, the strength value is always higher in healthy controls than in patients, whatever the band or the calculation channel. (Figure 4). This figure presents some visuals which led to the above conclusion, all of the visuals having the same appearance. The path of the patients is shown in red, while that of the healthy witnesses is symbolized in blue.

The x-axis shows the nineteen (19) channels, and the y-axis shows the average estimate of density, degree and strength, as appropriate. The observation that the average estimate of the degree is between 16.8 and 17.7, that of the strength is between 2.4 and 3.2 and that of the density between 2 and 5 is also made in the views of this figure.

IV. CONCLUSION AND DISCUSSION

In this article, PLI was calculated for each frequency band. Then, the degree, the strength, the density were calculated, analyzed and made it possible to compare the EEG of the patients compared to those of the healthy people. The observation is that there is a significant difference (significance = 0.032) between the degree of patients compared to that of non-patients. Also, when a three-factor ANOVA that is groups, channel and bands is made, the result is the same for all channels : the degree and density of healthy people are lower than those suffering from schizophrenia on each band, frequency and each channel. However, the strength of healthy people is greater than that of sick people on each frequency band and each channel. In addition, spectral analysis also showed that the power (absolute and relative), frequency peaks and coherence of an EEG signal on each frequency band could also be determined. Thus, the inputs of the future intelligent system could be chosen according to whether a spectral analysis or a study of cerebral connectivity is made, or even both for more precision. Also, the fact of writing the source code personally made it possible to touch the finger at the EEGs as files, to master the programming language python, which is the most used language in the field of Machine Learning, Big data and data science according to the online magazine “big data” [20]. What seems to be a plus to approach the continuation of the work which consists in setting up an artificial intelligence allowing to diagnose
cerebral diseases such as schizophrenia. For this, we will have to enlarge the dataset, because who says artificial intelligence says big data. In addition, it would be very important in future work to collaborate with doctors in order to make good configurations during the pretreatment stages, that is to say having the exact frequencies, eliminating the artifacts and the inappropriate channels according to the disease to be treated to detect and the conditions of acquisition of EEGs.

The main interest of this work is that it has great potential for real world applications and can change many lives very significantly and in a relatively short time. Provided that we can have a large volume of data, that a deep work is done with psychiatrists, neurologists among others to be able to build a stable system that can help the whole world, in particular the Africa which suffers from a shortage of qualified mental health care personnel.

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Références


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