Early Detection Method of Alzheimer's Disease Using EEG Signals

Dhiya Al-Jumeily[1], Shamaila Iram[1], Abir Jaffar Hussain[1], Vialatte Francois-Benois[2], and Paul Fergus [1]

[1] Applied Computing Research Group, Liverpool John Moores University, Byroom Street, Liverpool, L3 3AF, UK
[2] Laboratoire SIGMA, ESPCI ParisTech, Paris, France
{D.Aljumeily,P.Fergus,A.Hussain}@ljmu.ac.uk, francois.vialatte@espci.fr

Abstract. Different studies have stated that electroencephalogram signals in Alzheimer's disease patients usually have less synchronization as compare to healthy subjects. Changes in electroencephalogram signals start at early stage but clinically, these changes are not easily detected. To detect this perturbation, three neural synchrony measurement techniques have been examined with three different sets of data. This research work have successfully reported the experiment of comparing right and left temporal of brain with the rest of the brain area (frontal, central and occipital), as temporal regions are relatively the first ones to be affected by Alzheimer's disease. A new approach using principal component analysis before applying neural synchrony measurement techniques has been presented and compared with to other existing techniques. The simulation results indicated that applying principal component analysis before synchrony measurement techniques show significantly improvement over the lateral one. The results of the experiments were analyzed using Mann-Whitney U test.

Keywords: Electroencephalogram signals, EEG Signals, Alzheimer's Disease.

1 Introduction

Mild Cognitive Impairment (MCI) is characterized by impaired memory state of brain probably leads towards mild Alzheimer's disease (MiAD) or Alzheimer's disease (AD). This prodromal stage of AD is under a great influence of research for long time [1-3]. Different research work reported that 6-25% of MCI are transformed to AD annually and 0.2-4% transformed from healthy person to AD [2, 4], revealing the fact that MCI is a transition state of MiAD and AD.

Loss of functional connectivity between cortical and hippocampus has long been an important focus of many investigation to examine the cause of cognitive dysfunction in AD [5, 6]. Functional connectivity is a term which has been used to study the functional interaction among times series recorded from different brain areas [7]. Due to destructive characteristics of AD, it has also been characterized as a

D.-S. Huang et al. (Eds.): ICIC 2014, LNBI 8590, pp. 25–33, 2014.

neocortical “disconnection syndrome” [8]. Brain’s visualization as a complex network of subsystems has led us to find out the factors that can best identify functional disorders in the brain [9]. There is now ample evidence that formation of dynamic links in term of synchronization constitutes the functional integration of brain [10-12].

Electroencephalogram (EEG) signals are considered functional example to evaluate cognitive disturbances and a diagnostic tool, especially when a diagnostic doubt exists even after the initial clinical procedures [13, 14]. A great deal of research has already been conducted to detect the fluctuations in EEG signals [2, 5, 15]. Alteration in the regional cerebral blood flow (rCBF) has been considered one of the causes of abnormality in EEG signals of AD [16, 17]. Studies on MCI have shown a decrease of alpha power [18, 19] and an increase of theta (4-8 Hz) power [20] in cortio-cortical and subcortical parts of the brain. Babiloni et al [2] claimed that the reduction of the synchronization likelihood occurs both at inter-hemispherical (delta-beta2) and fronto-parietal (delta-gamma) electrodes. Topographically analyzing the EEG signals, Micheal et al [22] reported a less synchronization of upper alpha band between central and temporal cortex. In line, a correlation between higher low-frequency amplitude and alpha-beta activity at frontal region may reflect an early sign of cortical atrophy during the course of AD. The concept of local and global methods is used to analyze synchronization between pairs of signals and entire EEG channels at the same time, respectively [15]. This paper proposes a novel approach using principal component analysis before applying neural synchrony measurement techniques; the proposed technique was benchmarked with other existing techniques. The simulation results indicated that applying principal component analysis before synchrony measurement techniques show significantly improvement over the lateral one. The reminder of this paper is organised as follows. Section 2 will discuss synchrony measurement techniques while section 3 will shows the data description and filtering. Section 4 is concerned with the methodology and section 5 shows the conclusion and future direction.

2 Synchrony Measurement Techniques

In this section, we briefly review the synchrony measurement techniques that we have implemented on our datasets which include phase synchrony, cross correlation and coherence.

2.1 Phase Synchrony (Hilbert Transform)

Synchronization of two periodic non-identical oscillators refers to the adjustment of their rhythmicity, i.e. the phase locking between the two signals. It refers to the interdependence between the instantaneous phases $\varphi_1(t)$ and $\varphi_2(t)$ of the two signals $s_1(t)$ and $s_2(t)$, respectively. It is usually written as:

$$\varphi_{n,m} \quad n\varphi_1(t) \quad n\varphi_2(t) \quad \text{constant} \tag{1}$$

Where n and m are integers indicating the ratio of possible frequency locking, and $\varphi_{n,m}$ is their relative phase or phase difference. To compute the phase synchronization, the instantaneous phase of the two signals should be known. This can be detected using analytical signals based on Hilbert Transform [9].

$$z(t) \quad x(\tau) + i\tilde{x}(t) \tag{2}$$

Here z(t) is complex value with x(t) is a real time series and $\tilde{x}$(t) is its Hilbert transform.

2.2 Cross Correlation

Cross correlation is a mathematical operation used to measure the extent of similarity between two signals. If a signal is correlated to itself, it is called auto-correlated. If we suppose that *x(n)* and *y(n)* are two time series then the correlation between them is calculated as:

$$\hat{R}_{xy}(m) \begin{cases} \sum_{n=0}^{N-m-1} x_{n+m} y_n & m \geq 0 \\ \hat{R}_{yx}(-m) & m < 0 \end{cases} \tag{3}$$

Cross correlation returns a sequence of length 2*M−1 vector, where x and y are of length N vectors (N>1). If x and y are not of the same length then the shorter vector is zero-padded. Cross correlation returns value between −1 and +1. If both signals are identical to each other the value will be 1, otherwise it would be zero [15].

2.3 Magnitude Squared Coherence

The coherence functions estimates the linear correlation of signals in frequency domain [15]. The magnitude squared coherence is defined as the square of the modulus of the mean cross power spectral density (PSD) normalized to the product of the mean auto PSDs. The coherence $C_{xy}(f)$ between two channel time series is computed as:

$$C_{xy}(f) \frac{|P_{xy}(f)|}{P_{xx}(f)P_{yy}(f)} \tag{4}$$

$P_{xy}(f)$ is the cross PSD estimate of x and y. $P_{xx}(f)$ and $P_{yy}(f)$ are the PSD estimates of x and y respectively. For computation, each signal is divided into a section of 650ms and default value of 50% is used. Coherence returns the values between 0 and 1, showing how well the input x corresponds to the output y at each frequency.

3 Data Description and Data Filtering

3.1 Data Description

The datasets we are analyzing, have been recorded from three different countries of European Union. Specialist at memory clinic referred all patients to the EEG department of the hospital. All patients passed through a number of recommended tests; Mini Mental State Examination (MMSE). The Rey Auditory Verbal Learning Test, Benton Visual Retention test and memory recall tests. The results are scored and interpreted by psychologists and a multidisciplinary team in the clinic. After that, each patient is referred to hospital for EEG assessment to diagnose the symptoms of AD. Patients were advised to be in a resting state with their eyes closed. The sampling frequency and number of electrodes for three datasets are all different. Detailed information is described in the following sections.

3.1.1 Database A

The EEG dataset A contains 17 MiAD patients (10 males; aged 69.4 ± 11.5 years) while 24 healthy subjects (9 males; aged 77.6 ± 10 years). They all are of British nationality. These data were obtained using a strict protocol from Derriford Hospital, Plymouth, U.K. and had been collected using normal hospital practices. EEG signals were obtained using the modified Maudsley system which is similar to the traditional 10-20 international system. EEGs were recorded for 20 sec at a sampling frequency of 256 Hz (later on sampled down to 128 Hz) using 21 electrodes.

3.1.2 Database B

This EEG dataset composed of 5 MiAD patients (2 males; aged 78.8 ± 5.6 years) as well as 5 healthy subjects (3 males; aged 76.6 ± 10.0 years). They all are of Italian nationality. Several tests, for instance; MMSE, the clinical dementia rating scale (CDRS) and the geriatric depression scale (GDS) were conducted to evaluate the cognitive state of the patients. The MMSE result for healthy subjects is (29.3 ± 0.7) while for MiAD patients is (22.3 ± 3.1). EEGs were recorded for 20 sec at a sampling frequency of 128 Hz using 19 electrodes at the University of Malta, Msida MSD06, Malta.

3.1.3 Database C

This dataset consists of 8 MiAD patients (6 males; aged 75 ± 3.4 years) and 3 healthy subjects (3 males; aged 73.5 ± 2.2 years). They all are of Romanian Nationality. The AD patients have been referred by a neurologist for EEG recordings. All subjects are diagnosed with AD by means of psychometric tests (MMSE, CDR, OTS), neuroimaging (CT) and clinical examination (gender, age, disease, duration, education and medication). The MMSE result for healthy subjects is (28-30) while for MiAD patients is (20-25). EEG data is recorded using a large equidistant 22-channel arrangement conforming to the international federation of clinical neurophysiology (IFCN) standards for digital recording of clinical EEG from the Ecological University

of Bucharest. The time series are recorded for 10 to 20 min at a sampling frequency of 512 Hz using 22 electrodes. The signals are notch filtered at 50 Hz.

For current research work, we have obtained a version of data that is already preprocessed of artifacts by using Independent Component Analysis (ICA), a blind source separation technique (BSS). Details of these procedures can be found in [43]. For ICA processed data, least corrupted 20s recordings have been selected for further analysis.

3.2 Data Filtering into Five Frequency Bands

EEG time series are classified into five frequency bands. Each frequency band has its own physiological significance [6].

1. Delta (δ: $1 \leq f \leq 4$ Hz): these are characterized for deep sleep and are correlated with different pathologies.
2. Theta (θ: $4 \leq f \leq 8$ Hz): they play important role during childhood. High theta activities in adults are considered abnormal and associated with brain disorders.
3. Alpha (α: $8 \leq f \leq 12$ Hz): they usually appear during mental inactive conditions and under relaxation. They are best seen during eye closed and mostly pronounced in occipital location.
4. Beta (β: $12 \leq f \leq 25$ Hz): they are visible in central and frontal locations. Their amplitude is less than alpha waves and they mostly enhance during tension.
5. Gamma (γ: $25 \leq f \leq 30$ Hz): they are best characterized for cognitive and motor functions.
6. Bandpass filter is applied to each EEG channel to extract the EEG data in specific frequency band [F:(F+W)] Hz. Butterworth filters were used (of 2nd order) as they offer good transition band characteristics at low coefficient orders; thus, they can be implemented efficiently.

4 Methodology

In this research work, a novel methodology using PCA and neural synchrony measurement of the brain is proposed. We have compared our proposed method with other method which takes the average of synchrony measures for all channels in one region of the brain. As mentioned previously, we are comparing right and left temporal with frontal, central and occipital so there are total 7 comparisons of the brain ((left temporal-right temporal (LT-RT)), (left temporal-frontal (LT-F)), (left temporal-central (LT-C)), (left temporal-occipital (LT-O)), (right temporal-frontal (RT-F)), (right temporal-central (RT-C)), and (right temporal-occipital (RT-O))) for all frequency bands (δ, θ, α, β, γ). A brief description of these methods is given below.

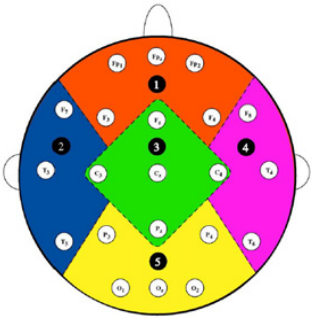

Fig. 1. The 21 Channels used for EEG recording

4.1 First Method (Taking Average of Synchrony Measures)

First we apply neural synchrony measurement technique on each channel pair (time series of two channels) of two different regions for all frequency bands and then we take the average of those results. For instance, we apply phase synchrony measure on each channel pair of right and left temporal ((F7-F8), (F7-T4), (F7-T6), (T3-F8), (T3-T4), (T3-T6), (T5-F8), (T5-T4), (T5-T6) and then we take the average result of right temporal-left temporal. We compare the left temporal with frontal (FP1, FP2, FPz, F3, F4), central (Fz, C3, Cz, C4, Pz) and occipital (P3, P4, O1, O2, Oz). Similarly, we compare the right temporal (F8, T4, T6) to rest of the brain area. The same technique has been used for rest of the synchrony measures i.e. cross correlation and coherence.

After getting the results, we compare the neural synchronization of AD patients and healthy subjects, for all three measurement techniques (phase synchronization, cross correlation and coherence), by Mann-Whitney U test. Figure 2 shows all the steps of our Average method.

4.2 Second Method (PCA Based Neural Synchrony Measure)

In this method, instead of applying synchrony measurement technique directly on the filtered data, first we apply Principal Component Analysis (PCA) technique on all channels of one region. This eliminates any redundant information that a region could provide. For instance, we apply PCA on all three channels of left temporal (F7, T3, T5) and consequently it provides a single signal without any redundant information. Then we apply PCA on all channels of right temporal (F8, T4, T6). After that, we apply synchrony measure on these two regions. Similarly, we apply PCA on all other channels of a region; frontal (FP1, FP2, FPz, F3, F4), central (Fz, C3, Cz, C4, Pz) and occipital (P3, P4, O1, O2, Oz) and compute the synchrony measure with left and right temporal. Rest of the procedure is similar to the first proposed method.

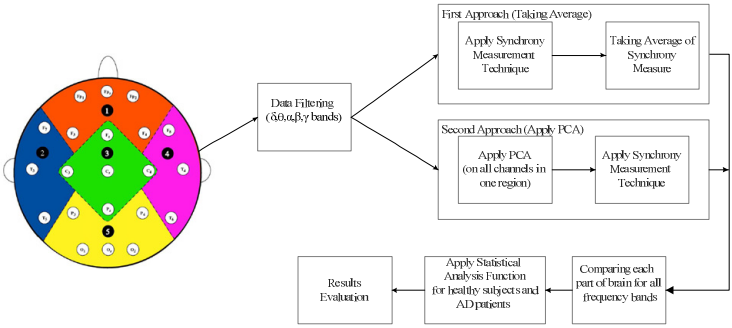

Fig. 2. Average and PCA Methods

4.2.1 Principal Component Analysis (PCA)

The basic purpose of PCA is to reduce the dimensionality of a dataset to convert it to uncorrelated variables providing maximum information about a data while eliminating interrelated variables. In other words it transforms highly dimensional dataset (of m dimensions) into low dimensional orthogonal features (of n dimension) where n<m.

In our case we apply PCA on all channels in one particular region, for instance, the application of PCA for the left temporal as is shown in Fig.3 (a) using channel (F7, T3, T5) are converted into a single signal as shown in Fig. 3(b). The generated temporal signal contains almost all information from the left temporal while eliminating any redundant information.

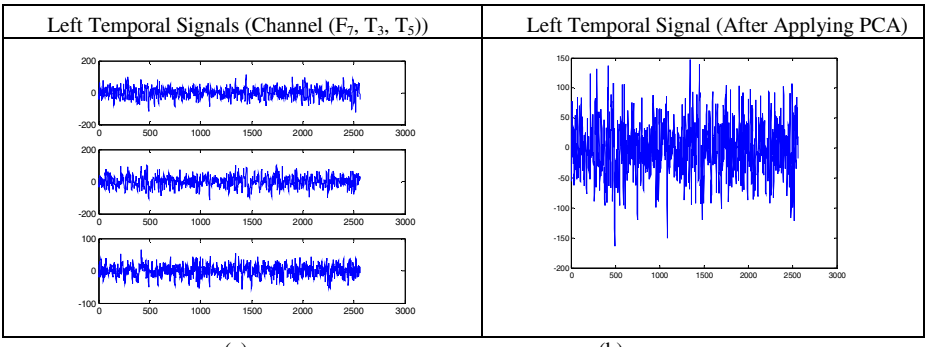

Fig. 3. Application of PCA on left temporal channels signals

5 Conclusion

The aim of the current study was to show the significance of applying PCA method to eliminate redundant information from the datasets to get more reliable results. In this study, three different datasets are selected with different specifications and three

different synchrony measures are applied to prove the significance of our approach. Moreover we have compared our proposed method with Average method to compute synchronization in MiAD patients as well as in control subjects. Results revealed that cross correlation measure showed higher difference in synchronization of MiAD and control subjects as compare to phase synchrony while coherence function did not perform very well. They have also indicated that alpha and theta bands play a major role in identifying the change in synchronization from MiAD and control subjects especially in right temporal-central region (RT-C) and also in left temporal-occipital (LT-O) region. Furthermore, we have successfully shown the importance and significance of our proposed method, to detect lower synchronization in MiAD patients, as compare to the Average method for all three datasets. Future work will involve the study of much significant results of lower synchronization in case of datasets B and datasets C as compare to dataset A.

References

1. Rogers, J., Webster, S., Lue, L.F., Brachova, L., Civin, W.H., Emmerling, M., Shivers, B., Walker, D., Mcgeer, P.: Inflammation and Alzheimer's Disease Pathogenesis. Neurobiology of Aging 17, 681–686 (1996)
2. Babiloni, C., Ferri, R., Binetti, G., Cassarino, A., Forno, G.D., Ercolani, M., Ferreri, F., Frisoni, G.B., Lanuzza, B., Miniussi, C., Nobili, F., Rodriguez, G., Rundo, F., Stam, C.J., Musha, T., Vecchio, F., Rossini, P.M.: Fronto-Parietal Coupling of Brain Rhythms in Mild Cognitive Impairment: A Multicentric EEG Study. Brain Research Bulletin 69, 63–73 (2006)
3. Babiloni, C.G., Frisoni, B., Pievani, M., Vecchio, F., Lizio, R., Buttiglione, M., Geroldi, C., Fracassi, C., Eusebi, F., Ferri, R., Rossini, P.M.: Hippocampal Volume and Cortical Sources of EEG Alpha Rhythms in Mild Cognitive Impairment and Alzheimer Disease. Neuroimage 44, 123–135 (2009)
4. Frisoni, G.B., Padovani, A., Wahlund, L.O.: The Predementia Diagnosis of Alzheimer Disease. Alzheimer. Dis. Assoc. Disord. 18, 51–53 (2004)
5. Jelles, B., Scheltens, P., Van Der Flier, W.M., Jonkman, E.J.: Global Dynamical Analysis of The EEG in Alzheimer's Disease: Frequency-Specific Changes of Functional Interactions. Clinical Neurophysiology 119 (2008)
6. Faustino, M.C., Serquiña, R.P., Rapp, P.E., Albano, A.M.: Phase Synchronization of Electroencephalographic Signals in The Different Frequency Bands. Philippine Science Letters 5, 131–137 (2012)
7. Fingelkurts, A.A., Fingelkurts, A.A., Kähkönen, S.: Functional Connectivity in The Brain—Is It An Elusive Concept? Neuroscience & Biobehavioral Reviews 28, 827–836 (2005)
8. Delbeuck, X., Van Der Linden, M., Collette, F.: Alzheimer' Disease As A Disconnection Syndrome? Neuropsychology Review 13, 79–92 (2003)
9. Stam, C.J., Nolte, G., Daffertshofer, A.: Phase Lag Index: Assessment of Functional Connectivity From Multi Channel EEG and MEG With Diminished Bias From Common Sources. Human Brain Mapping 28, 1178–1193 (2007)
10. Singer, W.: Neuronal Synchrony: A Versatile Code for The Definition of Relations? Neuron 24 (1999)

11. Fries, P.: A Mechanism for Cognitive Dynamics: Neuronal Communication Through Neuronal Coherence. Trends in Cognitive Sciences 9, 474–480 (2005)
12. Varela, F., Lachaux, J.P., Rodriguez, E., Martinerie, J.: The Brainweb: Phase Synchronization and Large-Scale Integration. Neuroscience 2 (2001)
13. Claus, J.J., Strijers, R.L.M., Jonkman, E.J., Ongerboer De Visser, B.W., Jonker, C., Walstra, G.J.M., Scheltens, P., Van Gool, W.A.: The Diagnostic Value of Electroencephalography in Mild Senile Alzheimer's Disease. Clinical Neurophysiology 110, 825–832 (1999)
14. Gallego-Jutgla, E., Elgendi, M., Vialatte, F., Sole-Casals, J., Cichocki, A., Latchoumane, C., Jaesung, J., Dauwels, J.: Diagnosis of Alzheimer's Disease From EEG By Means of Synchrony Measures in Optimized Frequency Bands. In: International Conference (EMBC), pp. 4266–4270 (2012)
15. Dauwels, J., Vialatte, F.B., Cichocki, A.: A Comparative Study of Synchrony Measures for The Early Detection of Alzheimer's Disease Based on EEG. In: Ishikawa, M., Doya, K., Miyamoto, H., Yamakawa, T. (eds.) ICONIP 2007, Part I. LNCS, vol. 4984, pp. 112–125. Springer, Heidelberg (2008)
16. JÓHannesson, G., Brun, A., Gustafson, I., Ingvar, D.H.: EEG in Presenile Dementia Related to Cerebral Blood Flow and Autopsy Findings. Acta Neurologica Scandinavica 56, 89–103 (1977)
17. Szelies, B., Grond, M., Herholz, K., Kessler, J., Wullen, T., Heiss, W.D.: Quantitative EEG Mapping and PET in Alzheimer's Disease. Journal of the Neurological Sciences 110, 46–56 (1992)
18. Huang, C., Wahlund, L.O., Dierks, T., Julin, P., Winblad, B., Jelic, V.: Discrimination of Alzheimer's Disease and Mild Cognitive Impairment By Equivalent EEG Sources: A Cross-Sectional and Longitudinal Study. Clinical Neurophysiology 111, 1961–1967 (2000)
19. Grunwald, M., Busse, F., Hensel, A., Kruggel, F., Riedel-Heller, S., Wolf, H., Arendt, T., Gertz, H.J.: Correlation Between Cortical Theta Activity and Hippocampal Volumes in Health, Mild Cognitive Impairment, and Mild Dementia. J. Clin. Neurophysiol. 18 (2001)
20. Fonseca, L.C., Tedrus, G.M., Prandi, L.R., Andrade, A.C.: Quantitative Electroencephalography Power and Coherence Measurements in The Diagnosis of Mild and Moderate Alzheimer's Disease. Arq Neuropsiquiatr 69 (2011)
21. Stam, C.J., Jones, B.F., Manshanden, I.A., Van Cappellen Van Walsum, M., Montez, T., Verbunt, J.P.A., De Munck, J.C.B., Van Dijk, W., Berendse, H.W., Scheltens, P.: Magnetoencephalographic Evaluation of Resting-State Functional Connectivity in Alzheimer's Disease. Neuroimage 32, 1335–1344 (2006)
22. Hogan, M.J., Swanwick, G.R., Kaiser, J.J., Rowan, M., Lawlor, B.: Memory-Related EEG Power and Coherence Reductions in Mild Alzheimer's Disease. International Journal of Psychophysiology 49, 147–163 (2003)