Diagnosis of Alzheimer Disease using EEG Signals

Nilesh Kulkarni
M.E Student, Department of Electronics Engineering
All India Shri Shivaji Memorial Society's Institute of Information Technology,
Pune, India.

Prof. Dr. V. K. Bairagi
Associate Professor, Department of Electronics & Telecommunication
All India Shri Shivaji Memorial Society's Institute of Information Technology,
Pune, India.

***Abstract*— Alzheimer Disease is the Neuro-degenerative disease, which consists of the common form of dementia. It is the most expensive disease in the modern society & characterized by cognitive, intellectual as well as behavioral disturbance. Due to this, the early diagnosis of the disease is essential as it helps the patients & also his family to take preventive measures. EEG can be used the standardized tool for diagnosis of Alzheimer disease. Various abnormalities are found in the EEG signals of the patients suffering from Alzheimer disease. Hence, the need is to develop the detection of the disease in early stage called as Dementia, the first stage called Mild cognitive impairment (MCI). Role of EEG in diagnostic & clinical research of Alzheimer disease has become more useful in present decades. In present, the most critical task includes the diagnosis of the AD & its early detection in the preclinical stage. The need is to improve the diagnosis accuracy of the EEG signal. The paper presents the ideas of increasing the accuracy of the signal by using various methods. Basically, abnormalities in the EEG signals are characterized by slowing of signals, shift of power spectrum to low frequencies etc. In this way, EEG can be as the tool for the early diagnosis of Alzheimer disease.**

Keywords*— Alzheimer Disease, Dementia, Electroencephalography, Mild Cognitive impairment (MCI).

I. INTRODUCTION

Alzheimer disease is one of the Neuro-degenerative diseases which are found to be complex in the present scenario. It is the common form of dementia & by the time it affects the brains cells [1] [2]. Its prevalence in the world is assumed to be doubled in next 20 years [3]. In 2012, the World Health Organization and Alzheimer's disease International released a report calling on governments to implement national dementia plans focusing on 1) raising public awareness about the disease and reducing stigma, 2) improving early diagnosis, and 3) providing better care and more support to Caregivers [4]. As AD is assumed to be increased in the near future due to the aging phenomenon, several measures are taken into the consideration for the early diagnosis of disease in the early stage. AD is mainly characterized by the neuronal widespread loss of cells, neurofibrillary tangles, and senile plaques in

Hippocampus, entorhinal cortex, neocortex and other brain regions [5]. In the pre-clinical stage of the disease, there are no basically reliable and valid symptoms detected to allow a very early diagnosis. In the mild stage of the disease, memory impairment & loss are noticed. In the moderate stage of dementia, language difficulties become more such as word finding difficulties, paraphasia etc. As the disease goes in progression, several deficits are found in cognitive abilities such as judgment, abstract or logical reasoning, planning, and organizing [6]. In the final stage called as the severe AD, almost all cognitive functions are severely damaged, and motor functions including chewing and swallowing are profoundly disturbed [7].

Presently, it was estimated that there are 44.4 millions of people suffering from dementia in the world. It was also estimated that this number will increase till 75.6 million in 2030, and 135.5 million in 2050. It was also observed that 61% of the people suffering from dementia are from the developed countries. The fastest growth in the elderly population is taking place in China, India, and their south Asian and western Pacific neighbors [8].

There are basically no proper symptoms for cause of AD. But, some cases are generally accepted for the genetic differences. Some of the hypothesis are used for the understanding the cause of AD. Some of the common hypothesis includes the genetics, cholinergic hypothesis, Amyloid hypothesis, tau hypothesis etc. Another hypothesis is also made that AD is also caused by the age related myelin breakdown in the brain. Air pollution is also one of the contributing factors for the development of the Alzheimer disease. Early diagnosis of the disease in early stage is essential in both the Mild AD & MCI stage as medications can be applied in an early stage. Early diagnosis of the disease also raises the chances of treating the disease at a nascent stage. It allows the patients family to take financial decisions related to the disease, and to plan for the future needs and care of the patients.

II. METHODS

Numerous clinical methods are extensively used for the diagnosis of Alzheimer disease such as neuroimaging techniques, physiological markers, and genetic analyses. Neuroimaging is one of the well-accepted methods for definitive diagnosis of dementia. Various Neuro-imaging methods are used for the diagnosis of the Alzheimer disease. Several methods such as single-photon emission computerized tomography (SPECT), positron emission tomography (PET), and magnetic resonance imaging (MRI) have been successful for recognizing AD at an early stage. But the main problem of PET & SPECT is they impose the radiation risks. Other disadvantages are their costs; which

are much expensive, time consuming & inconvenient. So, apart from all these Neuro-imaging methods; EEG is one of the standard methods used for the diagnosis of the Alzheimer disease.

The use of the Electroencephalography is considered as the one of the approach for mass screening the population at risk for Alzheimer's. EEG is noninvasive, repeatable, and can be easily executed at home through wireless body area networks as a personalized medical tool. EEG is also a direct correlate of brain function that is used clinically to monitor brain activity. It is shown that non-linear analysis of the sampled EEG data have shown the unique features to reveal the diagnosis of the neurological diseases such as Alzheimer, Epilepsy & Parkinson's [9][10].

Table.1 Comparative Study of various techniques developed by Researchers.

Sr. No	Reference	Method Used	Accuracy
1.	[30]	Independent Component Analysis	60%
2.	[33]	Conventional spectral analysis and nonlinear dynamical methods.	80%
3.	[34]	Nonlinear Analysis of EEG via Tsallis Entropy.	82%
4.	[35]	Quantitative (qEEG) method for measuring the EEG variability to improve the classification accuracy	88%
5.	[36]	Relative power and complexity measures as features to classify the disease.	83%
6.	[37]	Integrative EEG biomarkers to predict the diagnosis	88%
7.	[38]	M3 approach to classify AD. M3 is multi-modal imaging and multi-level characteristics with multi-classifier	89.4 %

A. EEG Based Diagnosis

As discussed earlier, EEG is one of the methods used for the diagnosis of the AD. The advantages of AD includes that they are inexpensive, convenient & cheap. Along with this, certain abnormalities are found in the EEG of the patients suffering from the Alzheimer disease or who are in the first stage called Mild Cognitive impairment (MCI). Numerous studies have investigated the potential of EEG as a diagnostic tool for AD [11][12][13][14][15].The abnormalities found in the patients are the i) Slowing of the EEG signals ii) reduced complexity of the EEG signals, and iii) perturbations in EEG synchrony [16][17][18][19][20][21].

a) Slowing of EEG signals:

It is one of the most important phenomenon observed in the EEG of patient suffering from AD. Studies have shown that an EEG signal slows down as the Mild Cognitive impairment & Alzheimer disease is caused. The MCI/AD is also associated with the increase in the power of the low frequencies (delta and theta band, 0.5–8Hz) and a decrease of power in higher frequencies (alpha and beta, 8–30Hz).

From the above of the signals it was shown that transient oscillations in the EEG of MCI and AD patients occur more often at low frequencies compared to healthy control subjects. Thus, these transients also exhibit slowing of the signals.

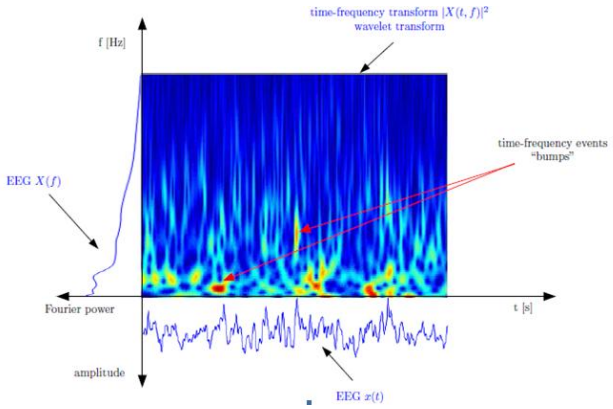

Fig 1.Slowing of the EEG signals: EEG signal, shown in time-domain x (t), frequency domain X (f), and time-frequency domain |X (t, f) |. [22]

From the above of the signals it was shown that transient oscillations in the EEG of MCI and AD patients occur more often at low frequencies compared to healthy control subjects. Thus, these transients also exhibit slowing of the signals.

b) Reduced Complexity of EEG Signals:

Various methods are used for the reducing the complexity of the EEG signals. Several methods have been used for the complexity of EEG signals in MCI and AD Patients. Different methods such as information theory [22] [23], Tsallis entropy [23], approximate entropy [25], multi-scale entropy [27, 28], sample entropy & mutual information and Lempel-Ziv complexity [24] are used to quantify EEG complexity.

c) Perturbation of Synchrony Measures:

Many different measures of synchrony have been employed in the physical sciences, signal processing and in the study of neurobiology. Numerous studies have shown the decreased EEG synchrony in MCI/AD patients. The main problem is that most studies use just one measure or very few measures, and many of those studies analyze different data sets; consequently, it is difficult to rigorously compare the various measures. Various synchrony measures obtained from the EEG signals are affected by the brain signals. Pearson Correlation Coefficient, Magnitude and Phase Coherence, Granger Causality, Phase Synchrony are some of the synchrony measures used for the diagnosis of the Alzheimer disease.

III. METHODOLOGY

In our proposed methodology, firstly we are acquiring the EEG signal by using the EEG electrodes. The EEG electrode cap is used for the signal acquisition which is put on the patient's head for recording of the signal. For the placement of the electrodes, we are using the standard 10-20 electrode system. The following figure shows the block diagram of proposed system.

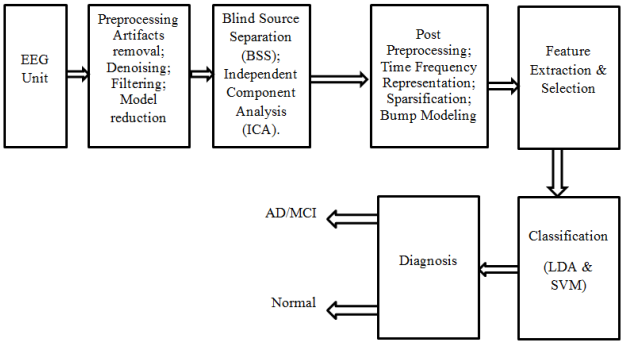

Fig 2. Block Diagram of Proposed System

a) **EEG Unit**: It is used for measurement of EEG signal. This is done by using the electrodes. Many BCIs use an *electrode cap*, in which the electrodes are already in the right places, typically according to the "international 10-20 system". It saves time because the electrodes do not have to be attached one by one. (Typically, less than 10 electrodes are used in online).

b) **Pre-Processing**: This includes amplification, initial filtering of EEG signal artifact removal. Also A/D conversion is made, i.e. the analog EEG signal is digitized. Additionally to obtain more enhanced EEG signals various methods such as the Blind Source separation [29], independent component analysis [30] are used. After the above method again the EEG signal is post processed using the time frequency domain. Various techniques such as the Wavelet transform, Sparsification & Bump Modeling [31] are used for the same.

c) **Feature Selection & Extraction**: In this stage, certain features are extracted from the pre-processed & digitized EEG signal. In the easiest form, a certain frequency range is selected and the amplitude relative to some reference level is measured. Typically the features are certain frequency bands of a power spectrum. The power spectrum (which describes the Frequency content of the EEG signal) can be calculated using, for example, Fast Fourier Transform (FFT), the transfer function of an autoregressive (AR) model or wavelet Transform. Also, after bump modeling, the signals under investigation are represented by the set of parameters that describe the bumps [31].

d) **Classification**: The features extracted in the previous stage are the input for the classifier. The classifier can be anything from a simple linear model to a complex non-linear neural network that can be trained to diagnose the disease. In our proposed methodology, Linear Discriminant Analysis (LDA) or Support Vector Machine (SVM) [32] can be used for the classification.

e) **Diagnosis:** Based on the output of the Classifier, we can detect whether the person is suffering from Alzheimer Disease or he is in the early stage of the AD called as the Mild cognitive impairment (MCI).

EEGLAB is found to be an interactive MATLAB toolbox which is used for processing the continuous and event-related EEG, MEG and other electrophysiological data using independent component analysis (ICA), time/frequency analysis, and other methods including artifact rejection. EEGLAB provides an interactive graphic user interface (GUI) allowing users to flexibly and interactively process their high-density EEG and other dynamic brain data using independent component analysis and/or time/frequency analysis (TFA), as well as standard averaging methods.

IV. RESULTS

At the end of the research, it is expected that we get the high accuracy (upto 95%) of the EEG signal for detection of the Alzheimer disease. By watching the nature of the above signal according to the frequency bands classified we can also detect stage of the Alzheimer disease for example the early stage dementia, later stage Mild cognitive impairment (MCI) & last stage Severe Alzheimer disease.

V. CONCLUSIONS & FUTURE SCOPE

In this way, we can use EEG as a means of diagnosis of Alzheimer disease. Various abnormalities are found in the EEG signals. Slowing of EEG signals, reduced complexity, Perturbations in synchrony measures are some of the abnormalities found. Various different features extraction methods as well as classifiers can be used for early detection of the disease. Thus, EEG can be used as the inexpensive, convenient tool for diagnosis of Alzheimer disease. In future, various different algorithms as well as classifiers such as neural networks can be used for increasing the accuracy of diagnosis of the disease in early stage. Research Challenges includes the increase of accuracy upto 95% of EEG signal to detect the disease in the early stage, use of different classifiers for classification purpose & to remove the artifacts in EEG signal are some them. In future, the above system can also be made portable.

ACKNOWLEDGMENT

Firstly, author would like to thank Prof.Dr.V.K.Bairagi for his valuable guidance, advice & support. Secondly, author would also like to thank Prof.D.K.Shedge, Head, Electronics Engineering for providing his valuable support. Author would lastly thank all the staff of PG section for their guidance & support.

Authors gratefully acknowledges the Principal of the institute Dr. P. B. Mane, Prof. D. K. Shedge, Head of Electronics Engg, Dept. & entire staff of Post Graduate section of the Institute for their support & guidance in the present work.

REFERENCES

[1]Mattson M., "Pathways towards and away from Alzheimer's disease", Nature, Vol. 430, Aug.2004, pp. 631–639.
[2] Meek P.D., McKeithan K., and Shumock G.T., "Economics considerations of Alzheimer's disease", Pharmacotherapy, Vol. 18, March-April 1998, pp.68–73,
[3] M. W. Weiner, D. P. Veitch, P. S. Aisen, L. A. Beckett, N. J. Cairns, R. C. Green, D. Harvey, "The Alzheimer's Disease Neuroimaging Initiative: A review of paperspublished since its inception", Alzheimer's & Dementia 8 (1 Suppl), 2012, pp. S1–S68.
[4] World Health Organization and Alzheimer's disease International (2012) Dementia: a public health priority. Technical report.
[5] De Carli C, Kaye JA, Horwitz B, Rapoport SI., "Critical analysis of the use of computer-assisted transverse axial tomography to study human brain in aging and dementia of the Alzheimer type.", Neurology, Vol .40, 1990,pp. 872–83.
[6] D. Fo¨rstl H, Kurz A., "Clinical features of Alzheimer's disease." Eur ArchPsychiatry Clin Neurosci, Vol.249, 1999, pp.288–90.
[7] Bianchetti A, Trabucch M., "Clinical aspects of Alzheimer's disease." AgingClin Exp Res, Vol 13, 2001, pp. 221–30.
[8] Béatrice Duthey, "A Public Health Approach to Innovation", Update on 2004 Background Paper written by SaloniTanna, February 2013.
[9] Beuter, C. Labric, and K. Vasilakos, "Transient dynamics in motor control of patients with Parkinson's disease," Chaos, vol.1, 1991, pp. 279-286.
[10] H. L. Glass, "Nonlinear dynamics of physiological function and control," Chaos, vol. 1, 1991, pp. 247-250.
[11] Sink K.M., Holden K.F., and Yaffe K., "Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence." JAMA, Vol .293, No.5, 2005, pp. 596–608.
[12] Baker M., Akrofi K., Schiffer R., and Michael W. O' Boyle, "EEG Patterns in Mild Cognitive Impairment (MCI) Patients." Open Neuroimage J., Vol.2, Aug. 2008, pp. 52–55.
[13] Besthorn C., Zerfass R., Geiger-Kabisch C., Sattel H., Daniel S., Schreiter-GasserU., and Frstl H., "Discrimination of Alzheimer's disease and normal aging by EEG data.", Electroencephalography and Clinical Neurophysiology, Vol.103, No.2, August 1997, pp.241–248.
[14] Van der Hiele K., Vein A.A., Reijntjes R.H., Westendorp R.G., Bollen E.L., van Buchem M.A., van Dijk J.G., Middelkoop H.A., "EEG correlates in the spectrum of cognitive decline., "Clinical Neurophysiology,Vol.118,No.9, Sept.2007, pp.1931–1939.
[15] Czigler B., Csik´os D., Hidasi Z., Anna Ga´al Z., Csibri E., Kiss E., Salacz P., Moln´ar M., "Quantitative EEG in early Alzheimer's disease patients—power spectrum and complexity features." , Int. J. Psychophysiol. , Vol. 68, No.1, April 2007, pp.75–80.
[16] Gianotti L.R., K¨unig G., Lehmann D., Faber P.L., Pascual-Marqui R.D., Kochi K., and Schreiter-Gasser U., "Correlation between disease severity and brain electric LORETA tomography in Alzheimer's disease.", Clin.Neurophysiol., Vol. 118 ,No.1, Jan 2001, pp.186–96.
[17] Herrmann C.S. and Demiralp T., "Human EEG gamma oscillations in neuropsychiatric disorders." Clin.Neurophysiology. Vol 116, No.12, Dec 2005, pp.2719–2733.
[18] Latchoumane C.F.V., Vialatte F.B., Cichocki A., and Jeong J., "Multiway analysis of Alzheimer's disease: classification based on space-frequency characteristics of EEG time series", Proc. World Congress on Engineering 2008, London, United Kingdom, 2–4 July, 2008.
[19] Latchoumane C.F.V, Vialatte F.B., Jeong J., and Cichocki A. EEC Classification of Mild and Severe Alzheimer's Disease using Parallel Factor Analysis Method. In Advances in Electrical Engineering and Computational Science, in press, 2009
[20] Schreiter Gasser U., Rousson V., Hentschel F., Sattel H., Gasser T., "Alzheimer disease versus mixed dementias: an EEG perspective.", Clin Neurophysiology, Vol.119 , No.10, Oct 2008, pp. 2255–2759.
[21] Moretti D.V., Fracassi C., Pievani M., Geroldi C., Binetti G., Zanetti O., Sosta K., Rossini P.M., and Frisoni G.B., "Increase of theta/gamma ratio is associated With memory impairment.", Clin.Neurophysiol. Vol .120, No. 2, Feb 2009, pp. 295–303.
[22] Justin Dauwels, Francois Vialatte, and Andrzej Cichocki, "Diagnosis of Alzheimer's disease from EEG Signals: Where Are We Standing?" Current Alzheimer Research, Vol. 7, No.6, Sep 2010, pp.487-505.
[23] Shannon C.E., "A Mathematical Theory of Communication. Bell System Technical Journal", Vol 27, pp. 379–423, 623–656, July-October 1948.
[24] Cover T. M. and Thomas J. A., "Elements of Information Theory." Wiley, New York, 1991.
[25] Pincus S.M., "Approximate entropy as a measure of system complexity", Proc.Natl Acad Sci, USA, Vol 88, March 1991, pp. 2297–2301.
[26] Lake D.E., Richman J.S, Griffin M.P., and Moorman J.R., "Sample entropy analysis of neonatal heart rate variability", Am J Physiol, Vol .283, No. 3, Sep 2007, pp. 789–797
[27] Costa M., Goldberger A.L., Peng C.-K., "Multiscale entropy analysis of physiologic time series." Phys Rev Lett, Vol.89, No.06, August 2002.
[28] Jeong J., Gore J., and Peterson B., "Mutual information analysis of the EEG in patients with Alzheimer's disease." Clinical Neurophysiology, Vol.112, No. 5, May 2001, pp. 827–835.
[29] Andrzej Cichocki, Sergei L. Shishkin, ToshimitsuMusha, Zbigniew Leonowicz , Takashi Asada, Takayoshi Kurachi, "EEG filtering based on blind source separation (BSS) for early detection of Alzheimer's disease", Clinical Neurophysiology, Vol 116, No.3, March 2005, pp.729-737.
[30] Co Melissant, Alexander Ypma, Edward E.E. Frietman, Cornelis J. Stam, "A method for detection of Alzheimer's disease using ICA-enhanced EEG measurements", Artificial Intelligence in Medicine, Vol. 33,No.3,March 2005 pp. 209-222.
[33] Jaeseung Jeong, "EEG dynamics in patients with Alzheimer's disease", Artificial Intelligence in Medicine, Vol 33, Issue 1 pp. 209—222, 2005.
[34] Thibaut De Bock, Satyajit Das, Maruf Mohsin, "Early Detection of Alzheimer's Disease Using Nonlinear Analysis of EEG via Tsallis Entropy", Proceedings of 15th International Conference, Warsaw, Poland,pp.1-4, September 11-15, 2005.
[35] Robert Sneddon, "EEG detection of early Alzheimer disease using psychological task.", Journal of Clinical EEG & Neuro Science, Volume 36, No.3, July 2005, pp.141-150.
[36] Justin Dauwels, K.Srinivasan, M. Ramasubba Reddy, Toshimitsu Musha, Franc¸ois-Benoˆıt Vialatte, Charles Latchoumane, Jaeseung Jeong and Andrzej Cichocki, "Slowing and Loss of Complexity in Alzheimer's EEG: Two Sides of the Same Coin?", Hindawi Access of Research, International Journal of Alzheimer's Disease, Volume 2011, Article ID 539621.
[37]Simon-Shlomo Poil, WillemdeHaan, Wiesje M.vAnder Flier, HuibertD.Mansvelder Philip Scheltens and KlausLinkenkaer-Hansen, "Integrative EEG biomarkers predict progression to Alzheimer's disease at the MCI stage", Frontiers in Aging Neuroscience, Vol.5, Oct 2013, pp. 1-6, Article ID 58.
[38] Zhengjia Dai, Chaogan Yan, Zhiqun Wang, Jinhui Wang, Mingrui Xia, Kuncheng Li, Yong He, "Discriminative analysis of early Alzheimer's disease using multi-modal imaging and multi-level characterization with multi-classifier (M3)", Journal of Neuroimage,Vol.59,No.3,Feb 2012,pp.2187–2195.