EUSIPCO 2013 1569744477

EVALUATION OF EEG SPECTRAL FEATURES IN ALZHEIMER DISEASE DISCRIMINATION

P. M. Rodrigues[1], *B. C. Bispo*[1], *D. R. Freitas*[1], *J. P. Teixeira*[2] *and A. Carreres*[3]

[1]University of Porto, Department of Electrical and Computer Engineering, Porto, Portugal,
Emails:{pmlr, bruno.bispo, dfreitas}@fe.up.pt
[2]Polytechnic Institute of Bragança, Department of Electrical Engineering, Bragança, Portugal,
Email: joaopt@ipb.pt
[3]Hospital Universitario Pío del Río Hortega, Servicio de Neurología, Valladolid, Spain,
Email: acarreres@saludcastillayleon.es

ABSTRACT

Alzheimer's disease (AD) is considered one of the most disabling diseases and it has a high prevalence in developed countries. It is as well the most common cause of dementia and it affects particularly the elderly. The current AD diagnosis accuracy is relatively low. It is therefore necessary to optimize the methods for AD detection. The electroencephalogram (EEG) is an inexpensive and noninvasive technique, that is able to record the electromagnetic fields produced by the brain activity. It has shown in the recent past a growing quality of the contribution to show brain disorders. The aim of this study was to evaluate the individual and combined power of several EEG features in AD discrimination. 95.00% of sensitivity, 100.00% of specificity, 97.06% of accuracy and 0.98 of AUC were the best classification results obtained in this work.

Index Terms— Alzheimer's disease, Electroencephalogram, diagnose, elderly people

1. INTRODUCTION

Alzheimer's disease (AD) is a brain illness characterized as being progressive, degenerative and irreversible. The origin of this disease still remains unknown. So far, no single factor has been identified as being responsible to cause AD. AD can affect several cerebral areas connected with memory, thinking, planning and attention [1]. It seems that a combination of several factors, such as: age, genetic inheritance, environment, lifestyle, obesity, diabetes, hypertension and cholesterol, may be responsible for this disease [2]. An autopsy or brain biopsy is the only way to make a definitive diagnosis of AD [3]. This disease, in 2001, reached more than 21.1 million of people around the world [3]. The greatest risk factor universally accepted for AD is increasing age. The number of people with AD will increase significantly all over the world, especially in western countries which have a high rate of aged population[3]. There is still no cure for this devastating disease and unfortunately there is no straightforward test for AD diagnosis. It is urgent to find an early and effective method for AD detection, because the disease should be prevented or treated effectively [3]. AD symptoms are often confounded with other normal symptoms of aging and they are often subtle at the beginning, that is why it is difficult to achieve an accurate diagnosis [4]. Significant advances have been achieved in recent decades to diagnose AD. Therefore, it is important to continue the research to successfully diagnose the disease in an early stage before substantial brain damage occurs [3].

The Electroencephalogram (EEG) has been used for several decades as a diagnostic tool for dementia. EEG is a noninvasive technique that records the electromagnetic fields of the brain with a high temporal resolution [5]. The convencional EEG frequency bands are delta (δ, 1-4 Hz), theta (θ, 4-8 Hz), alpha (α, 8-13Hz), beta (β, 13-30 Hz) and gamma (γ, 30-60 Hz) [5]. AD is associated with an increase of power in low frequencies (delta and theta band) and a decrease of power in higher frequencies (alpha and beta) [5]. This phenomenon also called "shift-to-the-left" appears in advanced and intermediate states of AD and can be seen notably in the peak occurring at alpha range. These changes are related to the destruction of cholinergic synapses in the Meynet nucleus where transferase, responsible for the synthesis of acetylcholine, is produced [6].

In this study, we want to evaluate the individual and combined power of several EEG features in AD discrimination. For this purpose, the Wavelet Transform (WT) was used to process the EEG signals and twenty eight parameters were calculated. The Linear discriminant analysis (LDA) with a leave-one-out cross-validation procedure was performed in order to evaluate the individual and the combined discriminant power of EEG extracted features.

2. MATERIALS AND FEATURES

2.1. Patients and controls selection/EEG recording

Thirty four subjects participated in the study (14 Control subjects and 20 AD patients). EEGs were recorded from the in-

ternational system 10-20 of 19 localizations (loci). Recordings were made with the subjects in a relaxed state and under the eyes-closed condition in order to minimize the occurance of artifacts. The sampling frequency was 200 Hz. Afterwards, EEGs were organized in 5 seconds artifact-free epochs. All recordings were digitally filtered with a 50Hz notch filter.

2.2. EEG Time-frequency representations

EEG signals, in general, tend to have rapid oscillations in short intervals or slow variations in long intervals [7]. The Fast Fourier Transform (FFT) was introduced in 1965 and it remains the spectral EEG signal processing most commonly used until today [8]. Despite fast, FFT is not able to provide information both in the time and frequency of signal characteristics. The spectral components do not reflect changes along time representing a problem to analyze non-stationary signals, as EEG [9]. Therefore, it is convenient to use a transformation that provides a variable resolution in time-frequency plane as is the case of Wavelet Transform (WT) which provides a good time resolution for the high frequencies and good frequency resolution for low frequencies [8]. The WT is an optimal tool for data analysis when time and frequency resolution are critical [8]. Equation 1 represents the calculation of WT per scale, sometimes called child WT($\psi(t)_{\tau,a}$).

$$\psi(t)_{\tau,a} = \frac{1}{\sqrt{|a|}} \cdot \psi\left(\frac{t-\tau}{a}\right); \quad (1)$$

where τ is the translational parameter, t represents the bins in the time domain, $\psi(t)$ is the Wavelet Mother and a represents the basis functions range which acts as an enlargement factor if a> 1 or as a compression factor if a <1.

The Discrete Wavelet Transform (DWT) was used in the implementation. It uses a multiresolution analysis that consists in obtaining increasingly smaller signal resolution versions by successive filtering. The DWT uses one set of two functions: a scale function ($\varphi[n]$) and a Wavelet function ($\psi[n]$) [8].

$$\varphi[n] = \sum_k h[k] \cdot \varphi[2 \cdot n - k] \quad (2)$$

$$\psi[n] = \sum_k g[k] \cdot \varphi[2 \cdot n - k] \quad (3)$$

where k is the discrete translation parameter and $h[k]$ and $g[k]$ respectively are the impulse responses of the lowpass and highpass filters used in the WT analysis. The signal decomposition in different frequency bands is achieved by successive low-pass filters and high-pass filters in time, followed by subsampling by factor of two until the maximum level of decomposition ($log_2(N)$) as is illustrated in the following equations 4 and 5 [8, 10].

$$DWT_A^{\varphi}[j,k] = \sum_{n=0}^{\frac{N}{2^{j-1}}} DWT_A^{\varphi}[j-1,n] \cdot h[2 \cdot k - n] \quad (4)$$

$$DWT_D^{\psi}[j,k] = \sum_{n=0}^{\frac{N}{2^{j-1}}} DWT_A^{\psi}[j-1,n] \cdot g[2 \cdot k - n] \quad (5)$$

where, $k = 0, ..., \frac{N}{2^j}; j = 0, ..., log_2(N)$, A represents the DWT approximated coefficients, D the DWT detail coefficients and N the signal length.

2.2.1. Feature extraction

Each 5 seconds of EEG signal epoch has undergone an average process per electrode and per subject. Fig. 1 explains the signal averaging process per electrode and subject. In order to extract some information from the EEG signals of AD patients and Control subjects, each signal resulting from the average process was decomposed to the level 5 by the $Bior3.5$ DWT (correct level of EEG signal decomposition to reach the conventional frequency bands of EEG). The $Bior3.5$ Wavelet proved to be a good choice in previous works [11, 12, 13]. The delta band corresponded to the approximated coefficients $A5$ of DWT decomposition, the theta band to the detail coefficients $D5$, the alpha band to $D4$, the beta band to $D3$ and the gamma band to $D2$. Each EEG convencional band was reconstructed in the time domain by the $Bior3.5$ DWT with the same length of the original average signal (5s - 1000 points).

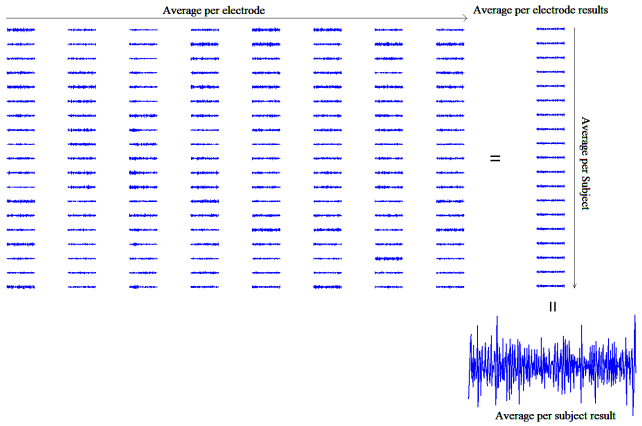

Fig. 1. Signal averaging per electrode and subject.

Several features were extracted from each EEG signal reconstructed component ($\delta, \theta, \alpha, \beta$ and γ). They characterized the waveform in terms of its faster or less rapid and of greater or smaller variability as will be needs to happen when observing the phenomenon "shift-to-the-left", described by the rate amount of maxima ($NMax$) and minima ($NMin$), the

zero-crossing (Zcr) rate, the mean derivative value at a point ($Mdif$), the signal energy (E) and the spectrum energy deceleration represented by the spectral ratios (r). The extracted features were:

- $NMax$ and $NMin$: Accounting and calculation of all signal maxima and minima, respectively, by the variation of the signal waveform derivative (view Fig. 2).

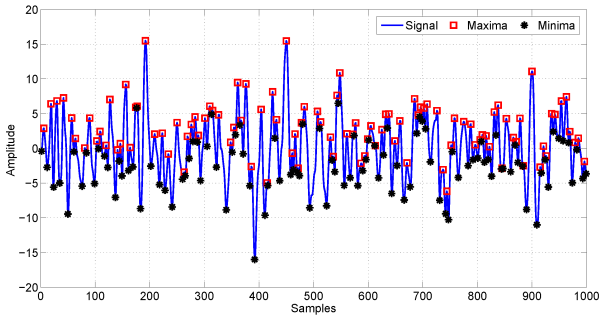

Fig. 2. Signal maxima and minima, example.

- Zcr: The zero-crossing rate was calculated as [14]:

$$Zcr_i = \frac{1}{N-1}\sum_{n=1}^{N-1}\mathbb{I}\{s_i(n)s_i(n)-1<0\}, \quad (6)$$

where $i = \{\delta, \theta, \alpha, \beta, \gamma\}$, s is a DWT coefficient signal of length N and $\mathbb{I}$ the indicator function. If the $\mathbb{I}$ value, in a certain position, is equal to 1 a signal zero crossing is found.

- $Mdif$: The mean derivative value at a point was obtained by the equation 7 [15],

$$Mdif_i = \frac{1}{N-6}\cdot\sum_{n=1}^{N-6}\left(s_i(n)-\sum_{b=n}^{n+5}s(b)\right), \quad (7)$$

where $i = \{\delta, \theta, \alpha, \beta, \gamma\}$.

- E: The Wavelet coefficients energies of δ, θ, α, β and γ were obtained by the following generic equation 8

$$E_i = \sum_{n=1}^{N} s_i(n)^2, \quad (8)$$

where $i = \{\delta, \theta, \alpha, \beta, \gamma\}$.

- r: Three spectral ratios were defined to resume the EEG spectrum deceleration [11, 12, 13]

$$r_1 = \frac{E_\alpha}{E_\theta}, \quad (9)$$

$$r_2 = \frac{E_\alpha + E_\beta + E_\gamma}{E_\delta + E_\theta}, \quad (10)$$

$$r_3 = \frac{E_\beta}{E_\delta}, \quad (11)$$

r_1 is a spectral ratio that enabled us to detect changes when a slight slowdown in the EEG spectrum appears. r_2 is an index that summarized the EEG global slowing. r_3 is an extension of the definition of r_1 to the whole power spectrum.

Finally, all EEG features of all AD patients and control subjects were normalized between 0 to 1.

3. STATISTICAL ANALISYS AND DISCRIMINATIVE RESULTS

The performance of the parameters to discriminate between groups was evaluated by means of a LDA with leave-one-out cross-validation procedure. The classifier ability to discriminate AD patients from control subjects was evaluated using ROC curves [16]. The ROC curve is a graphical representation of the trade-off between sensitivity and specificity [16]. Sensitivity represents the percentage of patients correctly identified, specificity represents the percentage of controls correctly classified and accuracy is the percentage of all study participants correctly identified. The area under ROC curve (AUC) summarized the system performance [16].

The LDA with a leave-one-out cross-validation procedure was done for each of the EEG features previously extracted (view Table 1).

Table 1. Discriminant results of LDA with a leave-one-out cross-validation procedure for each extracted features.

Feature	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC
$NMax_\delta$	85	64	76	0.80
$NMax_\theta$	80	50	62	0.58
$NMax_\alpha$	90	64	79	0.85
$NMax_\beta$	65	93	76	0.74
$NMax_\gamma$	50	86	65	0.54
$NMin_\delta$	85	64	76	0.80
$NMin_\theta$	80	50	62	0.64
$NMin_\alpha$	95	57	79	0.85
$NMin_\beta$	65	93	76	0.74
$NMin_\gamma$	65	50	59	0.53
Zcr_δ	85	71	79	0.81
Zcr_θ	80	57	62	0.57
Zcr_α	90	64	79	0.86
Zcr_β	65	93	76	0.70
Zcr_γ	50	86	62	0.57
$Mdif_\delta$	90	50	74	0.69
$Mdif_\theta$	80	50	68	0.63
$Mdif_\alpha$	90	56	68	0.62
$Mdif_\beta$	85	79	82	0.83
$Mdif_\gamma$	75	64	71	0.75
E_δ	75	79	77	0.80
E_θ	75	79	67	0.85
E_α	75	71	74	0.78
E_β	65	86	74	0.78
E_γ	75	50	65	0.63
r_1	75	86	79	0.86
r_2	75	93	82	0.88
r_3	70	100	79	0.81

In Table 1 it can be observed that it is in the alpha band that are located more differences between AD patients and

Table 2. Classification results of LDA with a leave-one-out cross-validation procedure for the best features combinations of 2 to 11.

Number of features	Best Features combination	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC
2	r_2,r_1	85.00	57.14	73.53	0.71
3	r_2,r_1, Zcr_α	90.00	71.43	82.35	0.81
4	r_2,r_1, Zcr_α,r_3	90.00	71.43	82.35	0.81
5	r_2,r_1, Zcr_α,r_3, $NMin_\delta$	85.00	71.43	79.41	0.78
6	r_2,r_1, Zcr_α,r_3, $NMin_\delta$, $NMin_\alpha$	90.00	71.43	82.35	0.81
7	r_2,r_1, Zcr_α,r_3, $NMin_\delta$, $NMin_\alpha$, $NMax_\delta$	95.00	85.71	91.18	0.90
8	r_2,r_1, Zcr_α,r_3, $NMin_\delta$, $NMin_\alpha$, $NMax_\delta$, $NMax_\alpha$	95.00	92.86	94.12	0.94
9	**r_2,r_1, Zcr_α,r_3, $NMin_\delta$, $NMin_\alpha$, $NMax_\delta$,$NMax_\alpha$, $Mdif_\beta$**	**95.00**	**100.00**	**97.06**	**0.98**
10	r_2, r_1, Zcr_α, r_3, $NMin_\delta$, $NMin_\alpha$, $NMax_\delta$, $NMax_\alpha$, $Mdif_\beta$, E_θ	95.00	92.86	94.12	0.94
11	r_2, r_1, Zcr_α, r_3, $NMin_\delta$, $NMin_\alpha$, $NMax_\delta$, $NMax_\alpha$, $Mdif_\beta$, E_θ, E_δ	95.00	92.86	94.12	0.94
12	r_2, r_1, Zcr_α, r_3, $NMin_\delta$, $NMin_\alpha$, $NMax_\delta$, $NMax_\alpha$, $Mdif_\beta$, E_θ, E_δ, $Mdif_\delta$	95.00	85.71	91.18	0.90

control subjects because this band provided features that have a slightly higher discriminant power than the other EEG convencional bands (for instance, better AUC results). This fact can be explained by the "shift to the left" phenomenon. One possible hypothesis to explain the concept of "EEG slowing" involves a loss of the acetylcholine neurotransmitter [5].

As in a previous work [10], with a different EEG processing technique, the spectral ratios provided good AUC results. In this study, r_2 offered the best individual AUC classification parameter. However, unlike previous studies, in present one ROC classification results with a high specificity in beta and gamma bands were obtained. It is the case of parameters $NMax_\beta$, $NMax_\gamma$, $NMin_\beta$, Zcr_γ and Zcr_β. One possible explanation for this is that in previous works the EEG spectrum was restricted between 1 and 40Hz and so the beta and gama bands were not accurately compared to the other EEG convencional bands. So, in this work, beta and gama bands provided features that allow to identify more precisely control subjects than in those previous works [10, 11, 12].

Finally, a LDA with a leave-one-out cross-validation procedure was performed to assess the combination of features which reached the best classification performance. Table 2 shows the classification results for the best features combinations of 2 to 11. The best features combinations were obtained by a forward process of feature selection with the Mahalanobis distance criterium. It can be seen that the best combinations of 2 to 11 were composed by the features that showed the best individual feature classification AUC results (view Table 1). The features combination of 9 provided the best results, 95.00% of sensitivity, 100.00% of specificity, 97.06% of accuracy and 0.98 of AUC.

4. CONCLUSIONS

The increasing incidence of AD is a fact more and more common in developed countries and so they have to optimize urgently all means of AD detection and treatment. In this study, were evaluated the individual and combined power of several EEG features in order to discriminate AD patients from control subjects. For this purpose, the WT was used to process the EEG signals and 28 features were extracted.

Table 3 summarizes the classification statistics obtained in some review studies that used leave-one-out cross-validation procedure to discriminate AD patients from control subjects. In short, we could say that our results were in line (sometimes they overcome) with the results achieved by other studies. Like Petrosian *et al.* [17] and Melissant *et al.* [18] studies, we find 100% of specificity, which means that our classifier identified correctly all the health subject. Concerning the accuracy and specificity, our classifier provided better results than the other previous review studies.

Table 3. Classification results of some review studies that used leave-one-out cross-validation procedure in AD classification.

Author	Sensitivity (%)	Specificity (%)	Accuracy (%)
Huang *et al.* [19]	84	78	81
Petrosian *et al.* [17]	80	100	90
Viallate *et al.* [20]	73	84	78.25
Melissant *et al.* [18]	93	95	94
Melissant *et al.* [18]	64	100	82
Present study	**95**	**100**	**97**

Despite we have obtained good classification results, some limitations for this type of study arise, because we lose some spatial information when we retain only the average measures over the channels. In the future we must have more EEG signals to ensure generalization. It should also be mentioned that the detected increase of EEG regularity is not specific to AD, it appears in others dementias including Parkinson's disease, epilepsy, vascular dementia and schizophrenia [5]. So, further works must be carried out with patients suffering from other neurodegenerative diseases.

5. ACKNOWLEDGMENTS

We would like to thank to the Biomedical Engineering Group - University of Valladolid (Spain) for their support during the work.

6. REFERENCES

[1] T.D. Bird, *Harrison's Principles of Internal Medicine*, chapter Alzheimer's disease and other primary dementias, pp. 2391–2399, McGraw-Hill, 2001.

[2] R. Mayeux, "Epidemiology of neurodegeneration," *Annual Review of Neuroscience*, vol. 26, pp. 81–104, 2003.

[3] C. Ballard, S. Gauthier, A. Corbett, C. Brayne, D. Aarsland, and E. Jones, "Alzheimer's disease," *The Lancet*, vol. 377, pp. 1019–1031, 2011.

[4] G. Waldemar, "Recommendations for the diagnosis and management of alzheimer's disease and other disorders associated with dementia," *EFNS European Journal of Neurology*, vol. 14, pp. 1–26, 2007.

[5] J. Jeong, "EEG dynamics in patients with alzheimer's disease," *Clinical Neurophysiology*, vol. 115, pp. 1490–1505, 2004.

[6] M. Gawel, E. Szmidt-Salkowska, and J. Kowalski, "The value of quantitative eeg in differential diagnosis of alzheimer's disease subcortical vascular dementia," *Journal of Neurology Science*, vol. 283, pp. 127–133, 2009.

[7] S. Sanei and J. Chambers, *EEG signal processing*, Wiley-Interscience, 2007.

[8] O. Rioul and M. Vetterli, "Wavelets and signal processing," *IEEE Signal Processing Magazine*, vol. 8, pp. 14–38, 1992.

[9] S. Haykin and B. V. Veen, *Signals and Systems*, John Wiley & Sons, 2003.

[10] P. M. Rodrigues, "Diagnóstico da doença de alzheimer com base no electroencefalograma," M.S. thesis, Instituto Politénico de Bragança - Escola Superior de Tecnologia e Gestão, 2011.

[11] P. Rodrigues and J.P. Teixeira, "Artificial neural networks in the discrimination of alzheimer's disease," *Communications in Computer and Information Science*, vol. 221, pp. 272–281, 2011.

[12] P. M. Rodrigues and J. P. Teixeira, *Information Systems and Technologies for Enhancing Health and Social Care*, chapter 7 - Alzheimer's Disease Recognition with Artificial Neural Networks, pp. 102–118, IGI Global, 2013.

[13] P. M. Rodrigues, D. Freitas, and J. P. Teixeira, "Alzheimer electroencephalogram temporal events detection by k-means," *Procedia Technology*, vol. 5, pp. 859–864, 2012.

[14] C. H. Chen, *Signal processing handbook*, Dekker, 1988.

[15] T. M. Apostol, *Calculus*, Editora reverté, 1998.

[16] C. Williams, S. Lee, R. Fisher, and L Dickerman, "A comparison of statistical methods for prenatal screening for down syndrome," *Applied Stochastic Models in Business and Industry*, vol. 15, pp. 89–101, 1999.

[17] A.A. Petrosian, D.V. Prokhorov, W. Lajara-Nanson, and R.B. Schiffer, "Recurrent neural network-based approach for early recognition of alzheimer's disease in eeg," *Clinical Neurophysiology*, vol. 112, pp. 1378–1387, 2001.

[18] C. Melissant, A. Ypma, E. Frietman, and C. Stam, "A method for detection of alzheimer's disease using ica-enhanced eeg measurements," *Artificial Intelligence in Medicine*, vol. 33, pp. 209–222, 2005.

[19] C. Huang, L. Wahlund, T. Dierks, P. Julin, B. Winblad, and V. Jelic, "Discrimination of alzheimer's disease and mild cognitive impairment by equivalent eeg sources: a cross-sectional and longitudinal study," *Clinical Neurophysiology*, vol. 111, pp. 1961–1967, 2000.

[20] F. Vialatte, A. Cichocki, G. Dreyfus, T. Musha, S.L. Shishkin, and R. Gervais, "Early detection of alzheimer's disease by blind source separation, time frequency representation, and bump modeling of eeg signals," *Lecture Notes in Computer Science*, vol. 3696, pp. 683–692, 2005.