Time delay autocorrelation analysis of EEG time series for the patients of early mild Alzheimer's disease

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Abstract: In this report, we applied non-linear time series modeling techniques to analyze the EEG time series for early Alzheimer's disease collected from the Kaohsiung Armed Forces General Hospital. Our study has revealed that electroencephalogram (EEG) signals in Alzheimer's disease (AD) patients is more chaotic than those of healthy subjects. The EEG measurements were approved by local IRB in June of the year of 2016. 25 subjects were collected and the changes in EEG signals start at early stage were found for five subjects specifically. To detect this changes, cross correlation of the EEG series modified with different delay time were applied to the 5 patients of mild AD and 60 healthy subjects. We have compared the right and left temporal lobes of the brain with the rest of the brain areas including frontal, central, and occipital as temporal regions are relatively the ones being affected by the neuron-pathogen of AD. At the end, all the data are assessed by statistical analysis.
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Introduction

EEG signals are functional time series to evaluate cognitive disturbances. It can be used as a clinical diagnostic tool. A great deal of research has already been conducted to detect the chaotic characteristics in EEG signals [1]. Alteration of the rhythm abnormality in EEG signals of AD [2] have shown a decrease of alpha power and an increase of theta (4–8Hz) power in corticocortical and subcortical parts of the brain [3]. Babiloni et al. [4] claimed that the reduction of the chaotic occurs both at interhemispherical (delta-beta2) and frontoparietal (delta-gamma) electrode for AD patients. Topographically analyzing the EEG signals, Hogan et al. [5] reported more chaotic evidence of upper alpha band between central and temporal cortices for the healthy subjects than early mild AD patients. The rhythm abnormality of autocorrelation 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 [6]. The concept of power spectral density analysis method is used to analyze the rhythm abnormality between pairs of signals and entire EEG channels at the same time respectively [97. Further study is still necessary to analyze the rhythm abnormality of brain [9]. Any disturbance in the brain, caused by a disease or any other infection, can highly affect the chaotic characteristics of brain. The previous reports indicated that chaotic characteristics exist in the EEG time series system. It is an interesting issue to find a technique based on phase space dynamics used to analyze and predict the source of the EEG signal perturbation of mild early AD. As EEG data is highly nonlinear and also varies with delay time [8-14]. It may change abruptly when entering the perturbation of pathogen signal. Therefore, EEG time series system is a complex entity. Here we explored the ability of a multitude of linear and non-linear autocorrelations at different delay times to discriminate between the EEGs of patients with mild early degree of AD and healthy control subjects. The EEG channels and their proper function are critical for acquiring high quality data for interpretation. As it is known from tomography, different brain areas should be related to different functions of the brain. Each channel is located near certain brain control areas, such as F7 is located the area for rational activities as well as intentional and motivational areas, F8 is located to sources of emotional impulses. Cortex around C3 and C4 are to deal with sensory and motor functions. P3 and P4 are located to contribute the activity of perception and differentiation. Near T3 and T4 emotional processors are located. At T5 and T6 are located for certain memory functions. Primary visual areas can be found bellow points O1 and O2 [15]. In

this study, we choice the observations in T5 channel to check the difference of correlation distribution between healthy subjects and AD patients.

Methods

Subjects

Twenty-five subjects including 5 patients diagnosed with early probable AD agreed to participate this study. Patients had been referred to the outpatient memory clinics of the Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan, ROC. Control subjects were recruited through web news. All subjects underwent general medical and questionnaire investigations as part of the standard diagnostic of dementia. The study was approved by the Institution Review Board in Kaohsiung Armed Forces General Hospital. Written informed consent was obtained from all subjects.

EEG Clinics

EEGs were recorded using a Nihon Kohden apparatus with 16 Ag electrodes placed according to the 10/20 system shown in Figure 1. The EEG was band-pass filtered from 0.16 to 70 Hz for display and analysis. EEG recorded at channel of T5 for an early AD patient and a healthy subject are shown in Figure 2.

EEG Analysis Algorithm

In Table I, it is listed the function of the brain versus EEG channels. In this study, we calculated the delay time τ determined under the criteria of $\frac{R(\tau)}{R(0)} \approx 1$ for EEG signals in channel T5 near the memory functions of brain, in which we can realize the variance of the auto correlation in a specific EEG channel between the AD patients and healthy subjects.

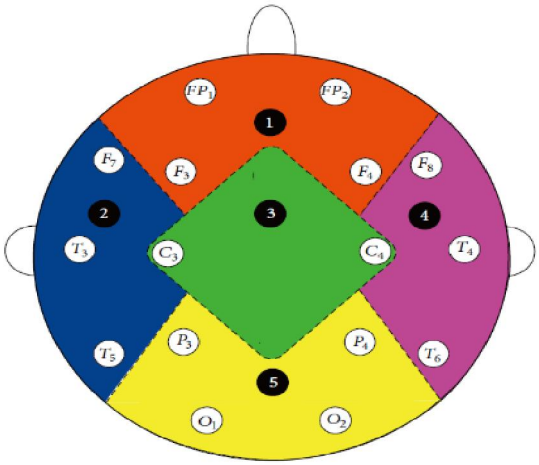
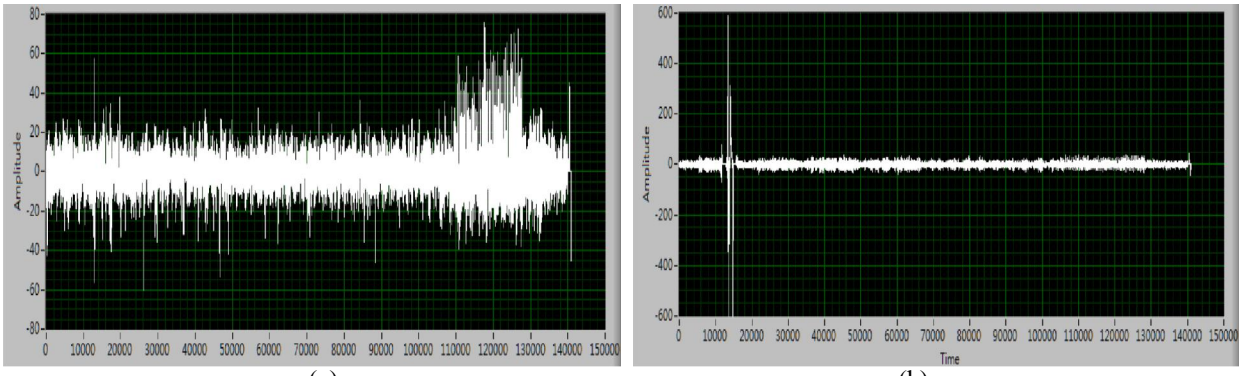


Figure 1: The 16 channels used for EEG recording [15]



(a) (b)

Figure 2: EEG recorded at channel of T5 for (a) an early AD patient and (b) a healthy subject

Table I The function of the brain correlated with the EEG channels

EEG Channel	Functions of the Brain
C3 and C4	Sensory and motor functions
P3 and P4	Perception and differentiation
T3 and T4	Emotional processors
T5 and T6	Memory functions
F7	Rational activities
F8	Emotional impulses
O1and O2	Primary visual areas

Results and Discussions

As the EEG observations are affected by the phase delay time τ of pathogen signal of AD, we could use it to determine $A_{i,n}^{d,\tau} = \frac{|X_{i+d\tau} - X_{n+d\tau}|}{|X_i - X_n|}$ to identify the early AD patients and normal subjects if the $A_{i,n}^{d,\tau}$ is clinically confined. The calculated d values are listed on Table II. Basically, d is used to determin how chaotic signal is [17], therefore, the

relationship between d and $A_{i,n}^{d,\tau}$ for AD patients as welll as normal subjects thus can show the chaotic characteristic of the EEG observations. Some previous researches reported that EEG signal of early AD patients was found leass chaotic than normal [16]. Inthis report, we specifically reveal d in EEG at T5 as a marker to identify early AD patients. Further studies are necessary to investigate the clinical meaning of $A_{i,n}^{d,\tau}$ and the phase delay when a neuron is pulled the trigger shown in EEG received at T5 channel or other channels.

Table II Calculated values of $A_{i,n}^{d,\tau}$ for AD patients and normal subjects ($p<0.001$)

	$A_{1,2}^{1,9772} = \frac{\lvert X_{9773} - X_{9774}\rvert}{\lvert X_1 - X_2\rvert}$	$A_{1,2}^{2,9772} = \frac{\lvert X_{19545} - X_{19546}\rvert}{\lvert X_1 - X_2\rvert}$
Early AD patients	1.53	1.66
Health subjects	0.99	0.98

Conclusion

This study is based upon EEG Chaos study through the calculation of $A_{i,n}^{d,\tau}$ to check the rhythm evoked potentials in EEG T5 for AD patients and health subjects. Software algorithm, mathematical model and causal analysis applied to the diagnosis of early mild AD are expected for further study.

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