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Research Article

Solving Reality Problems by Using Mutual Information Analysis

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Cross-mutual information (CMI) can calculate to time series for thousands of sampled points from corticocortical connection among different functional states of brain in Alzheimer's disease (AD) patients. The aim of this study was to use mutual information analysis in the multichannel EEG to predict the probability of AD disease. Considering the correlation between AD disease and ageing effect, the participants were 9 AD patients and 45 normal cases involving teenagers, young people and elders. This data revealed that both right frontal and temporo-parietal are differences between normal and AD participants. Besides, this study found the theta band is the main frequency to separate AD patients from all participants. Furthermore, this study suggested a higher distinguishable method by mutual information to predict the possibility AD patients.

1. Introduction

Alzheimer's disease (AD) is one of the most prevalent neurodegenerative diseases in recent years [1]. In 2000, there were 7.6 million people being reported as Alzheimer's disease (AD) in Europe [2], and there were 26.6 million cases of AD worldwide in 2006. It has been forecasted that AD will be 106.8 million in 2050 [3]. Therefore, predicting which individuals will progress as an AD patient is an important issue in clinical diagnosis and researches [4]. However, the rate of correctly identified AD cases in early AD stages only within a range between 29% and 42% by electrophysiological methods [5]. Two approaches to estimate AD disease are generally accepted: one is temporal resolution such as Event-Related Potentials (ERPs), and another is spatial resolution such as Functional Magnetic Resonance Imaging (fMRI) [6].

Many studies addressed that ERPs is the more reliable and sensitive method to diagnose AD disease [3, 4]. They also advised different ERPs components to diagnose mild AD disease such as P3, CNV, C145, C250, later components and so forth [4]. However, the individual ERPs component can not show the complex mutual connection of each electrode of EEG data. To combine with conventional and quantification of EEG data can enhance the analysis of brain's functional properties [5].

The quantification EEG analysis included linear and nonlinear analysis, several studies indicated the mathematics of nonlinear dynamical systems are advantaged to interpret the dynamic processing of brain work [5], and the other studies concerned the linear calculation of characteristics of EEG data. Na et al. [7] mentioned that cross mutual information does not matter if the signal is chaotic or not, it just calculate to time series for thousands of sampled points from different functional states of brain. Jeong et al. [8] also indicated that cross mutual information is a good way to assess the cortico-cortical connection between different cortical areas in AD patients. Hence, the main purpose of this study was to use mutual information analysis in the multichannel EEG to assess the cross-interaction of information between each electrode of AD patients and normal cases.

According to the quantitative ERPs analysis, auditory oddball might be a useful way to predict the conversion of AD, because the task spent a few time to collect EEG of AD patients, and it is simple but more accurate to know the brain work [9]. Therefore, this study used pure auditory of ERPs to elicit participants' response, and this study wanted

to establish a higher distinguishable method to predict the possibility AD patients.

2. Methods

2.1. Subjects. In this study, the data of subjects are the reality brain wave from human beings. There are 54 volunteers who participated in this research including normal and AD patients. AD disease is a continuous progressive degenerative disease, and it might be started in healthy young individuals and developed into a terminal stage of AD disease in elder [6]. Hence, this study collected the normal cases involving teenagers ($N = 28$, age: 17.5 ± 0.8), young people ($N = 13$, age: 21.7 ± 0.9), and elder ($N = 4$, age: 81.8 ± 7.3). Besides, this study collected the AD patients ($N = 9$, age: 80.7 ± 9.5) identified by doctor of Kaohsiung Veterans General Hospital.

None of the participants reported hearing loss or psychological diseases, and all were naive to electrophysiological studies. All participants gave informed consents and need to join the diagnosis of three tests included minimental state examination (MMSE), clinical dementia rating (CDR) and cognitive abilities screening instrument (CASI). In EEG data, the average accuracy rate of normal cases is 98% and of the AD cases is 92.8%. That means all participants can response to the tasks well. In normal group ($N = 45$), the average MMSE scores are 30 (SD = 0), the average CASI scores are 100 (SD = 0), and the CDR scores estimated as "normal". In AD group, the average MMSE scores are 16.9 (SD = 6.7), the CASI scores are 57.7 (SD = 19.4), and the CDR scores are 1.3 (SD = 0.7).

2.2. Data Acquisition. The auditory oddball was presented to two pure auditory: one was 2000 Hz, and the other was 1000 Hz that occurred regularly with a 0.20 probability. The participants need to press the response button when they heard the 1000 Hz sound, but no response is required when hearing the 2000 Hz sound.

EEG was recorded with the SynAmps/SCAN 4.4 hardware and software (NeuroScan, Inc., Herndon, VA) from 32 tin electrodes mounted in a commercial electrocap (Electro-Cap International, Eaton, OH), and electrode impedance was always kept below 5 kΩ. The common reference electrode for EEG measurements was placed on the mastoids behind the ears. Stimulus presentation was generated by Neuroscan Stim 3.3 Software. EEG channels were continuously digitized at a rate of 10000 Hz by a SynAmpTM amplifier. The signal was analog filtered (0.1–200 Hz), and A/D converted with a sampling rate of 10000 Hz and 14 bit precision and digitally filtered in the range 0.1–50 Hz. The EEG was segmented into 2048 ms epochs. Sweeps exceeding +/−80 μV were excluded by automatic artifact rejection, which was followed by visual artifact screening.

2.3. Data Analyses. EEG cross mutual information analysis was performed in the following frequency bands: delta band (1–4 Hz), alpha band (7–13 Hz), beta band (13–25 Hz), and gamma band (25–50 Hz) and was defined as (Jeong et al., 2001 [8])

$$I_{XY_\tau} = \sum_{x(t),y(t+\tau)} P_{XY_\tau}\left(x(t), y(t+\tau)\right) \times \log_2 \frac{P_{XY_\tau}\left(x(t), y(t+\tau)\right)}{P_X\left(x(t)\right) P_{Y_\tau}\left(y(t+\tau)\right)}. \quad (1)$$

The cross mutual information I_{XY_τ} is between time serials data $x(t)$ and $y(t+\tau)$. The τ of y function is timedelayed. $P_X(x(t))$, $P_{Y_\tau}(y(t+\tau))$, and $P_{XY_\tau}(x(t), y(t+\tau))$ are the normalized histogram of the distribution of values observed for the measurement $x(t)$ and $y(t+\tau)$. Based on the theory, this study analyzed all electrodes by mutual information methods from all participants, which involved the mean values between electrodes located over frontal and anterotemporal, temporal, parietal, and occipital regions. Also, this study calculated between the pairs of electrodes across the central line. Time serials data is 6000 data points, and sampling frequency is 1000 Hz (the average time delays of $\tau = 3$).

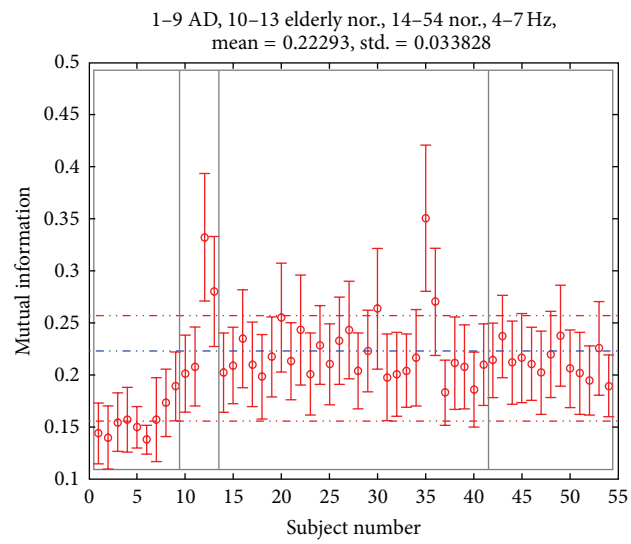

Figure 1: The theta band of right frontal and temporo-parietal area by cross mutual information analysis.

3. Results and Discussion

3.1. Analysis on Right Frontal and Temporoparietal. This study calculated the average cross mutual information of all normal participants. In addition, this study analyzed all electrodes by mutual information methods from all participants, which involved the mean values between electrodes located over frontal and anterotemporal, temporal, parietal, and occipital regions. Previous studies supported that EEG data which collected information from cortex is validity and sensitivity to predict the attention and semantic memory differences between normal and AD patients by using different instruments.

In this study, Figure 1 presented that the average cross mutual information is about 0.225, and all normal cases'

mutual information analyses are located within 2 times of standard deviation. But 78.8% AD cases' mutual information analyses are located without 2 times of standard deviation. The results showed that theta bands (4–7 Hz) of right frontal and temporo-parietal are higher differentiate from normal and AD cases. In other words, this study increased the percentage of AD predictability by analyzing the EEG data with cross mutual information.

Khachaturian [10] mentioned that number of neurofibrillary tangles (NFT) in brain regions could be a definite diagnosis in AD disease. Almkvist [6] also indicated that the first clinical stage of AD could be defined by NFT in the cortex. These studies supported that EEG data which collected information from cortex is validity and sensitivity. Almkvist's review paper mentioned that the medial temporal lobe could show the differences between normal and AD cases with NFT analysis. Then, Johannsen et al. [11] using Positron Emission Tomography (PET) to investigate sustained attention of AD patients which indicated the right middle frontal gyrus showed significant differences between normal and AD cases. To sum up, the right medial temporal lobe and the right and inferior frontal and the temporo-parietal regions are important factors to predict the attention and semantic memory differences between normal and AD cases by using different instruments.

In this study, we found both right frontal and temporo-parietal are higher differences than other brain areas between normal and AD cases, especially in F4 and CP3 electrodes. In other words, the results of this study contained a lot of important predictable factors of attention and semantic memory about AD disease.

3.2. Analysis on Theta Band. This paper analyzed different frequency included delta band (1–4 Hz), theta band (4–7 Hz), alpha band (7–13 Hz), beta band (13–25 Hz), and gamma band (25–50 Hz). The results revealed that theta band (4–7 Hz) of F4 and CP3 electrodes are higher differentiate from normal and AD cases. Although this study analyzed by 1–50 frequency band, delta band (1–4 Hz), alpha band (7–13 Hz), beta band (13–25 Hz), and gamma band (25–50 Hz), there are no significant differences on normal and AD cases. The results of this study showed that theta band is the main frequency to separate AD cases from all participants. Scheeringa et al. [12] mentioned that frontal theta activity is less pronounced than the alpha activity. But frontal theta power has been reported for increasing with working memory loading [13, 14].

4. Conclusion

The findings of this study support a lot of important predictable factors of attention and semantic memory about AD disease. Moreover, this study increased the percentage of AD predictability by analyzing the EEG data with cross mutual information.

The results showed that AD patients eliminate from 2 times standard deviation of average by calculating EEG theta power of normal participants in right frontal and temporo-parietal area by cross mutual information analysis. Frontal theta power has been reported for increasing with working memory loading [13, 14]. Nevertheless, Scheeringa et al. [12] mentioned that frontal theta activity is less pronounced than the alpha activity. This study preferred finding both right frontal and temporo-parietal are higher differences than other brain areas between normal and AD cases more accurate. This study supposed that in auditory oddball task testing, participants need to expend working memory loading to remember the different sounds and pay attention to response to different stimuli to induce participants' EEG.

The implication of this study is to prove that the reality nonlinear problems such as brain waves could be solved by using mathematical analysis such as mutual information. Furthermore, these mathematical analyses could provide predictions of the reality of AD disease.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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