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DCCA cross-correlation coefficients reveals the change of both synchronization and oscillation in EEG of Alzheimer disease patients

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HIGHLIGHTS

- DCCA cross-correlation coefficient was applied to analyze EEG signals.
- Comparing to healthy controls, AD patients has a lower DCCA coefficient, and a higher max-correlation scale.
- DCCA coefficient reveals the change of both oscillation and synchrony in AD.
- DCCA coefficient is a powerful tool to differentiate AD patients from healthy elderly individuals.

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ABSTRACT

Alzheimer's disease (AD) is a degenerative disorder of neural system that affects mainly the older population. Recently, many researches show that the EEG of AD patients can be characterized by EEG slowing, enhanced complexity of the EEG signals, and EEG synchrony. In order to examine the neural synchrony at multi scales, and to find a biomarker that help detecting AD in diagnosis, detrended cross-correlation analysis (DCCA) of EEG signals is applied in this paper. Several parameters, namely DCCA coefficients in the whole brain, DCCA coefficients at a specific scale, maximum DCCA coefficient over the span of all time scales and the corresponding scale of such coefficients, were extracted to examine the synchronization, respectively. The results show that DCCA coefficients have a trend of increase as scale increases, and decreases as electrode distance increases. Comparing DCCA coefficients in AD patients with healthy controls, a decrease of synchronization in the whole brain, and a bigger scale corresponding to maximum correlation is discovered in AD patients. The change of max-correlation scale may relate to the slowing of oscillatory activities. Linear combination of max DCCA coefficient and max-correlation scale reaches a classification accuracy of 90%. From the above results, it is reasonable to conclude that DCCA coefficient reveals the change of both oscillation and synchrony in AD, and thus is a powerful tool to differentiate AD patients from healthy elderly individuals.

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1. Introduction

Alzheimer's disease (AD) is a degenerative disorder of neural system that affects mainly senior individuals over the age of 70. It is estimated that the prevalence of the disease is increasingly spreading over the younger population in China. As a progressive disorder, all of the present-day treatments remain palliative. Timely diagnosis of AD is critical for curing and delaying symptoms. Especially, early diagnosis of AD allows prompt treatment where the medication is most effective [1]. Although histologic confirmation is the only way to make definite diagnosis of AD [2], An increasing number of researchers are actively involved in seeking for a biomarker that can distinguish AD patients from the age-matched healthy participants.

The characteristic neuropathology of AD reveals the existence of β-amyloid peptides in neuritic plaques, which contribute to the loss of neuronal cells and synapses, and hence induced cognitive impairment [2,3]. The loss of neuronal cells and synapses would change the patterns of local field potentials (LEP), which hence influence electroencephalograms (EEG). Since EEG is inexpensive, (potentially) portable, noninvasive and high resolution in time domain, several research groups have started to look into the potential role of EEG in AD diagnosis over the past few years, and found three major EEG characteristics in AD patients: EEG slowing, enhanced complexity of the EEG signals, and perturbations in EEG synchrony [2].

To date, numerous studies have reported the fluctuations in EEG synchrony. And a large variety of measures has been proposed to quantify EEG synchrony, in time or in frequency domains. Most of these measures showed a decrease in AD EEG coherence in different cortical regions of AD patients [2], but the detailed results are different and seem to capture a specific kind of interdependence. For instance, Koenig et al. found global field synchronization decreased in Alpha, Beta, and Gamma frequency bands, and increased in the Delta band [4]. The synchronization likelihood of AD patients significantly decreased in the upper alpha (10–12) and beta (12–30) bands [5], in fronto-parietal and inter-hemispherical regions [6]. Coherence studies showed a significant decrease in AD patients between central and right temporal electrodes [7] and in the fronto-parietal regions [8]. Cross-correlation analysis showed decrease in EEG synchrony of AD patients as compared to healthy subjects [9,10]. Dauwels et al. examined the performance of various synchrony measures in diagnosis AD, and they found the results generated are much alike regardless of the specific measures applied [2]. These studies only measured the synchrony at a single scale, did not, however, expand to multi scale measurements. EEG signals are usually characterized by multi-scale structures and non-stationarities. From this aspect, traditional synchronization analysis may not be suitable for EEG signals and if applied can generate erroneous results. On the other hand, according to many cross-correlation studies, the measure of cross-correlation would change as the scale evolves [11]. Therefore, Choosing appropriate scale may improve the sensitivity for detecting AD from EEG.

In 2011, Zebende used a cross-correlation coefficient to quantify the level of long-range cross-correlation [12]. This method was based on detrended fluctuation analysis (DFA), a method measuring the long-range correlation in a single time series, and detrended cross-correlation analysis (DCCA), a method extending DFA to measure the long-range cross correlation in two time series [13]. Because these two measures examined the correlation in multi-scales, the scale of correlation analysis was extended. Delignières and Marmelat used windowed detrended cross-correlation coefficients to improve the measure of signal coherence [14]. As indicated by Kristoufek, DCCA coefficient is able to estimate the true correlation coefficient between series precisely regardless the non-stationarity strength [15]. Even though the performance varies with some of the parameters, DCCA coefficient remains a very promising tool for measuring the dependence between non-stationary series [15]. Recently, DCCA and its revised version [11–17] has been applied to measure financial time series [18–27], meteorological time series [28,29], human behavior data [14], EEG signals [28], seismic data [30], traffic flows [31], and geophysical systems [32]. Balocchi et al. provided proof for applying DCCA in EEG analysis [28]. They found that DCCA coefficient start from a value above zero and increase up to near 1, suggesting the presence of both short- and long-range cross correlation. However, they applied DCCA analysis only to a single EEG sample, not to any disorder. Whether DCCA cross-correlation coefficient can be used to distinguish the EEG signals of AD patients from that of the normal controls, or reflect other additional information of AD patients, are still unclear.

In order to explore this problem, in this paper, we apply multi-scale cross correlation analysis to EEG, and detect the abnormalities of EEG signals in AD patients through DCCA cross-correlation coefficients. Our aim is to examine the effect of scale variation on EEG synchrony, of both AD patients and control subjects, and to improve the performance of correlation measure in diagnosis AD. A major hypothesis is that the correlation (synchronization) will change as scale changes. Based on this hypothesis, we extract DCCA cross-correlation coefficients at each timescale and examine their performance in detecting AD patients from the health controls. Accordingly, the subsequent parts of this paper are organized as follows: in Section 2, we give a description of the experiments, including the information of subjects, the EEG data recording and preprocessing; in Section 3, we introduce DCCA approach, and explain the statistical analysis in detail; in Section 4, analysis results of the two groups (AD patients and health controls) are presented; In Section 5, Discussion and Conclusion are given.

2. Experiment design and EEG recording

Experiments were performed upon two groups of subjects: AD group and control group. The AD group included 15 right-handed patients (age: 72–78 years old; eight females and seven males) with a diagnosis of probable AD according to NINCDS-ADRDA [33] and DSM-IV criteria. The symptom severity was assessed using the Mini-Mental Status Examination (MMSE) [34]. The MMSE scores ranged from 12.5 to 15.7, which indicated a severe cognitive impairment. In addition, neuroimaging diagnostic procedures (CT or MRI) and complete laboratory analyses were carried out to exclude other causes