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Functional brain networks in Alzheimer's disease: EEG analysis based on limited penetrable visibility graph and phase space method

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HIGHLIGHTS

- Complex network theory is applied to EEG series to study nonlinear characteristic.
- Functional brain connectivity is constructed from clustering coefficient sequences.
- Effective techniques are developed to explore features of functional brain network.
- The abnormalities of brain connectivity are investigated from AD patients.

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ABSTRACT

In this paper, EEG series are applied to construct functional connections with the correlation between different regions in order to investigate the nonlinear characteristic and the cognitive function of the brain with Alzheimer's disease (AD). First, limited penetrable visibility graph (LPVG) and phase space method map single EEG series into networks, and investigate the underlying chaotic system dynamics of AD brain. Topological properties of the networks are extracted, such as average path length and clustering coefficient. It is found that the network topology of AD in several local brain regions are different from that of the control group with no statistically significant difference existing all over the brain. Furthermore, in order to detect the abnormality of AD brain as a whole, functional connections among different brain regions are reconstructed based on similarity of clustering coefficient sequence (CCSS) of EEG series in the four frequency bands (delta, theta, alpha, and beta), which exhibit obvious small-world properties. Graph analysis demonstrates that for both methodologies, the functional connections between regions of AD brain decrease, particularly in the alpha frequency band. AD causes the graph index complexity of the functional network decreased, the small-world properties weakened, and the vulnerability increased. The obtained results show that the brain functional network constructed by LPVG and phase space method might be more effective to distinguish AD from the normal control than the analysis of single series, which is helpful for revealing the underlying pathological mechanism of the disease.

1. Introduction

Alzheimer's disease (AD), the most prevalent form of neuropathology leading to dementia, is a progressive, disabling neuro-degenerative disorder that affects mainly older person. Experimental studies show that it may be caused by the

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degeneration of synapses and death of neurons in the brain regions, such as hippocampus, entorhinal cortex, neocortex. It usually results in a loss in cognition, memory, judgment, even language and functional skills [1,2]. Although AD clinical diagnosis is achieved only by necropsy the symptoms in early state are easily neglected as normal consequences of aging [3], discriminating AD patients from the normal should be attempted. Electroencephalograph (EEG) could characterize the cerebral cortex electrical information directly by recording multi-channel neural electrical signals in different cortex areas of the brain simultaneously, so that to reflect the brain functions [4].

Nowadays, EEG has been widely used to detect the structural and functional abnormality of AD brain due to its high temporal resolution, non-invasion and relatively low cost as compared with imaging tools [5,6]. Such abnormalities are reported as the slowing of the EEG [7,8], reduction of complexity in EEG [3] and perturbations in EEG synchrony [9]. Therefore, EEG has been extensively used to assess AD in individuals. Jeong et al. [7] have found that the hallmark of EEG abnormalities in AD patients is a shift of the power spectrum to lower frequencies and a decrease in coherence of fast rhythms. Dauwels et al. [3] have further demonstrated that the loss of complexity in AD is strongly related to the slowing of EEG. Additionally, numerous studies have reported that the EEG synchrony is decreased in AD patients, indicating that the information transmission and synergies in different brain regions are decreased [7–9]. It is worth noted that these viewpoints all base on EEG series. Currently, complex network analysis has gained considerable attention and has been proposed to analyze nonlinear dynamics of the time series and capture the dysconnectivity of AD through topological properties of the network mapping from EEG series [10–19]. Several approaches have been proposed for transforming time series into networks. Zhang and Small have constructed complex networks from pseudo-periodic time series, with each cycle represented by a single node in the network, and found that time series with different dynamics exhibit distinct topological network structures [11]. Marwan has introduced the transformation of a time series into a network based on the corresponding recurrence plots [12]. Moreover, by reconstructing phase space to time series and taking each phase space point as a node in the network, Xu et al. have proposed the phase space network (k nearest neighbors) method and transform time series into networks, in which each node is connected with its four nearest neighbors [13]. More recently, Lacasa et al. have presented visibility graph (VG) to convert a time series to a graph, whose structure is related to self-similarity and complexity of the time series [14]. It has been applied in a very broad area covering many topics, such as economics, climatology, physics, biology, neurosciences and so on [15–19]. For instance, Long Yu has applied visibility graph network analysis to the gold price time series to explore the underlying mechanism of the gold price fluctuation from the perspective of complex network theory [18]. Ahmadlou et al. have discovered that the mathematical markers and classification features of AD patients obtained by visibility graph analysis are effective, and a high diagnostic accuracy of 97.7% is obtained [19].

However, the aforementioned complex network analysis is devoted to investigating single time series, and could not provide insight into the biological phenomena due to the degeneration of synapses and death of neurons in AD brain. While brain functional network is thought to provide the physiological basis for information processing and mental representations [20,21], capturing the dysconnectivity of AD through functional network has attracted so much attention and developed rapidly [22–24]. It is extensively reported that AD brain is characterized by the conversion from small-world network architecture to less optimal functional topologies [25,26]. For instance, Stam et al. have identified the disruption of small-world properties of AD brain functional network extracted from EEG and fMRI resting-state data [23,24]. Andrew et al. have further demonstrated that the structural AD brain is "disconnection syndrome" by using graph theoretical techniques and connectivity information derived from anatomical and diffusion-weighted MRI [27]. Tahaei et al. found a decrease in the synchronizability of brain networks across delta, alpha, beta, and gamma EEG frequencies in AD patients [28]. In conclusion there has been a loss of highly connected areas in AD according to findings from functional graphs [29]. However, whether the abnormalities of AD brain could be detected by both local network of specific electrode and global functional network are still unclear.

In order to explore this problem, in this work we investigate the abnormalities of EEG signals from ADs based on limited penetrable visibility graph and phase space network analysis. We first transform each EEG series into complex network by using the two methods, and extract the network topological characteristic to make a primary distinction between AD patients and the controls. We further extract the functional connectivity from the clustering coefficient sequence of visibility graph and phase space networks. And then the graph analysis is applied to the functional connectivity of the two groups and used to investigate the global brain functional network properties. Accordingly, the subsequent parts of this paper are organized as follows: in Section 2, we give a description of the experimental design and the EEG recording, including information of the subjects, the EEG data recording and preprocessing; in Section 3, we introduce the complex network analysis of local brain region: limited penetrable visibility graph and phase space network, the extraction of the global brain functional network and its topological characteristics in detail; in Section 4, analysis results of the two groups are presented; which is followed by discussion and conclusion in Section 5.

2. Experiment design and EEG recording

2.1. Subjects

Experiments were performed in two groups of subjects. (a) 14 right-handed patients with a diagnosis of probable AD (age: 74–78 years old; eight females and six males) according to the international Classification of diseases (ICD-10) of the world health organization and the diagnostic criteria of dementia in the Diagnostic and Statistical Manual of