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Graph theoretical analysis reveals disrupted topological properties of whole brain functional networks in temporal lobe epilepsy

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HIGHLIGHTS

- Graph theory and resting fMRI were used to compare brain networks in temporal lobe epilepsy patients and controls.
- Epilepsy patients showed greater clustering between nodes and longer path length than controls.
- Memory and language nodes were abnormally connected with other nodes in epilepsy.

ABSTRACT

Objective: Temporal lobe epilepsy (TLE) is one of the most common forms of drug-resistant epilepsy. Previous studies have indicated that the TLE-related impairments existed in extensive local functional networks. However, little is known about the alterations in the topological properties of whole brain functional networks.

Method: In this study, we acquired resting-state BOLD-fMRI (rsfMRI) data from 26 TLE patients and 25 healthy controls, constructed their whole brain functional networks, compared the differences in topological parameters between the TLE patients and the controls, and analyzed the correlation between the altered topological properties and the epilepsy duration.

Results: The TLE patients showed significant increases in clustering coefficient and characteristic path length, but significant decrease in global efficiency compared to the controls. We also found altered nodal parameters in several regions in the TLE patients, such as the bilateral angular gyri, left middle temporal gyrus, right hippocampus, triangular part of left inferior frontal gyrus, left inferior parietal but supramarginal and angular gyri, and left parahippocampus gyrus. Further correlation analysis showed that the local efficiency of the TLE patients correlated positively with the epilepsy duration.

Conclusion: Our results indicated the disrupted topological properties of whole brain functional networks in TLE patients.

Significance: Our findings indicated the TLE-related impairments in the whole brain functional networks, which may help us to understand the clinical symptoms of TLE patients and offer a clue for the diagnosis and treatment of the TLE patients.

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1. Introduction

Temporal lobe epilepsy (TLE) is one of the most common forms of drug-resistant epilepsy, in which seizures originate from the temporal lobe and propagate through interconnected brain networks limited to or extending beyond the temporal lobe (Guye et al., 2006). In TLE patients, the normal pattern of brain activity is generally believed to become disturbed, causing strange sensations, emotions, and behaviors (Gupta et al., 2007). With the development of neuroimaging techniques, an increasing number of studies have begun to evaluate the impact of TLE on brain networks (Bernhardt et al., 2012; Bettus et al., 2009; Bonilha et al., 2004; Sidhu et al., 2013).

Resting-state functional magnetic resonance imaging (rsfMRI) has been widely used to explore the intrinsic functional organization of the human brain (Anand et al., 2009; Greicius, 2008; Lynall et al., 2010). Based on rsfMRI data, several studies have revealed the TLE-related alterations in some specific local functional networks, such as the epileptogenic network (Bettus et al., 2009; Morgan et al., 2010), default mode network (DMN) (Liao et al., 2011; Zhang et al., 2010), and functional networks of language (Brazdil et al., 2005), memory (Voets et al., 2009), attention (Zhang et al., 2009b), alertness (Zheng et al., 2012), and perception (Zhang et al., 2009a). For example, Bettus et al. (2009) studied the basal functional connectivity (FC) within the temporal lobe in 11 TLE patients and 26 controls, and detected the decreased basal FC within epileptogenic networks. Zhang et al. (2009b) extracted the dorsal attention network using the independent component analysis (ICA), compared the FC in this network between 24 TLE patients and 24 controls, and found decreased FC in almost all the regions of dorsal attention networks in TLE patients. Actually, the whole brain can be modeled as a large-scale complex network, and its function can be fulfilled through simultaneously segregated or integrated specific FC patterns (He and Evans, 2010; van den Heuvel and Hulshoff Pol, 2010) with optimized efficiency (Bassett and Bullmore, 2006). The investigation of TLE-related alterations in the whole brain functional networks, instead of the FC in specific local networks, may give further network-level information about the pathology of TLE patients.

Graph theory offers a framework to quantify topological properties of a complex network, including the global and nodal properties. The whole brain functional network analysis has been widely used to study human brain development (Bullmore and Sporns, 2009) and to detect alterations of brain function in neuropsychiatry-related brain disorders, such as schizophrenia (Liu et al., 2008), attention-deficit/hyperactivity disorder (Wang et al., 2009b), and Alzheimer's disease (Supekar et al., 2008). For the TLE patients, Liao et al. (2010) studied the brain functional networks alterations using the rsfMRI data, but they mainly focused on the altered interregional FC in TLE patients. Up to now, little is known about the TLE-related alterations in topological properties, especially the topological efficiency, of the whole brain functional networks during resting state. Very few studies reported the relationship between the altered topological properties and an influential factor of epilepsy duration (Akman et al., 2010; Bernhardt et al., 2009; Bartolomei et al., 2013; Edefonti et al., 2011; van Dellen et al., 2009).

With the aim to investigate the TLE-related alterations in network properties, we constructed whole brain functional networks with rsfMRI data for the TLE patients and the controls, and compared their topological properties of the whole brain functional networks using graph theory analysis. In addition, we assessed the relationship between altered topological properties and the duration of epilepsy.

2. Materials and methods

2.1. Participants

Twenty-six TLE patients were recruited from the Guangdong 999 Brain Hospital. All patients underwent a comprehensive clinical evaluation including a careful interview, neurological examination, neuropsychological assessment, and neurophysiological monitoring according to the epilepsy classification of the International League Against Epilepsy ILAE (1989). Specifically, all patients had: (1) symptoms of TLE (such as complex partial seizures) and typical symptoms of TLE (such as abnormal emotional experiences and psychiatric symptoms, including depression, anxiety, confusion, and cognitive dysfunctions with memory and language complaints); (2) standard electroencephalogram (EEG) and video-EEG evaluations that clearly indicated interictal discharges in the unilateral temporal lobe; and (3) MRI manifestation of unilateral hippocampal sclerosis. In order to avoid confounding factors, we also excluded the patients with: (1) a history of neurological or psychiatric disorders other than TLE in this study; (2) mass lesion (tumor, vascular malformation, or malformations of cortical development) or traumatic brain injury; and (3) mismatch between the EEG localization and the clinical evidence. At last, a combination of EEGs and MRI was used to lateralize the focal side. Thus, all patients in this study were divided into two types: left TLE (lTLE) (three females and 10 males, 22.00 ± 5.07 years) and right TLE (rTLE) (five females and eight males, 26.31 ± 10.10 years). At the time of study, patients were on AED treatment with carbamazepine (200 mg/time, twice/day). All patients had discontinued antiepilepsy medication for about 24 h prior to the scans, and no seizure occurred during this period. The halt of medication might avoid or reduce its effects on the brain functions.

We also recruited 25 age- and gender-matched healthy volunteers (eight females and 17 males, 24.24 ± 5.31 years) as the controls from the staff of the Guangzhou 999 Brain Hospital by advertisement. All of the controls were interviewed to confirm that they had no history of neurological or psychiatric disorders or head injuries. Table 1 lists the demographic information of the TLE patients and the controls. All participants were right handed according to their self-report, and written informed consent was obtained from each participant prior to the study. The protocols were approved by the Institutional Review Board of the Guangdong 999 Brain Hospital, Guangzhou, China.

2.2. Data acquisition

MRI data were acquired on a 1.5 T Philips Intera MR scanner with an eight-channel phased array head coil. The rsfMRI data were obtained along the AC-PC plane using a GE-EPI sequence with the following parameters: repetition time (TR) = 3000 ms, echo time (TE) = 50 ms, flip angle (FA) = 90°, field of view (FOV) = 230 × 230 mm, data matrix = 128 × 128, slice thickness = 4.5 mm, gap = 0 mm, 31 interleaved slices covering the brain, and 160 volumes acquired in 8 min. During the scanning, all the participants were instructed to keep their eyes closed and not to think about anything in particular. In addition, we also acquired 3D high-resolution structural images for each subject with a T1-weighted MP-RAGE (magnetization-prepared rapid gradient echo) sequence. The sequence parameters were TR/TE/FA = 25 ms/4.6 ms/30°, data matrix = 256 × 256, FOV = 240 × 240 mm, slice thickness = 1.2 mm, and 140 sagittal slices. For each participant, both the rsfMRI data and the structural images were obtained in the same session.