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Altered characteristic of brain networks in mild cognitive impairment during a selective attention task: An EEG study

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ABSTRACT

The present study evaluated the topological properties of whole brain networks using graph theoretical concepts and investigated the time-evolution characteristic of brain network in mild cognitive impairment patients during a selective attention task. Electroencephalography (EEG) activities were recorded in 10 MCI patients and 17 healthy subjects when they performed a color match task. We calculated the phase synchrony index between each possible pairs of EEG channels in alpha and beta frequency bands and analyzed the local interconnectedness, overall connectedness and small-world characteristic of brain network in different degree for two groups. Relative to healthy normal controls, the properties of cortical networks in MCI patients tend to be a shift of randomization. Lower σ of MCI had suggested that patients had a further loss of small-world attribute both during active and resting states. Our results provide evidence for the functional disconnection of brain regions in MCI. Furthermore, we found the properties of cortical networks could reflect the processing of conflict information in the selective attention task. The human brain tends to be a more regular and efficient neural architecture in the late stage of information processing. In addition, the processing of conflict information needs stronger information integration and transfer between cortical areas.

1. Introduction

Mild cognitive impairment (MCI), characterized by cognitive decline more severe than expected in normal aging, is considered as the preclinical state between normal elderly cognition and dementia (Gauthier et al., 2006; Portet et al., 2006; Winblad et al., 2004). Individuals with MCI often have mild problems performing complex functional activities, and show a fourfold increased risk for the development of Alzheimer's disease (AD) when compared to healthy elderly people (Albert et al., 2011; Petersen, 2004). In recent years, studies in the general population suggest that AD or MCI may be associated with a deficit in selective attention early in the progression of the disease (Baddeley et al., 2001; Belleville et al., 2007; Fernandez-Duque and Black, 2006; Ko et al., 2005; Krinsky-McHale et al., 2008; Pignatti et al., 2005). Selective attention includes the ability to ignore perceptual distracters and the ability to withhold responses to goals. It reflects the top-down control (from frontal and parietal areas) of information processing based on task demands (Booth et al., 2005; Bressler et al., 2008; Geerligs et al., 2014). Furthermore, this modulation processing relies on long-range inputs from and interactions with a network of multiple regions (Gazzaley and Nobre, 2012; Zhang et al., 2014). In addition, the functional disconnection of brain regions in MCI and AD has been proved by many studies (Bai et al., 2008; Greicius et al., 2004; Jiang et al., 2014; Liu et al., 2012; Rombouts et al., 2005).

In recent years, the complex network analysis based on graph theoretical approaches has brought a method with a number of neurobiological meaningful and easily computable measures to the investigation of brain functional networks (Bullmore and Sporns, 2009; Deuker et al., 2009; He et al., 2007; Stam et al., 2007a, 2007b). An ordered network has a high clustering coefficient C (a measure that depicts the connectedness of immediate neighbors around individual vertices) and a long characteristic path length L (an index reflecting the overall integration of the network). In contrast, randomly organized networks are characterized by a low C and a short L. The small-world network, characterized by a high degree of clustering and short path length linking individual network nodes, has been an attractive model for the description of complex brain networks (Achard and Bullmore, 2007; Chen et al., 2008; Wu et al., 2012). Researchers found that both the anatomical and functional brain networks are small-world network (Bassett and Bullmore, 2006; Stam et al., 2007a, 2007b). Furthermore, comparisons of topologies between subject populations appear to reveal connectivity abnormalities in neurological and psychiatric disorders. The AD and MCI patients, for example, show abnormal properties of cortical networks and loss of small-world characteristics in recent functional magnetic resonance imaging findings,

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which reported that the local and global functional connectivity disruptions were found in these patients (Liu et al., 2012; Yao et al., 2010). In specific, AD patients showed the longest *L* and the largest *C*, and MCI exhibited intermediate values compared with normal controls. However, the whole-brain functional networks especially their transient activities during selective attention task of MCI are not yet fully understood.

Most studies show that the cortical neural synchronization of oscillations has been used to evaluate the brain functional network (Stam and van Straaten, 2012). And the scalp electroencephalogram (EEG) representing directly the ongoing neural activity, is appropriate for the investigation of networks related to various oscillatory frequency bands. The related studies on brain oscillations have revealed that the alpha and beta oscillation was correlated with cognitive decline (Bian et al., 2014; Jeong, 2004; Uhlhaas and Singer, 2006). The change of neural synchronous oscillation can be estimated with linear measures such as coherence and nonlinear techniques based on phase relationships. Relative to coherence, phase synchronization which overcome the confounding effects of mixing amplitude and phase and refers to the interdependence between the instantaneous phases of two EEG signals and, has been interpreted as a susceptive method to measure functional synchronization of EEG data (Basar et al., 2010; Bressler and Menon, 2010; Sun and Small, 2009). Related studies demonstrated a general decrease of phase synchrony in correlation with cognitive decline and AD (Knyazeva et al., 2010; Koenig et al., 2005). Compared with age matched control subjects, MCI and AD patients showed decreased global phase EEG synchrony values in alpha, beta, and gamma frequency bands, and increased global phase EEG synchrony values in the delta band in resting condition (Koenig et al., 2005; Park et al., 2008). In graph theory analysis, the brain function connectivity network can be constructed using the interaction between signals of all pair-wise combinations of the channels, such as correlation coefficients (Ahmadlou et al., 2014) and synchronization likelihood (Ponten et al., 2007). The phase synchronization analysis, which can separate the phase component from the amplitude component, is considered to be a valid method to construct and evaluate the graph parameters in specific oscillatory frequency bands (Wang et al., 2012; Wu et al., 2012).

In this study, we used phase synchronization index to measure the cortical neural synchronization of oscillations in alpha and beta bands and construct the brain functional networks for MCI patients and healthy controls. Then, the graph theoretical analysis was applied to study the network characteristics in different information process. Our hypotheses were as follows: (1) the small-world characteristic in patients with MCI was lost. (2) In a selective attention task, MCI patients had different network parameters compared with normal controls.

2. Methods

2.1. Participants

All the subjects were recruited from community by Xuanwu Hospital of Capital Medical University according to MMSE (mini-mental state examination) and MoCA (Montreal cognitive assessment) criteria. Ten human subjects diagnosed with mild cognitive impairment (in the following we use the term “MCI patients”) and seventeen elderly healthy control subjects with no history of psychiatric disorder participated in this study. Table 1 showed the socio-demographic characteristics of participants. All subjects had no personal neurological history, no drug or alcohol abuse, no current medication, and had normal or corrected-to-normal vision. Every subject signed an informed consent according to the guidelines of the Human Research Ethics Committee and was paid for participation after the experiment.

Table 1
Mean values ± standard deviation of socio-demographic characteristics.

	Normal Controls	MCI patients	Significance
Number of subjects	17	10	\
female/male	7/10	4/6	\
Age (years)	74.82 ± 5.54	75.20 ± 7.74	0.884
Education (years)	7.59 ± 3.86	7.0 ± 3.9	0.707

2.2. Stimuli and procedure

Selective attention can be studied in visual and spatial tasks. In visual task, one method is to ask participants to ignore some stimulus dimensions (e.g., identity, location) and respond based on a target dimension (e.g., color). In this study, we asked the subjects to attend to color and ignore the shape of stimuli.

The stimuli were some familiar colored shapes. Each stimulus had one of four colors (red, yellow, green, and white), and had one of four shapes (triangle, quadrangle, hexagon and round). The two stimuli in a pair were sequentially presented. The first stimulus and the second stimulus were presented on a monitor screen for 300 ms each with an inter-stimulus interval of 500 ms. Another trial began after 5 s ITI (inter-trial interval) (see Fig. 1). The stimuli were presented at the screen center of a computer-controlled monitor to each participant with a black background. The stimulus pairs were randomly presented 50 times in sequence and had equal probability. Subjects were seated at 1 m distance from the screen. They were instructed to sit quietly and to look at the cross in the center of the screen. The averaged visual angle of S1 and S2 was adjusted to 2.1°. In this task, participants were asked to discriminate whether the color of S2 was identical to that of S1 and ignored the shape of the stimulus. When the color of S2 was the same as that of S1, they were asked to press the left button of a push pad; when the color of S2 differed from S1, they pressed the right button. In statistic analysis, we divided the stimuli into two types (color match and color mismatch).

2.3. EEG recording and pre-processing

The electroencephalogram (EEG) was recorded using a sixty-four-channel EEG system with 60 surface electrodes mounted in an electrode cap (electrode impedance <5 kΩ, 0.05–100 Hz band pass, 1000 samples/s). Vertical and horizontal EOGs were simultaneously recorded to monitor eyes movement and blinks. The data were referenced to one electrode placed on nose. Trials with ocular, saccades artifacts and artifacts $>\pm 100$ μV were rejected before exporting. Artifact-free data were then segmented ranging from 200 ms before S1 to 1000 ms after S2 stimulus onset for all conditions.

Moreover, we chose 5 time windows (200–0 ms before S1, 0–200 ms, 200–400 ms, 400–600 ms, 600–800 ms after S2) for subsequent analysis in this study in order to explore the time-evolution of brain function network. In the following, each small epoch was decomposed into scale levels by wavelet packet decomposition (more details see reference (Akay, 1995)) in accordance with the traditional frequency bands in EEG analysis, i.e., beta: 16–32 Hz, alpha: 8–16 Hz. In the present work, the ‘db5’ mother wavelet which was better to reconstruct the original EEG signals from our prior study was employed with 7 levels decomposition.

2.4. Network analysis

2.4.1. Phase synchronization

It is well known at present that the phases of two coupled nonlinear oscillators may synchronize even if their amplitudes remain uncorrelated. So we use phase synchronization to analyze the characteristics of EEG during a cognitive task.