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Abnormal functional brain network in epilepsy patients with focal cortical dysplasia

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Summary
Purpose: Focal cortical dysplasia (FCD) is the second most common pathological entity in surgically treated neocortical focal epilepsy. Despite the recent increase of interest in network approaches derived from graph theory on epilepsy, resting state network analysis of the FCD brain has not been adequately investigated. In this study, we investigated the difference in the resting state functional network between epilepsy patients with FCD and healthy controls using whole-brain magnetoencephalography (MEG) recordings.
Methods: Global mutual information (MI_{glob}) and global efficiency (E_{glob}) were calculated for theta (4—7 Hz), alpha (8—12 Hz), beta (13—30 Hz), and gamma (31—45 Hz) bands in 35 epilepsy patients with FCD and 23 healthy controls.
Results: Resting state FCD brains had stronger functional connectivity (MI_{glob}) in the beta and gamma bands and higher functional efficiency (E_{glob}) in the beta and gamma bands than those of the controls ($p < 0.05$). The MI_{glob} and E_{glob} values of FCD type I and II brains in the beta band were higher than those of healthy control brains ($p < 0.05$). In the gamma band, the values of FCD type II brains were higher than those of control and FCD type I brains ($p < 0.05$).

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Conclusions: FCD brains had increased functional connectivity in the beta and gamma frequency bands at the resting state compared with those in healthy controls. In addition, patients exhibited different network characteristics depending on the type of FCD. The resting state network analysis could be useful in a clinical setting because we observed network differences even when there was no prominent interictal spike activity.

Introduction

Focal cortical dysplasia (FCD) is the second most common pathological entity in surgically treated neocortical focal epilepsy (Chung et al., 2005). Conventional clinical electrophysiological examination is insufficient to unravel the characteristics of FCD that are associated with less favorable surgical outcome when compared with those of epilepsy associated with hippocampal sclerosis or tumor.

Recently, functional connectivity and further network analyses have been used to reveal the intrinsic properties of the epileptic network (Engel et al., 2013; Horstmann et al., 2010; Liao et al., 2010; Morgan and Soltesz, 2008; Varotto et al., 2012; Wilke et al., 2011). Studies of focal epilepsies have reported enhanced connectivity in the region of the ictal onset zone, thereby revealing the existence of highly interconnected nodes that may play a crucial role in the onset and propagation of ictal activity (Morgan and Soltesz, 2008; Wilke et al., 2011). However, instead of including the entire brain, previous approaches covered only part of the whole brain, and such approaches may not grasp the full complexity of the brain as a network. Several previous studies utilized functional magnetic resonance imaging (fMRI) in network analyses of medial temporal lobe epilepsy (Liao et al., 2010; Pereira et al., 2010). However, with fMRI modality, it is difficult to investigate the dynamics of frequency bands above 0.1 Hz, which may play an important role in epileptogenesis.

In this respect, electrophysiological studies, such as electrocorticography (ECoG), electroencephalography (EEG), and magnetoencephalography (MEG), have advantages over fMRI. Recently, one study using ECoG investigated network characteristics in type II FCD patients (Varotto et al., 2012). Those authors reported that the interictal functional connectivity was higher in the seizure onset zone than in the non-involved zone in the gamma band. However, ECoG covers only part of the whole brain; moreover, it was not possible to study healthy controls in that study due to the method's invasiveness. Although one network study covered the whole brain with various frequency bands, that study compared only 5 healthy controls and 5 non-focal, absence seizure patients (Chavez et al., 2010).

To the best of our knowledge, there are no reports concerning whole-brain resting state network studies that compare focal epilepsy patients with FCD and healthy controls in various frequency bands. Unraveling such differences between FCD and healthy brains would enhance our knowledge of epileptogenesis in FCD. In this study, we investigated differences in the resting state functional network between patients with FCD and healthy controls by using whole-brain MEG signals. Global mutual information (MI_{glob}) as a measure of functional connectivity and global efficiency (E_{glob}) as a measure of network efficiency were used to compare the global resting state functional network between the two groups.

Materials and methods

Patients with FCD

Initially included in this study were 64 patients with intractable epilepsy and histologically proven FCD who underwent MEG examination before surgery between 2005 and 2011 at Seoul National University Hospital. Patients were screened for additional exclusion criteria: younger than 18 years of age at the time of surgery, FCD type III, which is associated with other pathologies, MEG recording after their first surgery for epilepsy, and a post-surgery follow-up period of less than two years. As a result, 35 patients (mean age at surgery ± SD = 30.0 ± 8.6 years; 18 males) were included in the study. Fig. 1 shows the flow chart of patient selection. Surgical outcome was classified according to the epilepsy surgery outcome classification system of the International League Against Epilepsy (Wieser et al., 2001).

Control subjects

Twenty-three healthy subjects (mean age ± SD = 24.7 ± 4.1 years; 12 males) were recruited as controls. There were no statistically significant differences in the gender mix between the patient and healthy subject groups ($p = 0.956$). Because there were a significant difference in ages between patients and healthy subjects ($p = 0.003$), we used age as a covariate in the statistical analysis. They had no history of neurologic or psychiatric disorders. The control subjects' MEG data were included in a previous study (Jin et al., 2011). All patients and healthy participants provided written informed consent. The study was approved by the institutional review board of Seoul National University Hospital (IRB H-0607-029-178).

MEG

Spontaneous magnetic activities were recorded inside a magnetically shielded room by using a 306-channel, whole-head MEG system (version 2.2, VectorView™, Elekta Neuromag Oy, Helsinki, Finland). The MEG sensors were arranged at 102 locations at which triplets consisting of two orthogonal planar gradiometers and one magnetometer were included. Data were collected for approximately 60 min (four 15 min sessions) from patients with their eyes closed. For healthy participants, MEG signals were recorded