Clinical Neurophysiology 126 (2015) 1482–1492

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Focal cortical dysplasia alters electrophysiological cortical hubs in the resting-state

Seung-Hyun Jin [a,b], Woorim Jeong [a,c], Chun Kee Chung [a,b,c,d,e,*]

[a] Department of Neurosurgery, Seoul National University Hospital, Seoul, Republic of Korea
[b] Neuroscience Research Institute, Seoul National University Medical Research Center, Seoul, Republic of Korea
[c] Interdisciplinary Program in Neuroscience, Seoul National University College of Natural Science, Seoul, Republic of Korea
[d] Department of Neurosurgery, Seoul National University College of Medicine, Seoul, Republic of Korea
[e] Department of Brain and Cognitive Sciences, Seoul National University College of Natural Sciences, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Accepted 7 October 2014
Available online 22 October 2014

Keywords:
Focal cortical dysplasia
Epilepsy
MEG
Cortical hubs
Resting-state

HIGHLIGHTS

- Focal cortical dysplasia (FCD) alters whole brain functional cortical hubs compared to healthy controls.
- FCD patients have enhanced nodal efficiency (Enodal) and betweenness centrality (BC) values in the functional network along the midline structures, which are indicative of electrophysiological cortical hubs in the epileptic FCD brain.
- Age at seizure onset was negatively correlated with Enodal in the beta band in FCD patients, which indicates unfavorable effects of cortical dysplasia on the functional network.

ABSTRACT

Objective: To test the hypothesis that epilepsy patients with focal cortical dysplasia (FCD) have different electrophysiological functional cortical hubs from those of healthy controls.
Methods: Resting-state functional networks in the theta, alpha, beta and gamma frequency bands were evaluated in 35 epilepsy patients with histopathologically verified FCD as a single pathology and in 46 age-matched healthy controls. Using magnetoencephalography (MEG), we investigated the network differences between the two groups by comparing the nodal efficiency (Enodal) and betweenness centrality (BC) values at the source level.
Results: The FCD patients had significant Enodal increases in the functional cortical hubs in the left anterior, middle, and posterior cortices and the medial orbital superior frontal cortex in the beta band. The left posterior cingulate cortex showed significant BC increases in the theta, alpha, and beta bands. There was a negative correlation between Enodal and age at seizure onset.
Conclusions: Cortical dysplasia alters whole brain functional cortical hubs compared to healthy controls. The age at seizure onset was negatively correlated with Enodal in the beta band in FCD patients.
Significance: Our study for the first time investigated the functional cortical hubs and their alteration in the resting-state functional network in epilepsy patients with FCD using noninvasive MEG signals.

1. Introduction

Cortical dysplasia is the second most common pathologic entity in surgically treated focal epilepsy (Chung et al., 2005), and epilepsy with focal cortical dysplasia (FCD) is a functionally and electrophysiologically integrated neural network disorder (Duchowny, 2009). Because the brain can be modeled by using network approaches, the application of networks based on graph theory

* Corresponding author at: Department of Neurosurgery, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 110-744, Republic of Korea. Tel.: +82 2 2072 2352; fax: +82 2 744 8459.
E-mail address: chungc@snu.ac.kr (C.K. Chung).

http://dx.doi.org/10.1016/j.clinph.2014.10.010
1388-2457/

can provide increased understanding of the brain's functional networks. With regard to epilepsy, altered brain functional networks have been reported in idiopathic generalized epilepsy (Zhang et al., 2011), medically intractable epilepsy (Wilke et al., 2011), absence epilepsy (Chavez et al., 2010), and temporal lobe epilepsy (TLE) (Ponten et al., 2007; Liao et al., 2010). In epilepsy patients with FCD, significantly different network patterns have been observed under inter-ictal, pre-ictal and ictal conditions by using stereo-electroencephalography (SEEG) (Varotto et al., 2012). However, no studies that compare resting-state brain functional networks in different frequency bands in epilepsy patients with FCD and in healthy subjects have been reported.

Because epilepsy with FCD is a neural network disorder (Duchowny, 2009), we hypothesized that FCD patients have altered resting-state functional networks and that, more specifically, they have alterations in highly connected network regions called "hubs" compared to hubs in healthy controls. Other pathologic entities such as hippocampal sclerosis (Haneef et al., 2014) or tumors (de Groot et al., 2012) could have different effects on the resting-state functional network; thus, we included only epilepsy patients with FCD as a single pathology in the present investigation into the effect of FCD on resting-state functional networks.

2. Materials and methods

2.1. Subjects

Thirty-five intractable epilepsy patients (right-handed) were enrolled in this retrospective study from among 64 epilepsy patients with histologically verified FCD who underwent magnetoencephalography (MEG) examination before surgery between 2005 and 2011 at Seoul National University Hospital. Excluded patients were those who were younger than 18 years of age at the time of surgery ($n = 9$), those who had FCD type III associated with other pathologies ($n = 18$), those who underwent post-surgical follow-up for less than 2 years ($n = 1$), and those who underwent MEG after their first surgery for epilepsy ($n = 1$). Detailed patients' characteristics are presented in Table 1. Summarized demographic data and surgical outcomes, based on the International League Against Epilepsy (ILAE) classification system (Blumcke et al., 2011), are summarized in Tables 2 and 3.

Forty-six age-matched healthy controls (mean age at the time of MEG study (range) = 29.9 (21–60); 19 males; right-handed) voluntarily participated in the study. There was no statistically significant difference in the age between the groups (Independent t-test, $p = 0.97$). The control subjects' MEG data are part of the data presented in our previous study (Jin et al., 2013). None of the participants had neurological abnormalities or magnetic resonance imaging (MRI)-detected lesions.

The study protocol was approved by the local Institutional Review Board at Seoul National University Hospital (IRB H-0607-029-178). Written informed consent was submitted by all of the subjects.

2.2. MRI evaluation

Preoperative MRI was performed on GE 1.5 T or 3 T scanners (GE Horizon Echospeed; GE Healthcare, Little Chalfont, UK) or on

Table 1
Detailed patients' characteristics.

#	Age at surgery	Sex	Age at seizure onset	Resection lobe	MRI findings	Pathology	ILAE outcome
1	26	F	25	T(Lt)	WNL	FCD IB	1
2	30	F	7	F(Rt)	Rt F gyrus and white matter, focal hyper SI	FCD IIB	1
3	28	F	21	F(Lt)	Lt F cortex, focal cortical thickening	FCD IIB	1
4	26	F	7	T(Lt)	WNL	FCD IA	1
5	27	F	15	T(Rt)	WNL	FCD IA	1
6	20	M	5	F(Lt)	Lt F cortex and gyrus, focal cortical atrophy and cortical tissue loss	FCD IA	1
7	36	M	31	T(Rt)	Rt T lobe, mild increased cortical thickness and hyper SI	FCD IA	1
8	21	F	4	T(Rt)	Rt T lobe, cyst like lesion	FCD IA	1
9	19	F	1	T(Rt)	Rt hippocampus, atrophy with hyper SI	FCD IA	1
10	23	F	11	T(Lt)	Lt F and T gyrus, cortical and subcortical lesions	FCD IIB	2
11	39	M	10	T(Rt)	WNL	FCD IA	2
12	51	F	21	F(Lt)	Lt F gyrus, localized cortical thickening	FCD IIB	2
13	26	M	5	F(Lt)	Lt F gyrus, focal cortical thickening with subtle hyper SI	FCD IIB	3
14	28	M	22	T(Lt)	WNL	FCD IA	3
15	22	M	14	T(Lt)	WNL	FCD IA	3
16	43	F	38	T(Rt)	WNL	FCD IA	3
17	19	F	5	T(Rt)	WNL	FCD IIB	3
18	47	M	42	T(Rt)	WNL	FCD IA	4
19	29	M	8	F(Rt)	WNL	FCD IA	4
20	33	M	1	F(Rt)	Rt F subcortical white matter and indistinct gray–white matter junction, focal subtle hyper SI	FCD IA	4
21	44	M	32	O(Rt)	WNL	FCD IA	4
22	41	M	13	F(Rt)	WNL	FCD IA	4
23	24	F	14	T(Rt)	WNL	FCD IA	4
24	39	M	15	T(Lt)	Lt hippocampus, atrophic change of	FCD IA	4
25	25	F	3	F(Lt)	WNL	FCD IA	4
26	32	F	8	F(Rt)	WNL	FCD IA	4
27	29	F	25	T(Lt)	Lt hippocampus, mild hyper SI	FCD IA	4
28	30	F	13	T(Rt)	Slightly asymmetric hippocampal head size	FCD IA	4
29	34	F	1	F(Lt)	WNL	FCD IA	4
30	25	M	22	F(Lt)	WNL	FCD IIB	4
31	25	F	13	T-O(Lt)	Lt F cortex and gyrus, focal decreased intensity and thickening	FCD IA	4
32	43	M	13	F(Rt)	Lt T, localized tissue loss and cerebromalacia	FCD IA	4
33	22	M	4	F(Rt)	WNL	FCD IA	5
34	18	M	13	F(Rt)	Rt parasylvian area, focal cortical thickening with subcortical hyper SI	FCD IA	6
35	26	F	16	T-P(Lt)	WNL	FCD IA	6

Abbreviations: F = frontal, FCD = focal cortical dysplasia, Lt = left, O = occipital, P = parietal, Rt = right, SI = signal intensity, T = temporal, WNL = within normal limit.