Journal of the Neurological Sciences 354 (2015) 79–85

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

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

# Altered resting state functional network connectivity in children absence epilepsy

Qifu Li [a,1], Weifang Cao [b,c,1], Xiaoping Liao [a], Zhibin Chen [a], Tianhua Yang [d], Qiyong Gong [e], Dong Zhou [d,**], Cheng Luo [b,*], Dezhong Yao [b]

[a] Department of Neurology, The Affiliated Hospital of Hainan Medical College, Haikou, China
[b] Key Laboratory for NeuroInformation of Ministry of Education, Center for Information in BioMedicine, High-Field Magnetic Resonance Brain Imaging Key Laboratory of Sichuan Province, University of Electronic Science and Technology of China, Chengdu 610054, China
[c] Department of Radiology, Taishan Medical University, Taian 271016, China
[d] Department of Neurology, West China Hospital of Sichuan University, Chengdu 610041, China
[e] Huaxi MR Research Center (HMRRC), Department of Radiology, West China Hospital of Sichuan University, Chengdu 610041, China

ARTICLE INFO

*Article history:*
Received 13 February 2015
Received in revised form 9 April 2015
Accepted 30 April 2015
Available online 8 May 2015

*Keyword:*
Resting state fMRI
Functional network connectivity
Independent component analysis
Antagonism
Absence epilepsy

ABSTRACT

Altered functional connectivity has been associated with the influence of epileptic activity. Abnormalities in connectivity, particularly in dorsal attention (DAN), salience (SN) and default mode (DMN) networks, might contribute to the loss of consciousness during seizures and cognitive deficits in patients with children absence epilepsy (CAE). The objective of the present study was to identify whether the functional network connectivity (FNC) is changed between patients with CAE and healthy controls. Using independent component analysis, twelve resting state networks (RSNs) were identified in resting state functional magnetic resonance imaging data sets in eighteen CAE patients and twenty-one healthy controls. Analyses of the group differences in FNC strength were conducted, controlling for age and gender effects. The findings showed that some functional networks were clustered into two subgroups, correlated within subgroups and antagonized with each other. Compared with the controls, patients with CAE demonstrated abnormal FNC strength among three networks: DMN, DAN and SN. In addition, the antagonism of two subgroups was altered. These results might reflect the underlying neuronal functional impairment or altered integration among these RSNs in CAE, suggesting that the abnormal functional connectivity is likely to imply the pathological mechanism associated with the accumulative influence of epileptic activity. These findings contribute to the understanding of the behavior abnormality in CAE, such as disturbed executive and attentional functions and the loss of consciousness during absence seizures.


## 1. Introduction

Childhood absence epilepsy (CAE) is the most common childhood epilepsy syndrome and is observed in 10–17% of all childhood onset epilepsy cases [1,2]. Typical absence seizures present as brief episodes of staring and unresponsiveness and are often accompanied by 2.5–4 Hz generalized spike and wave discharges (SWDs) in scalp electroencephalogram (EEG). The seizure duration is typically less than 10 s, and these seizures can occur up to hundreds of times per day. It has been suggested that the impairment of consciousness during absence seizures reflects the inhibition of the interactions among cortical and subcortical systems [3–6]. Impaired cognition, memory function and attentional deficits, as long-term outcomes of absence epilepsy, have been observed in behavior tests [7]. In addition, interictal epileptic discharges lead to transient cognitive impairment [8]. Neuroimages, such as simultaneous EEG and fMRI study, have demonstrated the transient effect of epileptic activity in which ictal and/or interictal epileptic discharges might lead to abnormalities in the thalamus and cortical cortex [9–12]. The fMRI studies in patients with CAE have shown altered functional connectivity in cortical and subcortical networks, such as the default mode network (DMN) [13], dorsal attention network (DAN) [14], and salience network (SN) [15]. Moreover, the structural alteration was also observed in thalamus, basal ganglia and cortical regions in patients with CAE [13,16]. These changes combined structural and resting state fMRI might reflect the chronic influence of epileptic activity associated with the relevant cognitive functions and/or the accumulative consequences of losses of

* Correspondence to: C. Luo, Key Laboratory for NeuroInformation of Ministry of Education, Center for Information in BioMedicine, High-Field Magnetic Resonance Brain Imaging Key Laboratory of Sichuan Province, University of Electronic Science and Technology of China, Chengdu 610054, China. Tel.: +86 28 83201018; fax: +86 28 83208238.
** Correspondence to: D. Zhou, Department of Neurology, West China Hospital of Sichuan University, Chengdu 610041, China. Tel.: +86 13980008088; fax: +86 28 85582944.
*E-mail addresses:* zhoudong66@yahoo.de (D. Zhou), chengluo@uestc.edu.cn (C. Luo).
[1] Qifu Li and Weifang Cao contributed equally to this work.

http://dx.doi.org/10.1016/j.jns.2015.04.054
0022-510X/

consciousness during absence seizures. However, a few studies have focused on the interactions between functional networks in CAE.

Functional connectivity analyses through fMRI focusing on resting state networks (RSNs) might provide underlying evidence to reflect the intrinsic interactions among discrete neuroanatomical regions [17,18]. In addition, resting state brain activity is intrinsically organized into dynamic dichotomic systems: task-positive and task-negative (or default mode, DMN) networks [19]. Indeed, the anti-correlation between the networks might reflect naturally occurring competition, which is functionally more important than the DMN activity itself [19,20]. Hence, the interaction between RSNs would contribute to the understanding of the neurophysiological mechanisms of the normal brain. An extension of functional connectivity, called functional network connectivity (FNC), was developed [21]. FNC is a powerful tool for characterizing distributed changes in the brain by examining the interactions among different RSNs. Jafri and colleagues conducted an FNC analysis of patients with schizophrenia, reporting significant differences between patients and controls that reflected deficiencies in cortical processing in patients [21]. In previous studies, disturbed FNC has been observed in schizophrenia [21], epilepsy [22], and attention deficit/hyperactivity disorder (ADHD) [23]. The abnormal integration between RSNs in mental disorder suggests the contribution of these networks to individual problems in behavior, such as attention deficits in ADHD and schizophrenia, and abnormal performance for introspective and extrospective orienting in a number of mental disorders [24]. In a number of studies of epilepsy, the dysfunctional connectivity among multiple brain regions is considered a central feature. Hence, the International League Against Epilepsy Commission on Classification and Terminology uses the terminology 'distributed networks' to describe epilepsy [25]. The abnormal functional connectivity between RSNs might be a feature of CAE observed in resting-state fMRI [13–15,26]. We hypothesized that the interactions between functional networks, particularly the antagonism between DMN and task-positive networks involved in brain baseline function and consciousness, would be disturbed in CAE. In the present study, eighteen patients with CAE were recruited to explore the FNC between RSNs. RSNs were isolated using group independent component analysis (ICA), FNC analyses were conducted.

## 2. Materials and methods

### 2.1. Participants

A total of twenty one right-handed children with absence epilepsy (mean age of 9.5 years old, 12 females) were recruited from West China Hospital of Sichuan University, Chengdu, China. The patients were diagnosed based on the International Classification of the Epilepsies (Commission on Classification and Terminology of the International League against Epilepsy, 2001) [27], and recruitment was based on video evidence, EEG telemetry, scalp EEG, and clinical manifestations. Eleven patients were newly diagnosed and untreated. All patients were seizure-free for at least one day before fMRI scanning. The mean age at onset was 7.7 years old (range: 4–10 years), and the mean duration of epilepsy was 34.6 months (range: 6–70 months) (Table 1). A total of 21 gender- and age-matched right-handed controls were also recruited (mean age of 10.2 years old, 13 females). None of the controls had neurological or psychiatric disorders. The years of education were also noted for each subject. The detailed information for the participants was also illustrated in a previous study [15]. The present study was approved through the ethics committee of West China Hospital, and the protocols were performed according to the standards of the Declaration of Helsinki. Written informed consent was obtained from each participant or parents (for children).

**Table 1**
Demographic, clinical and neuropsychological features of the subjects.

| | CAE | HC | p value |
|---|---|---|---|
| Gender (male/female) | 21 (9/12) | 21 (9/13) | – |
| Age (year) | 9.50 ± 2.75 (5–13 years) | 10.20 ± 2.89 (6–12 years) | 0.137 |
| Years of education (year) | 4.33 | 4.56 | 0.560 |
| Age at onset (year) | 7.70 ± 1. 64 | – | – |
| Epilepsy duration (month) | 34.60 ± 15.96 | – | – |

### 2.2. MRI data acquisition

All structural and functional MRI data were collected using a 3 T MRI system (EXCITE, GE Milwaukee, USA) with an research-dedicated eight-channel phased array head coil in Huaxi MR Research Center (HMRRC), Sichuan University, Chengdu, China. Structural T1-weighted images were acquired in axial orientation using a three-dimensional (3D) spoiled gradient recalled (SPGR) sequence (repetition time (TR) = 8.5 ms, echo time (TE) = 3.4 ms, field of view (FOV) = 24 cm × 24 cm, flip angle = 12°, matrix = 512 × 512, 156 slices) with a voxel size of 0.96 × 0.96 × 1.00 $mm^3$. MR images sensitized to changes in BOLD signal levels (TR = 2000 ms, TE = 30 ms, FOV = 24 cm × 24 cm, flip angle = 90°, matrix = 64 × 64, 30 slices) were obtained by a gradient-echo echo-planar imaging (EPI) sequence. The slice thickness was 5 mm (no slice gap) resulting in a voxel size 3.75 × 3.75 × 5.00 $mm^3$. According to patient endurance, 2–3 resting-state fMRI runs were performed, and each functional run contained 205 image volumes. The first five volumes were discarded to ensure steady-state longitudinal magnetization. During the resting-state scan, participants were instructed simply to keep their eyes closed and not to think of anything in particular.

### 2.3. Data preprocessing

The fMRI images were preprocessed using the Statistical Parametric Mapping software package, SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). The images were first corrected for timing differences between the slices and realigned to the first volume to correct head motions. After motion correction, the functional scans were normalized to the Montreal Neurological Institute (MNI) EPI template and resampled to 3 × 3 × 3 $mm^3$ voxels. Moreover, the images were spatially smoothed through convolution with a 6 mm full-width half maximum (FWHM) Gaussian kernel, resulting in a smoothed fMRI dataset. The transition and rotation were checked, and patients with head movement greater than 2 mm in any direction or head rotation greater than 1° were excluded.

### 2.4. Independent component analysis

ICA is a data-driven statistical analysis technique that yields independent components (ICs), representing a group of brain regions with a unique pattern of synchronized neural activity (time course), and these data can be conceptualized as a neural network. For all subjects, including absence epilepsy patients and health controls, a Group ICA analysis was performed to decompose the data into ICs using GIFT software [28] (version 2.0e; http://mialab.mrn.org/software/gift/). Minimum description length (MDL) criteria were used to define the number of ICs from all subjects [29]. The reduction of data dimensionality was performed using principal component analysis (PCA). The infomax algorithm was used as an independent component estimation [30]. This algorithm was repeated 20 times in ICASSO (http://research.ics.tkk.fi/ica/icasso), and the resulting components were clustered to estimate the reliability of the decomposition. Moreover, individual time courses and spatial maps were computed (called back reconstruction) [31], and the aggregate components and the data reduction results

were used to compute the individual subject components. The components were visually inspected for artifacts.

### 2.5. Functional network connectivity

The functional networks isolated through ICA were defined based on assumptions in which the time courses of brain regions within one component are synchronous. Although the components are spatially independent, significant temporal correlation can exist among time courses of different ICs. First, the temporal band-pass filter (pass band 0.01–0.08) was used to reduce the effects of low-frequency drift and high-frequency physiological noise on these time courses. Then, to measure the interaction, we calculated the constrained maximal lagged correlation using an extension of GIFT, the functional network connectivity toolbox (FNC; http://mialab.mrn.org/software/#fnc) [21].

The correlations between the time courses of two RSNs were computed for each subject. After the Fisher-Z-translation of correlation coefficient was performed, the significant temporal interactions between any two RSNs were examined using the one-sample t-test ($p < 0.05$, corrected by false discover rate, FDR) in patient and control groups separately. To better understand the distinctions of each FNC between two groups, two-sample t-tests were performed for all 66 potential connections among 12 RSNs, with a statistical significance level of $p < 0.05$ corrected by FDR.

## 3. Results

There were no significant differences between groups with respect to age ($p = 0.137$, two-tailed two-sample t-test) or years of education ($p = 0.56$, two-tailed two-sample t-test) (Table 1).

### 3.1. Identifications of the RSNs

Among the 34 components resulting from group ICA, 12 components were selected as non-artifactual, relevant networks through visual inspection in accordance with previously published results [19,32–35]. The spatial maps of these RSNs were highly stable (reliability index >0.90), as determined using ICASSO. The twelve RSNs are shown in Fig. 1. These networks were labeled as follows.

aDMN: The anterior region of the DMN, including primary clusters in the superior frontal gyrus and medial frontal gyrus. Typically, as an important network, the DMN primarily encompasses the PCC, the anterior cingulate cortex, and the bilateral

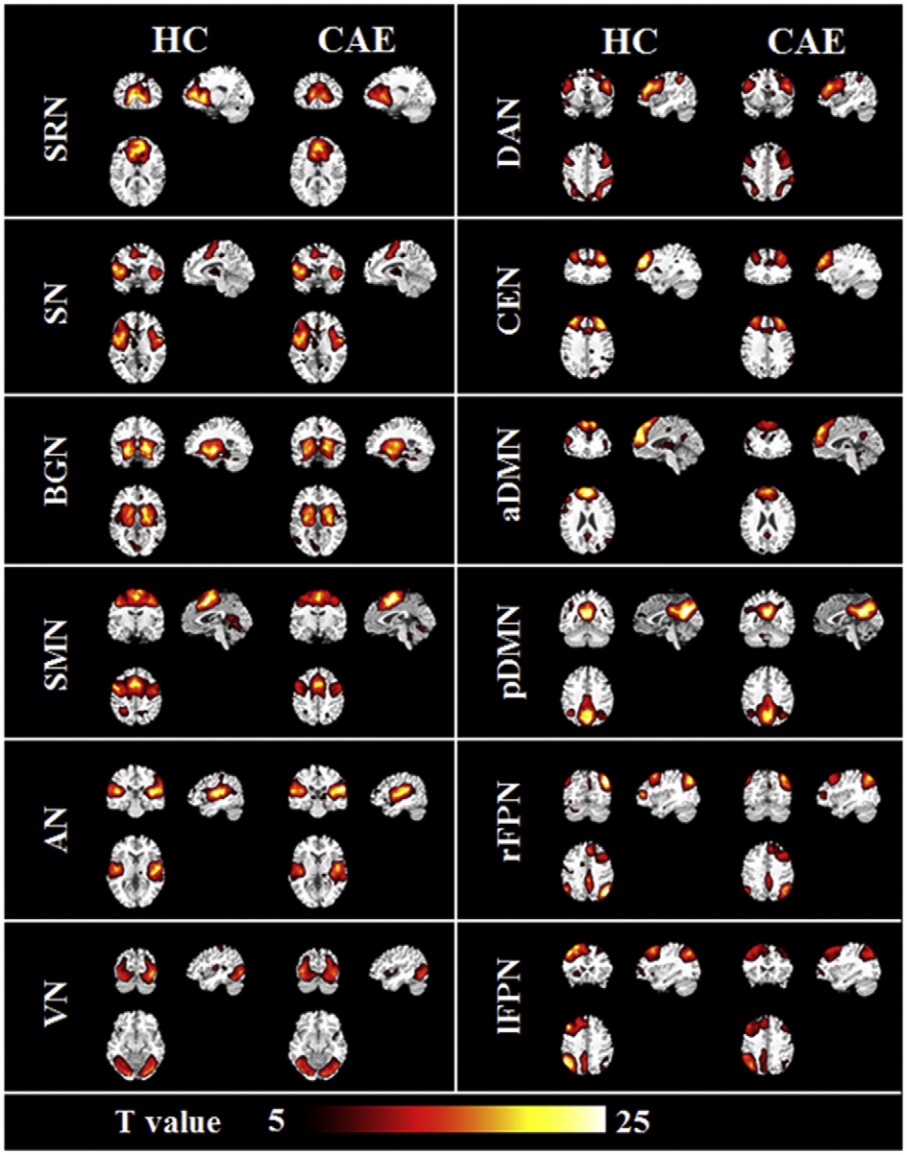


**Fig. 1.** The spatial maps of twelve RSNs. The group-level spatial maps are showed in two groups respectively.

inferior parietal lobule. Interestingly, in the present study, the DMN was divided into 2 components: the anterior areas (aDMN) and the posterior areas (pDMN). A similar decomposition of the DMN has been previously observed [22,36,37].

pDMN: The posterior region of the DMN involving the posterior cingulate cortex, bilateral inferior parietal gyrus, and angular gyrus [22,36].

SMN: The sensorimotor network (SMN) corresponds to sensorymotor function. This network includes the pre-central gyrus and the post-central gyrus, the primary sensorimotor cortices, and the supplementary motor area [22,36].

SRN: Self-referential network (SRN) putatively associated with self-referential mental activity, primarily including the medial–ventral prefrontal cortex and the pregenual anterior cingulate [22].

lFPN: Left lateral frontoparietal network (lFPN) and right lateral frontoparietal network showing similar spatial patterns with DAN comprising regions involved in goal-directed top-down processing [22,36]. This network primarily involves the precuneus, inferior parietal lobule, middle frontal gyrus, and superior parietal lobule.

rFPN: Right lateral frontoparietal network (rFPN), including clusters lateralized to the right hemisphere, putatively associated with DAN. The left and right lateral frontoparietal networks were the only strongly lateralized maps, shown as left–right mirrors of each other [22,36].

VN: Visual network (VN) showing spatial patterns comprising the middle temporal, superior temporal, insular and postcentral cortices, involved in visual processing [22,36].

AN: Auditory network (AN) primarily encompassing the middle temporal gyrus, superior temporal gyrus, and insular and temporal poles and corresponding to the auditory system [22,36].

CEN: Central executive network (CEN) showing spatial patterns comprising the superior and middle prefrontal cortices, anterior cingulate and paracingulate gyri, and the ventrolateral prefrontal cortex [38].

SN: Salience network (SN) showing spatial patterns comprising the bilateral anterior insular and anterior cingulate cortices and the temporal–parietal junction area [39].

BGN: Basal ganglia network (BGN) encompassing the middle temporal gyrus, superior temporal gyrus, insular and temporal poles and corresponding to the auditory system [35].

DAN: dorsal attention network (DAN), revealed in the present study as covering the bilateral intraparietal sulcus, frontal eye field and middle temporal lobe [33], with an anatomic pattern largely consistent with those mapped with the specific task.

### 3.2. FNC analysis between groups

Using one-sample t-test, 32 significant connections, including positive correlations (larger than zeros) in 18 connections and negative correlations (less than zeros) in 14 links, were observed in the HC group. The pattern of these connections is shown in Fig. 2; and positive correlation is represented by the red line, the negative by blue line. According to the pattern, these RSNs could be divided into two clusters, illustrating significantly positive within-cluster correlations and negative between-cluster correlations, with one cluster comprising aDMN, pDMN, SRN, lFPN, rFPN, and BGN and the other cluster comprising SN, DAN CEN, SMN, AN and VN. The CAE group demonstrated 15 connections with significantly positive correlations (red line in Fig. 3) and five connections with negative correlations (blue line in Fig. 3). Similar to the healthy control group, five negative connections were observed between the clusters. Although the main positive connections were situated within cluster, three positive connections were observed between clusters aDMN and CEN, CEN and rFPN, and BGN and AN.

To further understand the differences in FNC architecture, a two-sample t-test was used to identify difference between the groups (Table 2, Fig. 4). Compared with controls, patients showed three increased connections (represented by red line in Fig. 4) which represented significantly positive correlations in patients (Fig. 3), but no predominant connectivity was observed in healthy controls

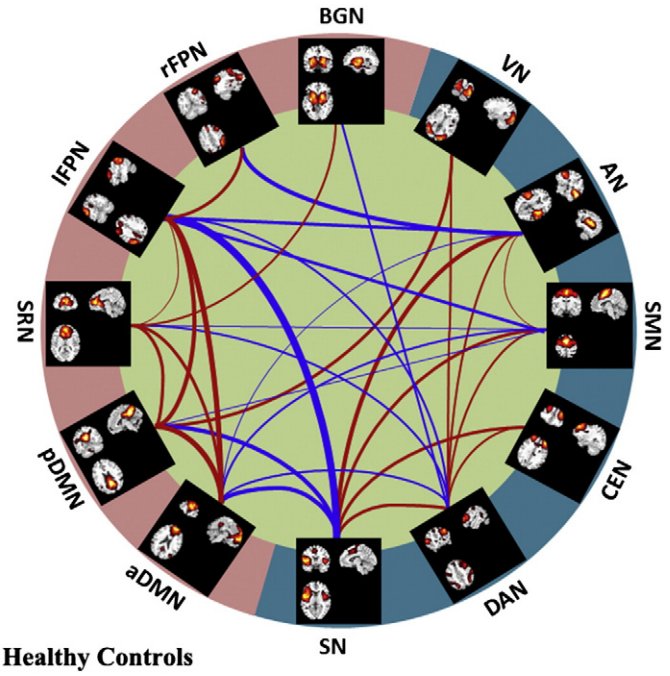


**Fig. 2.** The functional network connectivity in healthy control group. The red line represents the connection with positive correlation; and the blue line represents the connection with negative correlation.

(Fig. 2), including one connection between aDMN and CEN, one connection between aDMN and rFPN, and one connection between SN and BGN. Two antagonized connections observed in controls was distinctly decreased in patients (correlation coefficient approaching zero), including one between SN and aDMN and one between aDMN and DAN (represented by black line in Fig. 4). Finally, three positive connections in controls (Fig. 2) were reduced in patients including

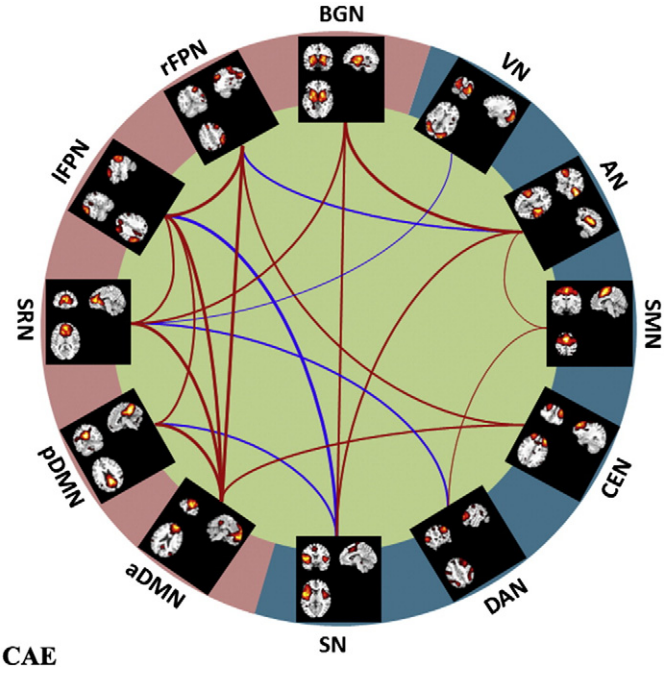


**Fig. 3.** The functional network connectivity in CAE group. The red line represents the connection with positive correlation; and the blue line represents the connection with negative correlation.

**Table 2**
The altered FNC between two groups.

| RSN1–RSN2 | Mean in CAE | Mean in HC | T-value | p-value |
|---|---|---|---|---|
| aDMN–CEN | 0.303[a] | −0.018 | 3.25 | 0.0023 |
| aDMN–rFPN | 0.384[a] | 0.148 | 3.03 | 0.0043 |
| SN–BGN | 0.320[a] | 0.035 | 3.06 | 0.0039 |
| aDMN–SN | −0.128 | −0.454[b] | 4.07 | 0.0002 |
| aDMN–DAN | −0.006 | −0.288[b] | 3.07 | 0.0038 |
| SN–DAN | −0.013 | 0.315[a] | 3.80 | 0.0004 |
| SN–SMN | 0.017 | 0.401[a] | 4.17 | 0.0001 |
| DAN–AN | 0.025 | 0.318[a] | 3.13 | 0.0033 |

[a] Means that the averaged value is significantly larger than zero.
[b] Means that the averaged value is significantly less than zero.

the associations between SN and DAN, SN and SMN, and DAN and AN (represented by blue line in Fig. 4).

## 4. Discussion

Using resting state fMRI, we investigated functional connectivity inter-RSNs in patients with CAE. Twelve RSNs were selected to conduct a systematical resting-state network analysis in a cohort of CAE patients and healthy controls. According to the within group findings, some RSNs could be clustered into two subgroups in which the interaction were antagonistic between subgroups, but associative within subgroups. Compared with controls, patients demonstrated altered FNC among three RSNs (aDMN, DAN and SN). On the one hand, functional network disconnectivity was observed in the links between DAN, SN and aDMN, reflecting the decreased antagonism between these networks. On the other hand, the connections between SN and DAN, SN and SMN, and DAN and AN were also decreased, suggesting that the disturbed attention in patients was associated with terrible monitoring in the external environment. In addition, patients with CAE showed increased FNC associated with DMN and BGN (red lines in Fig. 4), suggesting an association with the accumulative influence of epileptic activity in CAE. These findings indicate that analyzing connectivity strength among RSNs might be a valuable tool to assess the functional changes corresponding to epilepsy and contribute to our understanding of the neuro-pathophysiological mechanism of this condition.

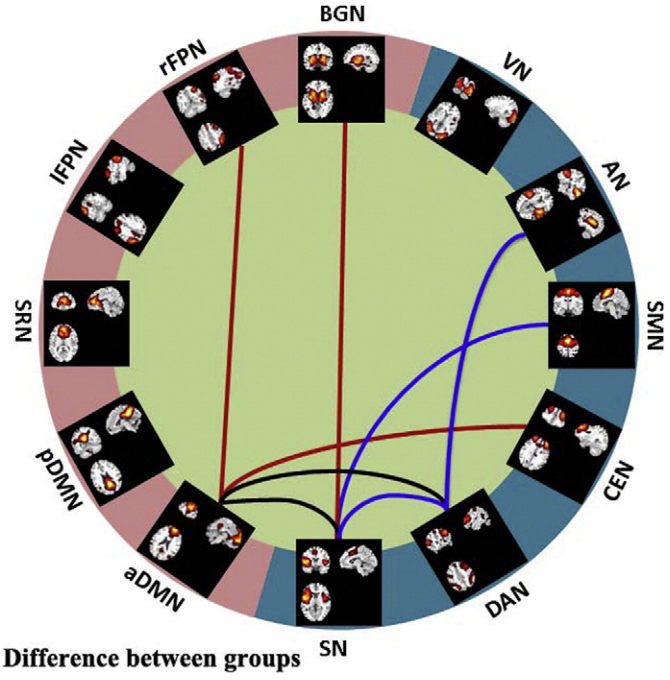


**Fig. 4.** The difference of functional network connectivity between two groups. The red line represents the connection with increased FNC with positive correlation in patients (the average correlation value of CAE group is significantly larger than zero); the black line represents the connection with increased FNC with negative correlation in patients (the average correlation value of healthy control group is significantly less than zero); and the blue line represents the connection with decreased FNC with positive correlation (the average correlation value of healthy control group is significantly larger.

### 4.1. Decreased antagonism between DMN, DAN, and SN

The DMN, which includes the medial prefrontal, posterior cingulate, and lateral parietal gyri, is often activated at rest, but deactivated during the performance of various goal-directed tasks [37]. In contrast, regions included in the DAN and SN, routinely activated during goal-directed task performance, were described as task-positive networks [33]. These two systems are temporally anti-correlated during resting state [19]. One hypothesis is that the reciprocal relationship might reflect the low-frequency toggling between introspective and extrospective states to ensure that an individual is attentive to novel or unexpected environmental events [24]. The potential degree of antagonism between two systems might be associated with the binding mechanism of the brain to process simultaneous multi-threads with consciousness. In this study, we observed significantly decreased FNC among the DMN, DAN and SN in the absence epilepsy patients, including increased anti-correlation and decreased positive coupling among task-positive systems (DAN and SN). The disconnection among these networks might contribute to the altered consciousness during absence seizures. The impairment of consciousness is a frequent behavioral manifestation in absence epilepsy. A previous study using SPECT, PET and fMRI showed that frontal–parietal association areas exhibit an important relationship with consciousness, playing a potential role in the genesis of consciousness [40]. Blumenfeld reported that abnormal activity in the frontoparietal association cortex in seizures was associated with the loss of consciousness [3]. In a previous study, we observed abnormal functional connectivity in DMN and SN in epilepsy [41,42]. Here, we further demonstrated the altered functional connectivity between these RSNs, suggesting that the abnormality in the two anti-correlated systems might reflect the disturbed management of introspective and extrospective information, thereby facilitating the loss of consciousness during absence seizures. This finding is consistent with previous suggestions of network inhibition or network disruption as a plausible mechanism for impaired consciousness during epilepsy seizure [3]. In addition, many studies have shown that the methods used in functional connectivity analyses would influence the anti-correlation in fMRI data [43–45]. For example, the preprocessing step with regression out globe-averaged single intensified the anti-correlation [45]. In current study, FNC analysis based on the time-course from ICA would shield the trap of globe regression.

### 4.2. Abnormal FNC with CEN

The executive control network, including the frontoparietal area and dorsal anterior cingulate, has been identified the association with task execution in previous studies [36,38]. The interaction between DMN and CEN showed anti-correlation. Two networks were classified into different clusters because CEN significantly positively correlated with DAN and SN anti-correlated with DMN, although no direct correlation between CEN and DMN was observed in healthy controls in the present study. However, in patients with CAE, CEN was significantly positively correlated with RFPN and aDMN, but not correlated with SN and DAN. Moreover, a significantly positive correlation between aDMN and CEN was observed in patients. These findings reflected the abnormal cooperation between CEN

and task-positive systems in patients, which might indicate disturbed executive and attentional functions in patients with CAE, consistent with the behavior findings in previous studies in CAE [7,11].

### 4.3. Abnormal FNC with DAN and SN

Previous studies in patients with epilepsy have shown decreased functional connectivity in DAN [14], motor-perception networks [22], and suggested that the decreased resting state functional connectivity might be a remarkable characteristic of epilepsy. In the present study, the three primary motor-perceptual RSNs (auditory, motor and visual network) were grouped into one cluster with DAN, CEN and SN in healthy controls. In general, the task-positive system would involve the extrinsic alertness, receiving input information and response to task. These primary RSNs would closely interact with the high-level task-processing RSNs (attention, execution and memory). Here, we observed the decreased connectivity between the primary and high-level RSNs (DAN–AN, SN–SMN) in patients with CAE, suggesting disturbed information procession in patients. We presumed that disconnection between primary and high-level function might cause the reduced cognitive function in CAE.

Increased FNC between SN and BGN was observed in patients with CAE in current study. BGN has been considered as a modulator of generalized epileptic discharges [46]. In previous study, we showed the abnormal functional integration of BGN in CAE patients, and aggravation was accompanied by an increased number of epileptic discharged during fMRI acquisition [35]. Although there was no evidence illustrating that SN is regulated through epileptic discharges, we proposed that the greater cooperation between BGN and SN might link epileptic discharges and the awareness system. These hypotheses, however, require further investigation.

There were several limitations that would be argued. First, the antiepileptic drugs might lead to the alteration of brain metabolism, the effects of medications would be considered in the future. Second, the longitudinal survey, rather than cross-section design, might investigate the link between diseases in children and the development clearly. Finally, ICA, as a data-driven method for fMRI data analysis, was used to identify the RSNs in this study. The network related with the epileptiform activity would be isolated in patients but not observed in healthy controls. Thus, the FNC among the common RSNs was investigated in this study. For the individual patient-specific network related with epileptiform activity, the seed-based functional connectivity analysis [47] and cluster analysis [48] might provide some valuable information in the comparison with health controls.

In summary, patients with CAE exhibit significantly disturbed functional connectivity strength among RSNs, particularly among DMN, DAN and SN. In addition, the altered antagonism of two subgroups was also observed. These results might reflect the underlying neuronal functional impairment or altered integration of these RSNs in patients with CAE. We proposed that the abnormal functional connectivity observed at resting state likely reflects the pathological mechanism associated with the accumulative influence of epileptic activity in patients with CAE. These findings contribute to the understanding of the behavior abnormality in CAE, such as the disturbed executive and attentional function and the loss of consciousness during absence seizures.

## Conflict of interest

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. None of the authors has any conflict of interest to disclose.

## Acknowledgments

This study was funded by grants from the 973 Project (2011CB707803), 863 Project (2015AA020505), the National Nature Science Foundation of China (81160166, 8121547, 91232725, 81371636, and 81471638), the PCSIRT Project (IRT0910), the '111' Project (B12027), the Special-Funded Program on National Key Scientific Instruments and Equipment Development of China (2013YQ49085908), and the Natural Science Foundation of Hainan Province of China (811218).

## References

[1] Tenney JR, Glauser TA. The current state of absence epilepsy: can we have your attention? Epilepsy Curr 2013;13(3):135–40.
[2] Crunelli V, Leresche N. Childhood absence epilepsy: genes, channels, neurons and networks. Nat Rev Neurosci 2002;3(5):371–82.
[3] Blumenfeld H. Impaired consciousness in epilepsy. Lancet Neurol 2012;11(9):814–26.
[4] Cavanna AE, Monaco F. Brain mechanisms of altered conscious states during epileptic seizures. Nat Rev Neurol 2009;5(5):267–76.
[5] Blumenfeld H, Taylor J. Why do seizures cause loss of consciousness? Neuroscientist 2003;9(5):301–10.
[6] Blumenfeld H. Consciousness and epilepsy: why are patients with absence seizures absent? Prog Brain Res 2005;150:271–86.
[7] Caplan R, et al. Childhood absence epilepsy: behavioral, cognitive, and linguistic comorbidities. Epilepsia 2008;49(11):1838–46.
[8] Hommet C, et al. Idiopathic epileptic syndromes and cognition. Neurosci Biobehav Rev 2006;30(1):85–96.
[9] Berman R, et al. Simultaneous EEG, fMRI, and behavior in typical childhood absence seizures. Epilepsia 2010;51(10):2011–22.
[10] Li Q, et al. EEG-fMRI study on the interictal and ictal generalized spike-wave discharges in patients with childhood absence epilepsy. Epilepsy Res 2009;87(2-3):160–8.
[11] Bai X, et al. Dynamic time course of typical childhood absence seizures: EEG, behavior, and functional magnetic resonance imaging. J Neurosci 2010;30(17):5884–93.
[12] Gotman J, et al. Generalized epileptic discharges show thalamocortical activation and suspension of the default state of the brain. Proc Natl Acad Sci U S A 2005;102(42):15236–40.
[13] Luo C, et al. Diffusion and volumetry abnormalities in subcortical nuclei of patients with absence seizures. Epilepsia 2011;52(6):1092–9.
[14] Killory BD, et al. Impaired attention and network connectivity in childhood absence epilepsy. Neuroimage 2011;56(4):2209–17.
[15] Luo C, et al. Altered intrinsic functional connectivity of the salience network in childhood absence epilepsy. J Neurol Sci 2014;339(1-2):189–95.
[16] Xue K, et al. Diffusion tensor tractography reveals disrupted structural connectivity in childhood absence epilepsy. Epilepsy Res 2014;108(1):125–38.
[17] De Luca M, et al. fMRI resting state networks define distinct modes of long-distance interactions in the human brain. Neuroimage 2006;29(4):1359–67.
[18] Fox MD, Raichle ME. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nat Rev Neurosci 2007;8(9):700–11.
[19] Fox MD, et al. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proc Natl Acad Sci U S A 2005;102(27):9673–8.
[20] Uddin LQ, et al. Functional connectivity of default mode network components: correlation, anticorrelation, and causality. Hum Brain Mapp 2009;30(2):625–37.
[21] Jafri MJ, et al. A method for functional network connectivity among spatially independent resting-state components in schizophrenia. Neuroimage 2008;39(4):1666–81.
[22] Luo C, et al. Disrupted functional brain connectivity in partial epilepsy: a resting-state fMRI study. PLoS One 2011;7(1):e28196.
[23] Choi J, et al. Aberrant development of functional connectivity among resting state-related functional networks in medication-naive ADHD children. PLoS One 2013;8(12):e83516.
[24] Broyd SJ, et al. Default-mode brain dysfunction in mental disorders: a systematic review. Neurosci Biobehav Rev 2009;33(3):279–96.
[25] Berg AT, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 2010;51(4):676–85.
[26] Yang T, et al. Altered resting-state connectivity during interictal generalized spike-wave discharges in drug-naive childhood absence epilepsy. Hum Brain Mapp 2013;34(8):1761–7.
[27] Engel Jr J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. Epilepsia 2001;42(6):796–803.
[28] Calhoun VD, et al. A method for making group inferences from functional MRI data using independent component analysis. Hum Brain Mapp 2001;14(3):140–51.
[29] Li YO, Adali T, Calhoun VD. Estimating the number of independent components for functional magnetic resonance imaging data. Hum Brain Mapp 2007;28(11):1251–66.
[30] Bell AJ, Sejnowski TJ. An information-maximization approach to blind separation and blind deconvolution. Neural Comput 1995;7(6):1129–59.

[31] Zhang H, et al. Subject order-independent group ICA (SOI-GICA) for functional MRI data analysis. Neuroimage 2010;51(4):1414–24.
[32] Dosenbach NU, et al. Distinct brain networks for adaptive and stable task control in humans. Proc Natl Acad Sci U S A 2007;104(26):11073–8.
[33] Fox MD, et al. Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. Proc Natl Acad Sci U S A 2006;103(26):10046–51.
[34] Luo C, et al. Altered functional connectivity in default mode network in absence epilepsy: a resting-state fMRI study. Hum Brain Mapp 2011;32(3):438–49.
[35] Luo C, et al. Resting state basal ganglia network in idiopathic generalized epilepsy. Hum Brain Mapp 2012;33(6):1279–94.
[36] Damoiseaux JS, et al. Consistent resting-state networks across healthy subjects. Proc Natl Acad Sci U S A 2006;103(37):13848–53.
[37] Raichle ME, et al. A default mode of brain function. Proc Natl Acad Sci U S A 2001;98(2):676–82.
[38] Beckmann CF, et al. Investigations into resting-state connectivity using independent component analysis. Philos Trans R Soc Lond B Biol Sci 2005;360(1457):1001–13.
[39] Menon V, Uddin LQ. Saliency, switching, attention and control: a network model of insula function. Brain Struct Funct 2010;214(5-6):655–67.
[40] Boly M, et al. Intrinsic brain activity in altered states of consciousness: how conscious is the default mode of brain function? Ann N Y Acad Sci 2008;1129:119–29.
[41] Liao W, et al. Default mode network abnormalities in mesial temporal lobe epilepsy: a study combining fMRI and DTI. Hum Brain Mapp 2011;32(6):883–95.
[42] Luo C, et al. Altered intrinsic functional connectivity of salience network in childhood absence epilepsy. J Neurol Sci 2014;339(1):189–95.
[43] Chai XJ, et al. Anticorrelations in resting state networks without global signal regression. Neuroimage 2012;59(2):1420–8.
[44] Anderson JS, et al. Network anticorrelations, global regression, and phase-shifted soft tissue correction. Hum Brain Mapp 2011;32(6):919–34.
[45] Murphy K, et al. The impact of global signal regression on resting state correlations: are anti-correlated networks introduced? Neuroimage 2009;44(3):893–905.
[46] Norden AD, Blumenfeld H. The role of subcortical structures in human epilepsy. Epilepsy Behav 2002;3(3):219–31.
[47] Luo C, et al. Patient-specific connectivity pattern of epileptic network in frontal lobe epilepsy. Neuroimage Clin 2014;4:668–75.
[48] Dansereau CL, et al. Detection of abnormal resting-state networks in individual patients suffering from focal epilepsy: an initial step toward individual connectivity assessment. Front Neurosci 2014;8:419.