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# Resting-State Functional Connectivity Analysis Using an Independent Component Approach

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***Abstract*****—**Refractory epilepsy is a complicated type of epilepsy that can be difficult to diagnose. Recent technological advancements have made resting-state functional magnetic resonance (rsfMRI) a vital technique for studying brain activity. However, there is still much to learn about rsfMRI. Investigating rsfMRI connectivity may aid in the detection of abnormal activities. In this paper, we propose studying the functional connectivity of rsfMRI candidates to diagnose epilepsy. 45 rsfMRI candidates, comprising 26 with refractory epilepsy and 19 healthy controls, were enrolled in this study. A data-driven approach known as Independent Component Analysis (ICA) was used to achieve our goal. First, rsfMRI data from both patients and healthy controls were analyzed using group ICA. The components that were obtained were then spatially sorted to find and select meaningful ones. A two-sample t-test was also used to identify abnormal networks in patients and healthy controls. Finally, based on the fractional amplitude of low-frequency fluctuations (fALFF), a chi-square statistic test was used to distinguish the network properties of the patient and healthy control groups. The two-sample t-test analysis yielded abnormal in the default mode network, including the left superior temporal lobe and the left supramarginal. The right precuneus was found to be abnormal in the dorsal attention network. In addition, the frontal cortex showed an abnormal cluster in the medial temporal gyrus. In contrast, the temporal cortex showed an abnormal cluster in the right middle temporal gyrus and the right fronto-operculum gyrus. Finally, the chi-square statistic test was significant, producing a p-value of 0.001 for the analysis. This study offers evidence that investigating rsfMRI connectivity provides an excellent diagnosis option for refractory epilepsy.

***Keywords*****—**Independent Component Analysis, Resting State Network, refractory epilepsy, rsfMRI.

## I. Introduction

EPILEPSY is a persistent brain illness that affects people of all ages is not contagious. According to recent statistics, epilepsy affects more than 50 million individuals globally [1], [2]. Refractory epilepsy, often known as drug-resistant epilepsy, is one of the most challenging forms to diagnose. The condition identified and the major reason for refractory epilepsy is still unknown, and doctors are still trying to figure out why some patients respond to medication while others do not, even though many researchers have studied uncover potential causes [3], [4]. The progress of neuroimaging technology has revealed fresh perspectives on detecting and treating brain disorders.

Brain signals were collected using a variety of methods that were designed for non-invasively studying brain function. One of the most important imaging techniques among them is functional magnetic resonance imaging (fMRI) [5], [6]. fMRI studies are produced using Blood Oxygenation Level Dependent (BOLD) imaging technology, which uses variations in cerebral blood flow between different regions to identify regional activity [7]. One of the two types of fMRI utilized in euroimaging is called resting-state fMRI, which is acquired while the subject is at rest [8]. Examining the resting state network (RSN) functional connectivity may significantly contribute to finding a cure for persons with refractory epilepsy.

The functional connectivity measurements can detect coherent spontaneous neuronal activities within a brain network [9], [10]. To do this, a range of techniques and resources could be employed. One of these is ICA, a data-driven, experimental method used in many fields and applications. The goal of ICA is to break down a multivariate signal into a set of features that represent some structure in the data [11], [12].

In this study, we propose to analyze rsfMRI data using the ICA approach. The current study aims to effectively aid in the identification of abnormal connectivity while also improving surgical precision. Our work is structured as follows: We intend to begin by preprocessing the rsfMRI data. The preprocessed data will then be subjected to group-ICA analysis. A spatial sorting analysis based on particular network masks was also performed to choose the significant components. In addition, a two-sample t-test was conducted based on the significant components between the patient and healthy control groups. Finally, the patient and healthy control groups' fALFF were extracted and statistically assessed using a chi-square test.

## II. Materials and Methods

### A. Participants

The data set for this study originally consisted of 63 subjects (30 patients and 33 healthy controls (HCs)). The image quality of all participants was succinctly inspected and selected. After applying the selection criteria to each candidate, 45 participants were considered for this investigation. The patient group included 26 subjects who underwent preoperative examinations at Shengjing Hospital of China Medical University from January 2018 to July 2019. The evaluation included a detailed

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medical history and neurological examination, complete neuropsychological evaluation, psychiatric evaluation, interictal and ictal onset patterns on long-term scalp video electroencephalography (video-EEG), magnetic resonance imaging (MRI), and fMRI results. All 26 patients underwent surgical resection for medically refractory epilepsy with histopathological confirmed focal cortical dysplasia (FCD). The healthy control candidates were collected by Yameng et al. [13]. After applying the selection criteria, 19 subjects were retained. The subjects had no history of medical, neurological, or psychiatric disease. None of the subjects was taking any medication at the time of testing. All of the patients were gathered and evaluated with clinical standards. The evaluation included a thorough clinical history, a neurological exam, inter-ictal and ictal onset patterns in long-term scalp video-EEG, MRI, and fMRI.

### *B. Data Acquisition*

Every single rs-fMRI measurement was taken and analyzed using a specific epilepsy methodology that is typically utilized in clinical practice.

The MR scans for the patient candidates were obtained using a SIGNA PET/MR scanner (GE Healthcare, Waukesha, WI, USA) with a 16-channel head coil scanner. The following steps were included in the protocol: T1w; TR = 8.5 ms, TE = 3.3 ms, flip angle = 12°, voxel size = 0.4690.4691.000 $mm^3$, FOV = 512512. Sag 3D T1BRAVO SIGNA PET/MR was used to acquire resting-state BOLD images (3.53.44.0 $mm^3$ voxel size, TR = 2000 ms, TE = 35 ms, Flip angle = 90°).

The candidates for the healthy controls group were scanned using a Siemens 20-channel receive-array coil on a 3 Tesla Prisma Siemens Fit scanner. An MPRAGE sequence (TR: 2300 ms, TE: 2.28 ms, 1 mm isotropic spatial resolution, FOV: 256 mm, flip angle: 8°, matrix size: 256256192, acceleration factor: 2) was used to capture the anatomical images. Each scanning section consisted of an anatomical session and two 10-min resting-state sessions. Using an EPI sequence, BOLD fMRI data were collected (TR: 2100 ms, TE: 25 ms, slice thickness: 4 mm, slices: 35, FOV: 240 mm, in-plane resolution: 3 mm).

### *C. Data Processing*

As shown in Fig. 1, we separated our work into three key parts for this investigation: data preprocessing, processing, and statistical inference.

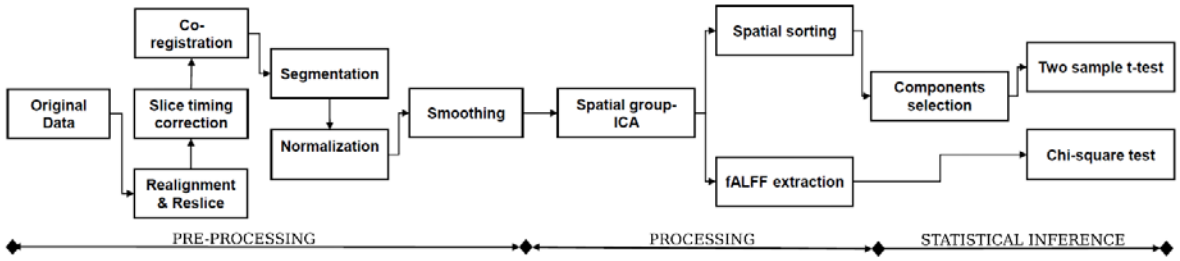


Fig. 1 General flowchart of the processing

During the preprocessing steps, the populations of patients and healthy controls will be examined separately. The preprocessing was carried out using Statistical Parametric Mapping (SPM12). SPM12 is a statistical tool used to investigate differences in brain activity recorded during functional neuroimaging experiments [14], [15]. The preprocessing step was carried out by the standard fMRI processing pipeline described in [16], [17]. Realignment, slice timing correction, co-registration, structural segmentation and normalization, functional normalization, and functional smoothing (with an 8-mm Gaussian kernel as the full-width-at-half maximum [FWHM]) were all performed.

After all preprocessing steps had been finished, the processing phase was carried out using an ICA technique. ICA is one of the most common data-driven methods for fMRI data processing. It can perform a full data-driven discovery of spatial patterns, temporal covariance, and even groups. ICA is an excellent choice for fMRI analysis because it is resistant to artifacts, makes few assumptions about the temporal process or spatial pattern form, and is simple to estimate. One of the most important properties of ICA is its ability to extract components from hybrid fMRI signals, representing large-scale neural networks [18]. In this study, ICA was used to analyze rsfMRI data using the fMRI toolbox GIFT (group ICA for fMRI) [19]. The Infomax algorithm, founded on maximal information transmission, was used to derive subject-specific components utilizing data from each subject concatenated over time [20]. The number of independent components (IC) was 25. Table I depicts four different template masks that were used to spatially sort the components. The default mode network (DMN) and dorsal attention network (DAN), as well as the middle frontal (MFG) and temporal gyrus (MTG), were among the masks used [21].

TABLE I
NETWORK AND THEIR COORDINATES

| RSN | Regions | Coordinate (x, y, z) |
|---|---|---|
| DMN | Medial Prefrontal Cortex (MPFC) | 1, 55, -3 |
| | Left Inferior Parietal (LIPC) | -39, -77, 33 |
| | Right Inferior Parietal (RIPC) | 47, -67, 29 |
| | Posterior Cingulate Cortex (PCC) | 1, -61, 38 |
| DAN | Intraparietal Sulcus (LIPS) | -39, -43, 52 |
| | Intraparietal Sulcus (RIPS) | 39, -42, 54 |
| FC | Left middle frontal gyrus (LMFG) | -45, 51, −7 |
| | Right frontal gyrus (RMFG) | 45, 53, −7 |
| TC | Left Temporal middle gyrus (LMFG) | -59, -29, -3 |
| | Right Temporal gyrus (RMFG) | 55, -29, -3 |

Following the spatial sorting, the components that show a

more significant correlation with a given mask were chosen as meaningful components and can be used for further analysis. Moreover, the fALFF was determined and extracted for the patient and healthy control groups [22].

TABLE II
SUMMARY OF THE RSN FINDINGS

| RSN | Regions | Power spectra | Dynamic range | Coordinates (x, y, z) | | |
|---|---|---|---|---|---|---|
| DMN | LSMG | 10.253 | 0.080 | -48 | -55 | 23 |
| | LSPL | 14.478 | 0.081 | -30 | -61 | 50 |
| | R AnG | 15.340 | 0.084 | 48 | -52 | 35 |
| DAN | RPCu | 16.339 | 0.077 | 12 | -67 | 41 |
| FC | mFG | 6.642 | 0.069 | 3 | 47 | 23 |
| TC | RMTG | 7.796 | 0.072 | 51 | -55 | 5 |
| | RFO | 5.467 | 0.059 | 39 | 11 | 5 |

L: left, R: right, m: medial, FO: frontal operculum, FG: frontal gyrus, SMG: supramarginal Gyrus, SPL: superior parietal gyrus, AnG; angular gyrus



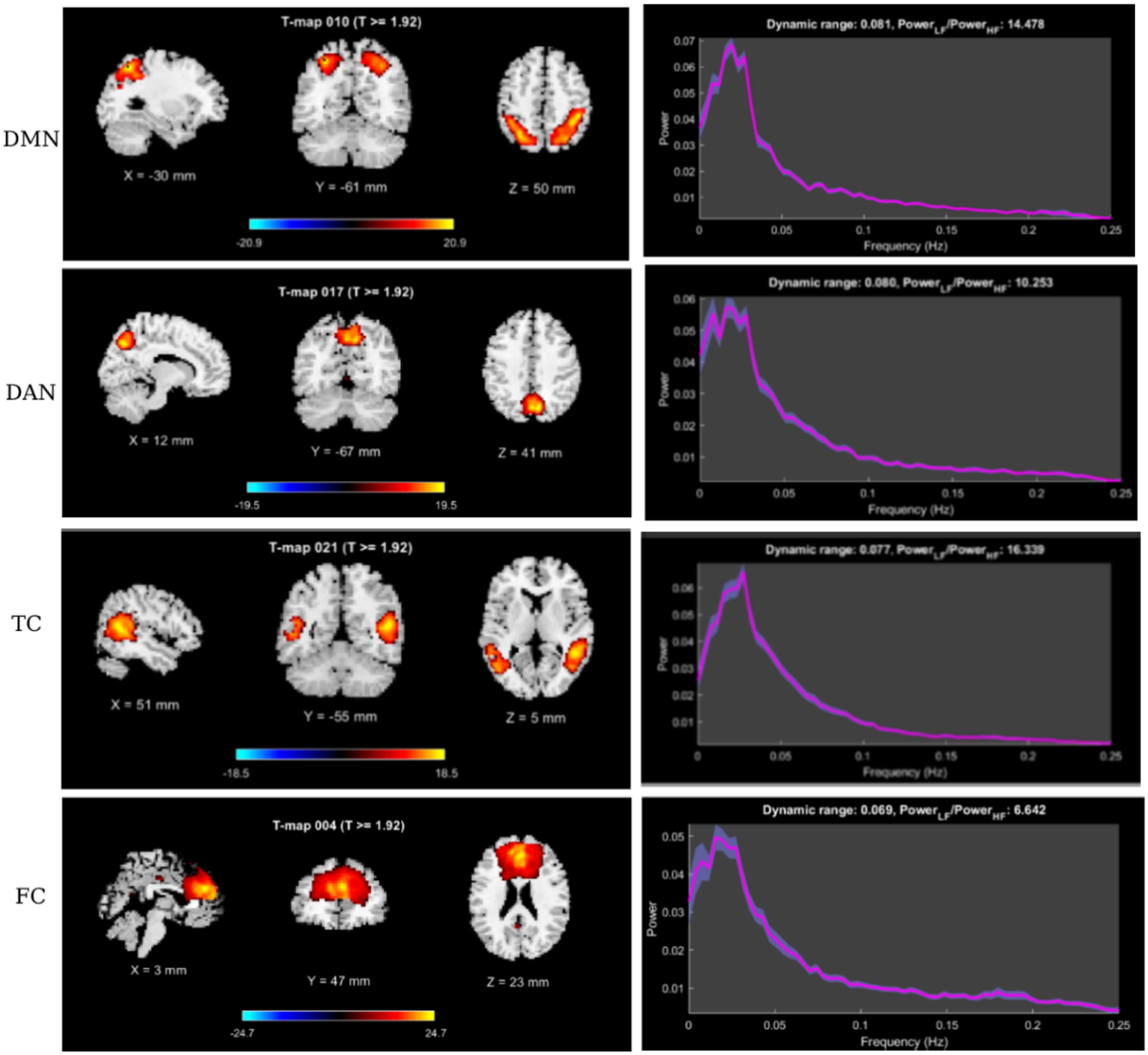


Fig. 2 The two-sample t-test findings (i.e., 10, 14, 17, and 21): Each row shown represents a specific network; column 1 highlights the statistical T-map, and column 2 shows the power spectra value and the dynamic range

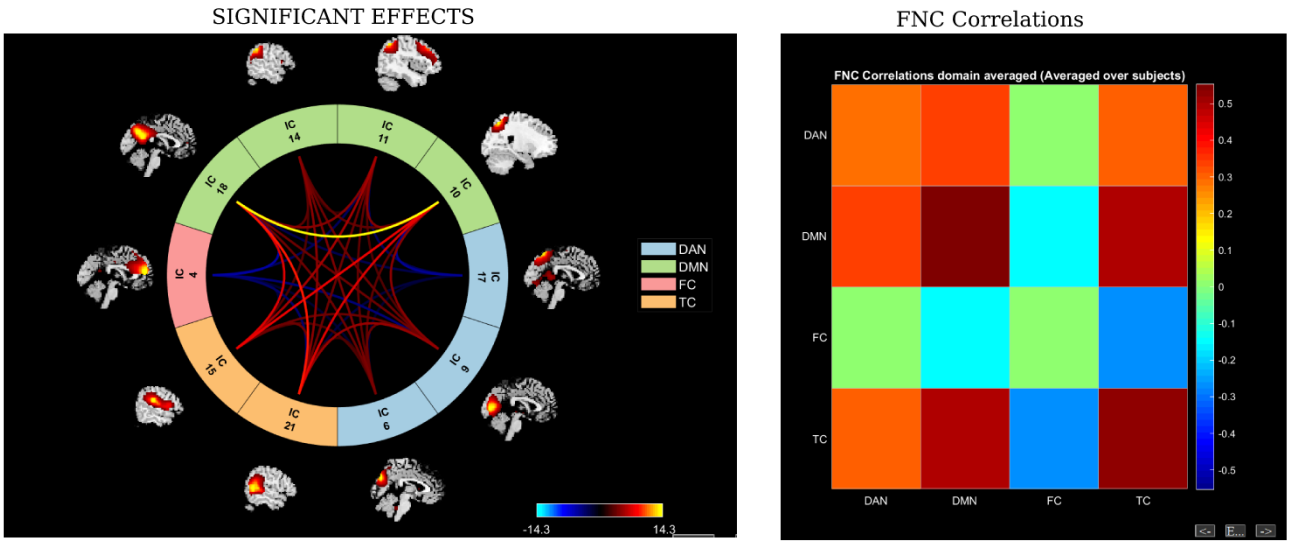


Fig. 3 The connectogram and the averaged FNC correlation

TABLE III
FALFF MEASURES OF THE PATIENT AND HEALTHY CONTROL GROUP

| Components | Controls | | Patients | |
|---|---|---|---|---|
| | fALFF | Dynamic range | fALFF | Dynamic range |
| 1 | 14.23 | 0.0346 | 11.92 | 0.0652 |
| 2 | 7.52 | 0.0283 | 7.88 | 0.0728 |
| 3 | 10.27 | 0.018 | 10.27 | 0.075 |
| 4 | 9.32 | 0.0167 | 11.0 | 0.0753 |
| 5 | 13.22 | 0.0167 | 9.77 | 0.0702 |
| 6 | 12.7 | 0.0224 | 5.99 | 0.0642 |
| 7 | 29.53 | 0.0217 | 16.18 | 0.0758 |
| 8 | 7.16 | 0.0191 | 11.98 | 0.078 |
| 9 | 19.31 | 0.0244 | 4.72 | 0.0596 |
| 10 | 5.89 | 0.0181 | 4.9 | 0.0593 |
| 11 | 5.95 | 0.0139 | 1.42 | 0.038 |
| 12 | 11.84 | 0.0199 | 2.9 | 0.0495 |
| 13 | 15.14 | 0.0228 | 5.72 | 0.0556 |
| 14 | 2.76 | 0.0107 | 6.9 | 0.0628 |
| 15 | 25.65 | 0.0197 | 8.68 | 0.0677 |
| 16 | 4.06 | 0.0106 | 5.95 | 0.0624 |
| 17 | 22.38 | 0.022 | 1.63 | 0.0383 |
| 18 | 20.36 | 0.0236 | 6.23 | 0.0618 |
| 19 | 6.31 | 0.016 | 7.29 | 0.063 |
| 20 | 9.38 | 0.0169 | 1.39 | 0.0336 |
| 21 | 4.3 | 0.0127 | 3.69 | 0.0568 |
| 22 | 16.46 | 0.0178 | 3.57 | 0.06 |
| 23 | 14.08 | 0.0239 | 4.98 | 0.0578 |
| 24 | 4.84 | 0.013 | 1.81 | 0.0378 |
| 25 | 29.42 | 0.0254 | 9.83 | 0.0716 |

The first column displays component No, and the second and third columns, respectively, display the control and patient measures for the patient and healthy control group.

The statistical analysis was performed after the processing step was completed. After identifying and selecting the meaningful components for the DMN, DAN, MFG, and MTG, the MANCOVA tool was set up and used to perform a two-sample t-test between the patient and healthy control. The covariate for the patient was set to '1', while the healthy control was set to '0'.

A chi-square statistical test was performed after the patients extracted and their healthy control's fALFF measurements. This strategy aims to statistically compare the variation between the patient and healthy control groups. The test is considered significant when the P-value is less than 0.05.

## III. Results and Discussion

### A. Results

The two-sample t-test analysis was completed successfully and yielded three important results. These results included the spatial maps (T-maps), the power spectra values, and the functional connectivity correlation. Fig. 2 highlights an example of two-sample t-test results. It contained spatial T-maps, power spectra, and dynamic range values. The T-map results revealed abnormal clusters. For the DMN, these findings included supramarginal gyrus, the left superior parietal lobe, and the right angular gyrus. The right precuneus revealed also a certain abnormality of the DAN. The same trend was observed at the medial frontal and right middle temporal gyrus, with irregularities in the frontal and temporal cortex. Therefore, Table II and Fig. 3 provide additional information about the findings. Furthermore, as shown in Table I, the fALFF measurements for the patients and the healthy control were determined successfully. The chi-square statistic test also yielded a significant result with a P-value of 0.001.

### B. Discussion

Recent research on brain disorders using rsfMRI has produced encouraging findings. It continues to be one of the most important neuroimaging methods used to identify brain disorders [23]. In this work, we used rsfMRI data to examine refractory epilepsy candidates. Our research's objective was to locate the aberrant areas of the brain. This investigation could be conducted using a variety of techniques, including the brain connectivity approach. In our study, we chose to investigate the resting state fMRI connectivity using an ICA data-driven approach. Our analysis strategy worked well and produced

valuable results.

Our research method revealed abnormal brain activity in various areas. This finding suggests that ICA is a good method for investigating abnormal connectivity in refractory epilepsy candidates. ICA has previously been used by numerous researchers to evaluate candidates for fMRI and epilepsy. Boerwinkle et al. [24] investigated the consistency of the seizure onset zone (SOZ) identified by intracranial electroencephalogram (ic-EEG) and the epileptogenic zones (EZ) localization using rsfMRI using the ICA technique. The researchers discovered a link between the gold standard for SOZ localization and rsfMRI-localized EZs. Ebrahimzadeh et al. [25] also compared the ICA results and the EEG-based GLM analyses of fMRI data from individuals with focal epilepsy. The study concluded that ICA findings might help process EEG-fMRI data when anomalies are not immediately visible on scalp EEG.

The chi-square statistic test revealed that the fALFF measures of the patient and healthy control groups were statistically different. This claim is supported by research from Egorova et al. [26], who examined the magnitude of low-frequency changes following a stroke (ALFF). They established fALFF's validity as a predictor of post-stroke depression. Wang et al. [27] also compared fALFF measurements in epilepsy patients with hippocampal sclerosis to healthy controls.

Even though our study performed well and yielded insightful results, some constraints must be removed. For starters, using a data-driven approach to analyze fMRI data may reveal unfavorable data characteristics, such as data corruption caused by motion. rsfMRI is extremely sensitive to movement and subjected to a great deal of noise. This can complicate the ICA analysis [28]. Another disadvantage is that ICA components are susceptible to all types of movement, including rapid shifts and steady, linear drifts [29]. They also provide an accurate reflection of the data. Furthermore, for some networks, multiple clusters were produced, making it difficult to evaluate the results of our investigation. This could be explained by the presence of artifacts, or noise or by the fact that the patient has multiple anomaly locations.

## IV. Conclusion

Resting-state fMRI is a promising tool in the field of neuroimaging. In this study, candidates for refractory epilepsy were evaluated using rsfMRI data and an ICA technique. Our investigation produced encouraging results and essential conclusions. Abnormal brain activity in various areas was observed at the group level. Furthermore, the chi-square test revealed a statistical difference between the patient and healthy control brain properties. The present findings show that rsfMRI can be used to identify candidates who are resistant to epilepsy treatment.

## Acknowledgments

### *Data Availability Statement*

The datasets presented in this article are not readily available because of the requirement of the Ethics Committee of Shengjing Hospital of China Medical University (Shenyang, China). Requests to access the datasets should be directed to Han Li, leoincmu@gmail.com.

### *Ethics Statement*

Shengjing Hospital of China Medical University reviewed and approved the studies involving human participants. The participants' legal guardian/next of kin provided written informed consent to participate in this study.

### *Conflicts of Interest*

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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