Independent Component Analysis Using Resting State-Functional MRI in Patients with Pediatric Epilepsy

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Purpose and Background

Epilepsy is a major cause of neurologic, psychosocial, and socioeconomic morbidity for children throughout the world. In many cases, seizures are refractory to medical therapy and may benefit from neurosurgical intervention. MRI is typically used in children with refractory focal epilepsy to localize the epileptogenic zone (EZ). However, standard MRI fails to identify the epileptogenic zone in many cases. Recently, resting state functional MRI (rs-fMRI) has been used to identify epileptogenic zones (EZ) in children, and to guide neurosurgery for epilepsy (1,2). In this study, we apply previously published techniques to analyze rs-fMRI data in 10 pediatric epilepsy patients retrospectively, with the goal of establishing a working data processing and independent component analysis (ICA) pipeline to sort independent components (IC) into noise, normal resting state network and possible epileptogenic zones. The results of this study will inform a future prospective study utilizing optimized rs-fMRI in pediatric epilepsy patients.

Methods

A total of 10 patients underwent rs-fMRI as part of epilepsy evaluation. MR images were acquired on a 3 Tesla MRI Siemens Prisma scanner. Approximately six-minute rs-fMRI scans were acquired using echo planar imaging sequence with the following parameters: included TR 2,550 msec, TE 33 msec, matrix size 72 x 72, flip angle 900, number of slices 46, slice thickness 3.3 mm with no gap, in-plane resolution 3 x 3 mm, and number of total volumes: 140. Data were processed using eFMRIB Software Library (FSL) tools. Pre-processing steps include slice-timing correction followed by motion correction using MCFLIRT and removal of non-brain structures. These volumes were registered using an affine transform with optimization using boundary-based registration (3). Data underwent independent component analysis using FSL's MELODIC tool. Number of ICs per subject was obtained using dimensionality estimate that utilizes an established Bayesian approach (4). The range of ICs for the 10 subjects included was 31-68. Each IC was rated as typical resting state network or noise or possible EZ independently by 2 raters based on techniques developed by Boerwinkle, et al (1,2). One rater has several years of experience in interpreting functional MRI for pediatric epilepsy. The other rater has several years of experience performing group-wise ICA using rs-fMRI. Language lateralization was attempted by applying previously published techniques (5) and compared to task-based fMRI language lateralization when available.

Results

Rs-fMRI data from 10 patients resulted in 515 ICs total. Most IC's were noise (74%), followed by RSNs (20%) and EZs (6%). Inter-rater reliability for sorting ICs as noise, resting state network and possible EZ was 96.5%. Among the ICs that were not suspicious for EZ by either rater, inter-rater reliability was 98.6%. Tallies shown in Table 1 for noise, RSN and EZ's reflect a consensus between raters for all ICs originally categorized differently (Table 1). If one rater suspected an EZ IC that the other rater did not, it was included as EZ IC. Individual subject data are shown in Table 1. Example of a right sided language network in patient Examples of spatial maps, time courses and power spectra for normal resting state network, noise, and possible EZ ICs are shown in Figures 2, 3 and 4 respectively. Attempted language lateralization via rs-fMRI, task-based fMRI results for language lateralization, MRI findings, EEG findings and rs-fMRI based EZ hypothesis are also shown in Table 1. Agreement between rs-fMRI and EEG lobar localization was 30%. Agreement between rs-fMRI and MRI abnormality was 90%.

Figure 1

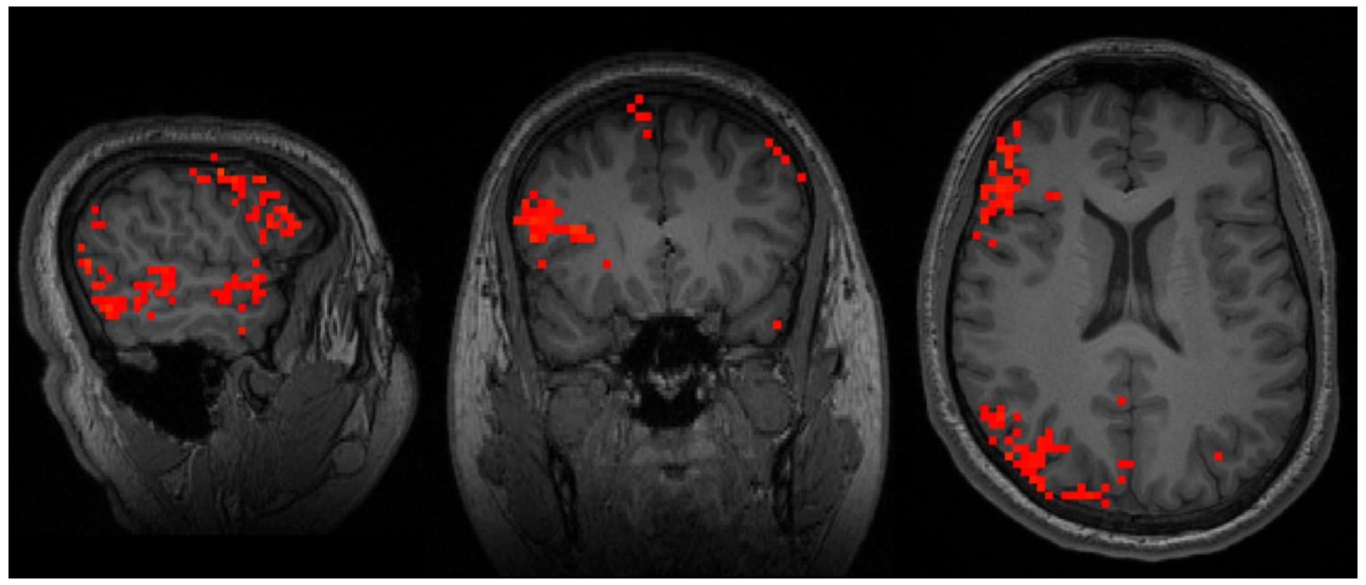

Figure 1 – Co-registered 3D T1 weighted sequence and IC demonstrating functional connectivity in the right frontal operculum and right superior temporal gyrus in patient 9, compatible with language network.

Conclusions

- In this study, we applied previously published techniques to sort ICs obtained from 6-minute rs-fMRI data in 10 pediatric epilepsy patients. The large number of noise ICs was a major limiting factor in this study. Nonetheless, EZs were suspected in multiple patients, with strongest evidence for EZs in patients 2,4, 6 and 10. Low agreement between rs-fMRI and EEG and low language lateralization in this study were likely due to low number of useful, non-noise ICs. This study shows that rs-fMRI is promising for EZ localization and that further studies are necessary to validate the technique. The experience gained from this study will be applied towards a larger pediatric epilepsy cohort prospectively using optimized rs-fMRI acquisition to study EZ detection and language lateralization.

References

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Figure 2

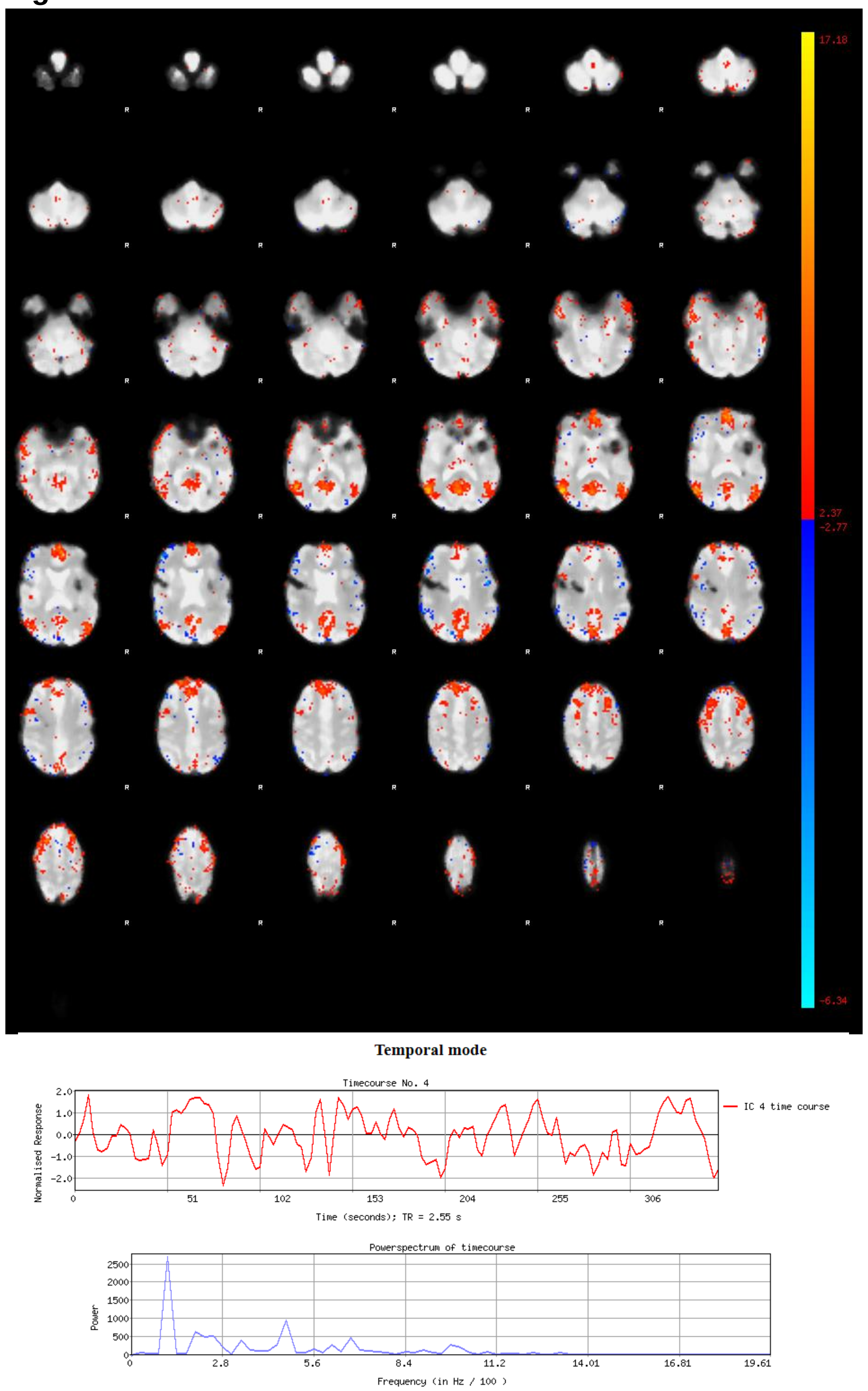

Figure 2 – Normal resting state network in patient 1. Spatial maps demonstrate default mode network. Time course and power spectrum demonstrate broad low frequency oscillations.

Figure 3

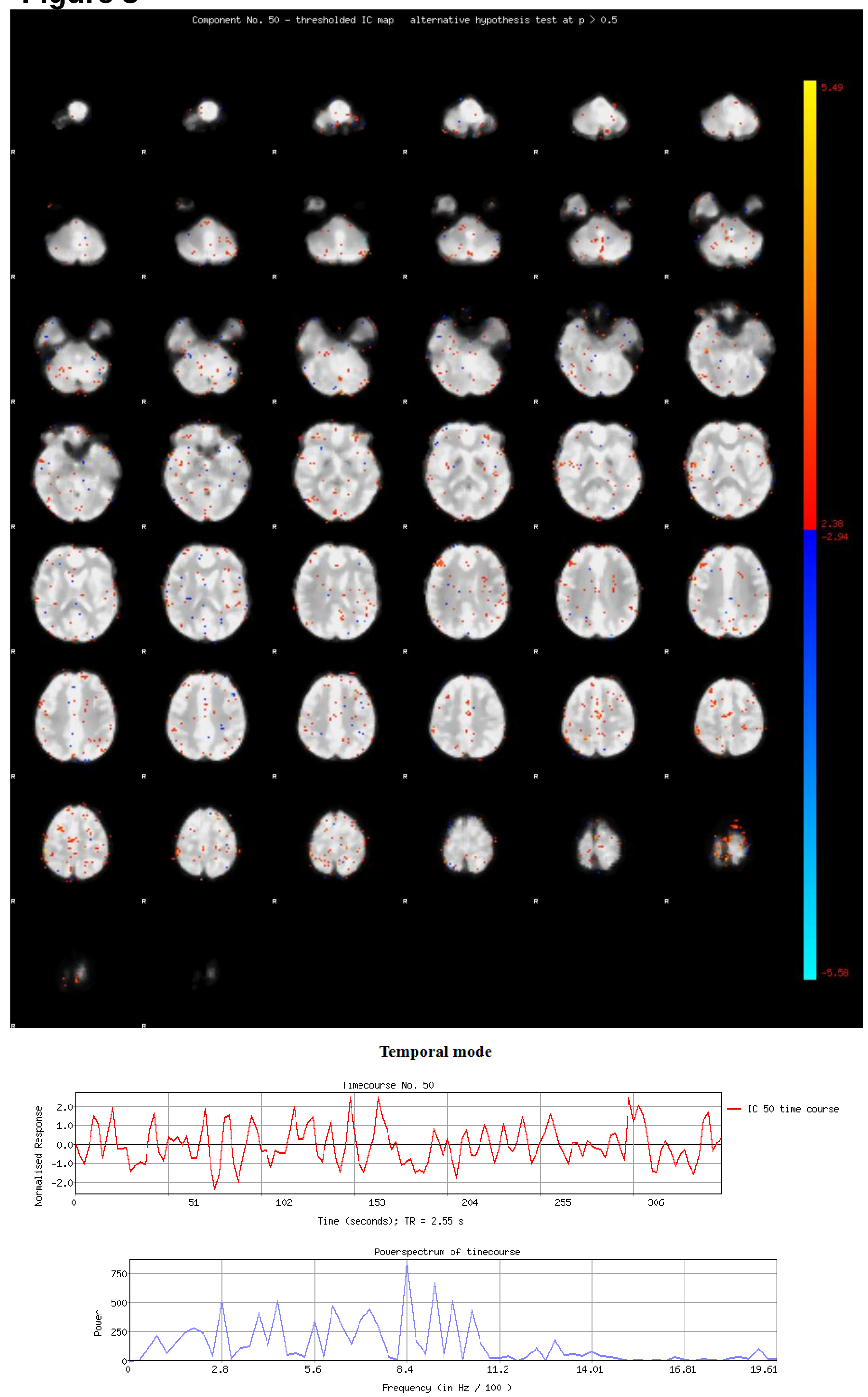

Figure 3 – Clearly noise IC in patient 1. Spatial maps demonstrate no gray matter signal in a known resting state network. Time course and power spectrum demonstrate sharp, oscillations with a spectrum of low to high frequency peaks.

Figure 4

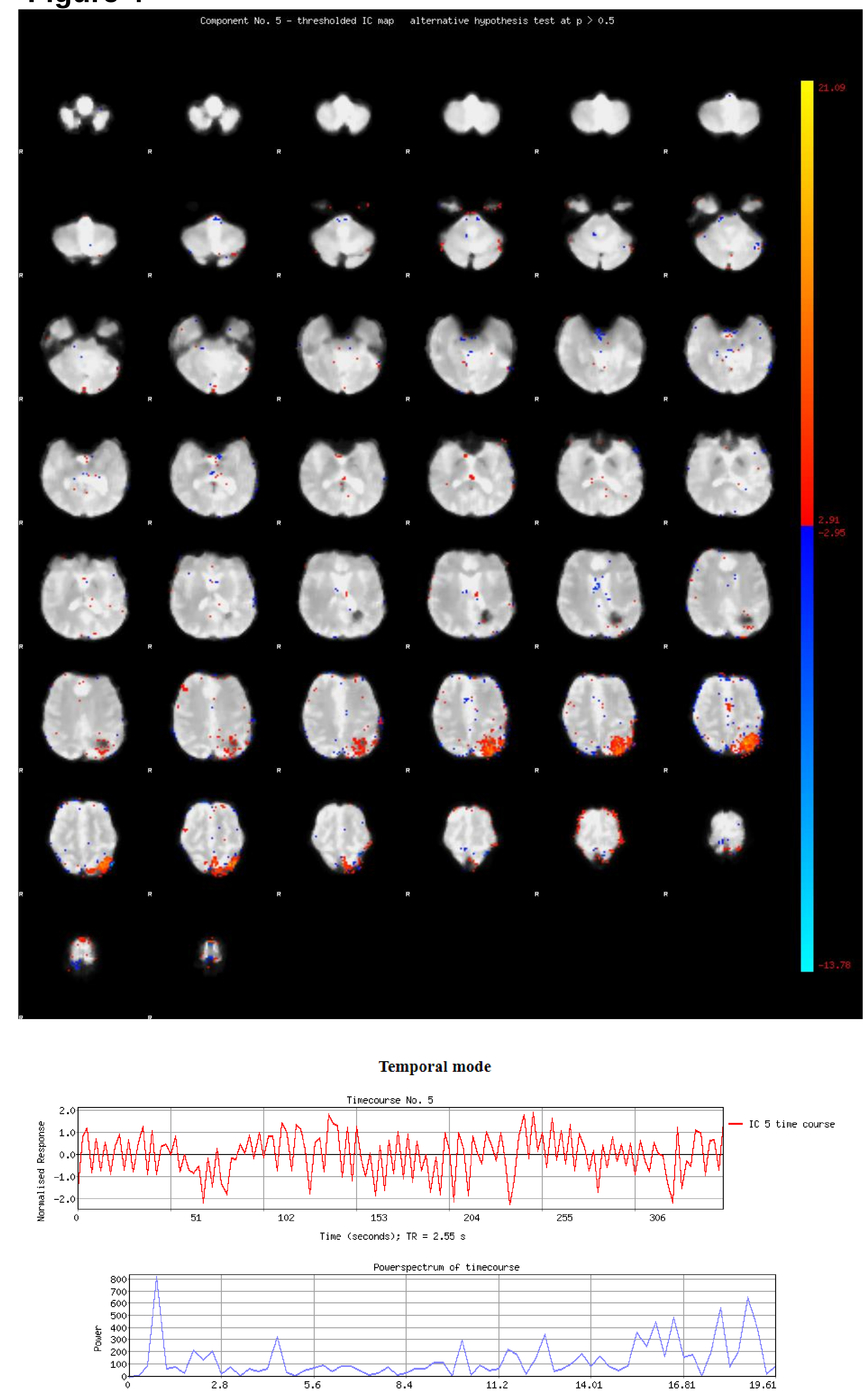

Figure 4 – Possible epileptogenic zone in patient 4. Spatial maps demonstrate a signal source in the left parietal lobe, near a known left parietal AVM. Time course and power spectrum demonstrate sharp oscillations with a spectrum of low to high frequency peaks.

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Table 1

N=10	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Total
Total ICs (sum of Noise, RSN and EZ ICs)	35	68	60	39	52	67	45	61	31	57	515
Noise ICs	18	48	56	20	40	50	29	57	16	47	381
Resting State Network (RSN) ICs	14	12	3	11	12	11	15	4	15	7	104
Possible Epileptogenic Zone (EZ) ICs	3	8	1	8	0	6	1	0	0	3	30
Language ICs and attempted lateralization	1, Left	1, Bilateral	1, Left	1, Right	1, Right	2	2, Right	0	3, Right	0	---
Task-based fMRI language lateralization	Left	Bilateral	Task-based fMRI failed to lateralize language	No task-based data available	Left	No task-based data available	Left	Left	Left	Left	---
MRI abnormality	Cavernomatosis*	Right greater than left periventricular gray matter heterotopias	Right perisylvian, frontotemporal polymicrogyria	Left parietal arteriovenous malformation	Left temporal pole focal cortical dysplasia	Right occipital polymorphous low-grade neuroepithelial tumor of the young	None identified	None identified	None identified	Left frontal encephalomalacia, prior cerebritis	---
Focal EEG epileptiform findings	Left temporal	No focal abnormality	Right temporal	Left posterior temporal	Left temporal	None available	Right frontotemporal and frontocentral	Normal	Left basal temporal	Left superior frontal gyrus, left frontal operculum	---
Lobe (s) containing EZ based on rs-fMRI ICA	Right frontal	Right frontal and temporal	Right temporal	Left parietal	Right occipital	Right occipital and temporal	None	None	None	Left frontal	---

*Patient 1 had multiple cavernous malformations, including a resected lesion in the left insula and a large lesion in the right frontal lobe.