Method for epileptogenic focus localization using BOLD signal complexity analysis

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Target audience: Neuroimaging and neuroscience researchers and clinicians (neurologists/neurosurgeons) interested in Epilepsy.

Purpose: A new approach to the epileptogenic focus localization is proposed in this study using a data-driven methodology applied to functional magnetic resonance imaging (fMRI) data. The aim of this new approach is to complement the work of Morgan and colleagues (2008)[1], in which a bi-dimensional temporal clustering analysis (2dTCA) was developed to identify brain regions with similar temporal profile. In order to identify which of those regions actually correspond to epileptogenic tissue Morgan et al[1] use information from other monitoring techniques, such as structural MRI, electroencephalography (EEG) and positron emission tomography. In the new approach it is proposed a complexity analysis of the blood oxygen level-dependent (BOLD) signals of the regions found with 2dTCA for the identification of the epileptogenic focus. For that purpose two methods were implemented: a multiscale entropy (MSE) analysis[2], modified in order to measure the entropy of BOLD signals with a low number (<1000) of time points, and a detrended fluctuation analysis (DFA)[3] to measure the long-range temporal correlations (LRTC) of the signal. The main hypotheses underlying this new approach are the following: (1) the epileptogenic focus presents a BOLD signal with a distinct temporal profile from the remaining brain parenchyma during interictal activity[1,4]; (2) the epileptogenic focus BOLD signal shows different complexity (lower entropy and stronger LRTC) than healthy parenchyma[5-7]. The innovation of this work is the development of a method able to characterize the complexity of BOLD signals and its application to the localization of the epileptogenic focus.

Materials and Methods: The method was developed in MATLAB environment and its pipeline analysis is depicted in Fig. 1. The first step in this method was to perform a basic preprocessing of the fMRI data comprising slice timing and motion corrections, normalization to MNI template, spatial smoothing, detrending, and bandpass filtering at 0.01-0.1 Hz using DPARSF toolbox[8]. Then, 2dTCA was used to identify the potential epileptogenic foci. The complexity of those potential foci's BOLD signals was measured with the modified MSE and DFA wherefrom two complexity parameters were, respectively, extracted: the complexity index (CI), representing the sum of the entropy values across all scales analyzed[9]; and the scaling exponent (α), representing the quantitative measure of the LRTC.

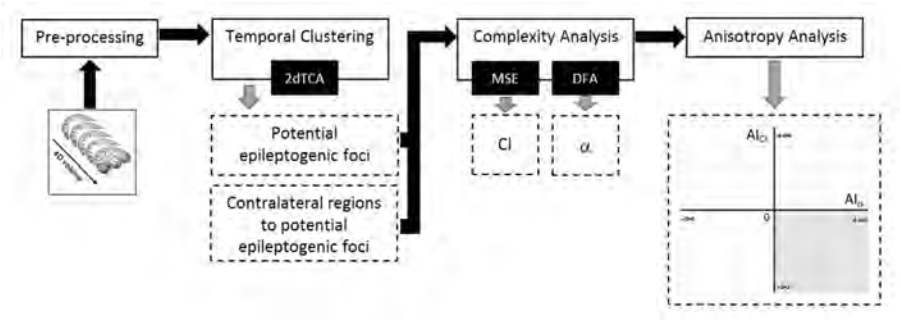

Fig. 1- Flowchart illustrating the pipeline analysis followed to localize the epileptogenic focus. The gray shadow on the right chart of the figure, represents the target region in which the anisotropy analysis result of the most likely epileptogenic focus should lie. 2dTCA: bi-dimensional temporal clustering analysis. MSE: multiscale entropy. DFA: detrended fluctuation analysis. CI: complex index. α: scaling exponent. AI: anisotropy index.

The complexity assessment was accomplished by computing the normalized difference [or anisotropy (AI)] between the complexity parameters CI and α of the regions found by 2dTCA and those of the corresponding contralateral regions. The most likely epileptogenic focus was chosen as the one with lowest AI_{CI} and highest AI_{α}. The anisotropies are associated with CI and α parameters, respectively, (see grey shadow in the chart of Fig. 1). Finally, the functional connectivity (FC) between the epileptogenic focus found by the method and the remaining brain was computed using Pearson's correlation.

In order to demonstrate the applicability of these methods, two epileptic patients, one with left temporal lobe epilepsy (P1), and the other with bilateral temporal epilepsy with right temporal-parietal predominance (P2), were studied. Functional scanning was performed using a Magneton Avanto 1.5T MRI scanner (Siemens, Erlanger, Germany) and a T2* weighted single-shot gradient echo sequence with echo planar imaging readout (matrix = 64x64, voxel size = 3.44x3.44x5.5 mm^3, 21 interleaved slices, TR/TE = 2 s/50 ms, 150 volumes).

Results and Discussion: The epileptogenic foci found by the method match known clinical information and EEG studies for both patients. In particular, it was observed that the epileptogenic tissue has a temporal behavior different from healthy tissue. Further, the epileptogenic foci have lower entropy of BOLD signals than the corresponding contralateral regions signals (Fig. 2, left), thus supporting the main finding in Protzner (2010)[7]. Regarding the LRTC hypothesis[5,6], only one patient (P2) exhibited stronger LRTC of BOLD signals of the epileptogenic focus than the ones of the corresponding contralateral regions. For the other patient (P1) the AI_{α} is close to zero. This is in agreement with FC results (Fig. 2, middle) which show that the region contralateral to the focus is part of an epileptic network strongly correlated with the epileptogenic focus. Finally, the FC result of patient P2 shows correlations between bilateral parietal and temporal regions which are in agreement with known clinical information.

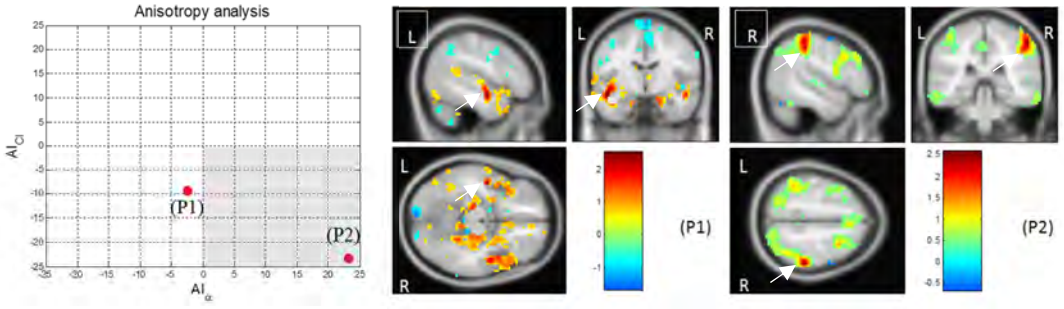

Fig. 2- Results from the anisotropy analysis (**left**) and from functional connectivity of the epileptogenic focus (white arrow) found by the method and the remaining brain (**right**) for the patient with left temporal lobe epilepsy (P1), and the patient with bilateral temporal epilepsy with right temporal-parietal predominance (P2). CI: complex index. α: scaling exponent. AI: anisotropy index. L: left; R: right.

Conclusion: New perspectives are envisioned concerning the use of this method in the medical care of epilepsy, in particular, to complement/validate conventional epileptogenic focus localization methods. Furthermore, this methodology could also be used to study the BOLD signal dynamics of both task and resting-state networks, and characterize them in terms of their complexity.

References: [1] Morgan et al. (2008) Hum. Brain Mapp., 29:57–69. [2] Costa et al. (2002) Phys. Rev. Lett.. 89:068102. [3] Peng et al. (1994) Phys. Rev. E 49:1685–89. [4] Salek-Haddadi et al. (2006) Brain Res, 1088:148-166. [5] Parish et al. (2004) Neuroscience, 125:1069–76. [6] Monto et al. (2007) Cereb. Cortex, 17:1386–93. [7] Protzner et al. (2010) Arch Ital Biol, 148:289–97. [8] Chao-Gan et al. (2010) Front. Syst. Neurosci., 4:13. [9] Yang et al (2013) Neurobiol Aging 34:428–38.

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