Enhanced Regional Clustering Algorithm in Seizure Location Identification

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Abstract - Epilepsy is a chronic condition that is characterized by frequent occurrence of seizure. The treatment of epilepsy using anticonvulsants that suppress the rapid neuron spikes in brain is promising; however, a permanent fix is always lacked. The region on brain that is responsible for seizure if identified exactly, the diseased area can be expelled and that could be a permanent fix. Generally, IEEG (Intracranial Electroencephalogram) an invasive procedure is adopted to diagnose the location of seizure, though the results are very reliable and considered as a golden standard, the procedure is a complex and risky one. To overcome these difficulties, fMRI (Functional magnetic resonance imaging) is used to read the internal anatomical and metabolic nature of brain, an algorithm (erKNOTS, enhanced regional K based Numbering Out of Time Slices) that analyse each individual voxel is developed and implemented. The result obtained by the developed algorithm is found to be in agreement with those obtained through IEEG. The findings were further validated with Regional homogeneity and Functional connectivity.

1. Introduction

Epilepsy, an abnormality in brain is considered in different way in different parts of the world. It has a rich history and it was considered in different ways from; a cause of evil spirits as mentioned in the Holy Bible to considering it’s as a Goddess in certain tribal group. This disease until up the past few decades was not of its exact reason of cause, however now with advancement in medical field with the help of signal and imaging the epilepsy study is been made lighter and effective. The complex nature of the brain, its anatomy and the related metabolic activities were understandable.

Epilepsy is condition in which a decent measure of cases can be constrained by drugs whenever taken all along life, yet an everlasting fix is not guaranteed. To the epileptic patients who are impervious to drugs preoperative epilepsy assessment followed by careful surgical treatment had led to numerous benefits including the improvement in nature of the epileptic patient’s life, improved to almost complete seizure free patients. The pre-surgical medical procedure is intended to recognize the specific area of the locale where neurological lop-sidedness is and helping the doctor in eliminating the specific ailing area to bring about complete seizure removal in patient. The main difficulty is that its probability of growing resulting in new neurological issues. This writing demonstrates that there is a need in the current clinical environment to draw out another technique to distinguish the epileptic seizures without affecting the normal functionalities of the brain by harming its tissues at vicinity. The intracranial EEG stayed as the perfect norm; however a surgical approach just for the assessment of the illness is excessively hazardous and might prompt some other issue inferable from the intricacy of the procedure [1].

This gave rise to the idea of developing a methodology using advanced imaging modalities to learn the internal anatomical and metabolic functionalities of brain which in turn would replace the highly risky and invasive evaluation procedure, the IEEG with a non-invasive, possibly non-contact procedure, fMRI.

fMRI, functional Magnetic Resonance imaging alongside EEG Electroencephalohraphy has end up being of a lot higher use in finding out the localization of the epilepsy in adults. This imaging methodology, fMRI has demonstrated many promising outcomes and the system in addition, is a non-intrusive and a non-contact strategy. The idea of the imaging methodology requires the patient to stay inert while images are being procured subsequently, youngsters are generally given sedation and the grown-ups are taught to wait all through the technique which may take from 2 to 10 minutes. Another significant feature of this methodology fMRI, is the patient explicit brain functions can likewise be concentrated with high spatial resolution, as against EEG. A task based fMRI is utilized in which the patient is given a specific errand and the brain movement associated with that is studied [2]. This is valuable in distinguishing the right elements of the areas of the mind and it can likewise be utilized in making a standard guide on the capacities over the regions of brain of the individuals of various demography. The non-intrusive nature of this system suggests the closing of fMRI as the apt investigation tool to distinguish epileptic areas of brain.

The therapy of this illness starts with a promising finding; from the day of verification of this affliction, there have been countless indicative methodologies to precisely perceive the territory of the seizure. The characteristic systems include strategies from the IEEG (intracranial Electroencephalography) to the non-invasive fMRI (Functional Magnetic Resonance Imaging). The invasive IEEG system was the solid and proven procedure. However, in any case it encounters a real trouble of prominence and various difficulties. A further study expresses that dubious results like cerebral agonies or below average fever were
observed in 10 of 18 (56%) patients after Stereo EEG, an Invasive EEG methodology [3]. This writing was exceptionally valuable in thinking of a system to supplant the obtrusive IEEG with fMRI.

To conquer these issues, a non-contact imaging module fMRI is used for the distinguishingly recognizing the epileptic seizure territory. Rather than the MRI, the functional MRI (fMRI) shows the anatomical and metabolic, Functional qualities of the area of brain [4]. fMRI is non-intrusive, non-contact imaging that has high spatial and transient resolution and it can additionally be utilized in brain complexity study [5]. fMRI is extraordinarily informative as the resulting slices are made as thin as possible to intensify the fMRI quality [6]. As the resolution is amazingly high, a little development can moreover impact the crudeness of the information, consequently it is basic in keeping up the subject exceptionally still all through the assessment. To make the examination more practical information of around 450 people were utilized from a confidential source and pre-processed [7]. To eliminate the fundamental aggravations and development, the slices of the information are continually overlooked. The readied fMRI picture can help in decisively choosing the territory of the seizure in epileptic patients.

2. Pre-processing
The fMRI image for this study is obtained from a 3T MRI machine and the images are in raw form, hence to make the images into much more meaningful form the data obtained is pre-processed in steps as shown in the Figure 1.

![Data Processing of fMRI to identify epileptic seizure](image)

**Fig. 1: Data Processing of fMRI to identify epileptic seizure**

**Initial slice correction**
A patient made to lie on a calm environment with the headsets on will take initially few time to get acustomized to the new environment [8]. To get at his best comfort level he will try to move his head on all possible ways till he finds an optimum degree at which he will rest his head and lie unaffected. The time the patient took to adjust his head will also be considered as the image acquisition time, however if the slices of image taken at this time interval is considered under study, it would give false results. To set it right the initial time slices are removed from the raw data as the first step in processing the image.
**Slice time correction**

A fMRI produced image will be in raw format and the slices will be overlapping on each other. This images are meaningless unless it is seperated as separate slices and then reoriented such that they all have a standard apex and base. To have the slices seperated, a small time correction is adopted such that all the images are started acquiring from the same initial point. This step ensures number of slices are unique, therby forming a better 3 Dimensional image as shown in Figure 2 [9].

![Fig. 2: Slice time correction](image)

**Reorientation**

The slice time corrected images are unique however they are in completely different orientation owing to the shape of the scanners that acquire image from different axis. As the images ae taken at different angle from different origin point and time, overlapping them into a single 3D image will result in a meaningless data. To set them apart and retain a common orientation they are made to undergo certain physical reorientation. The images are translated and rotated so as to fit in according to the common reference point. In this study AC (Anterior Commissure) which is considered to be the anatomical center is considered as the reference point. The slices are reoriented into a standard template frame [10]. By reorientation they go through translation that is the linear movement so that they overlie on each other, rotation so that their origin angle is the same. The reorientation adopted is shown in Figure 3. The reoriented image is much meaningful and provides the fullest information.

![Fig. 1: Reorientation, Translation and rotation of the image](image)

**Co registration**

Cooregisteration in the fMRI imaging as like the other steps is very useful as it is the reason behinf the complete The anatomical data is to be side referenced when the metabolic actovoty is being traced. To do the same it is necessary that we use both the T1 and T2 weighed images as well the structural data. They are overlapped over each other such that they both, the structural and functional volumes co-exist on the same place. The coregistered image is shown in Figure 4.

![Fig. 2: Co-registration of the structural and functional image](image)

**Segmentation**

The human brain is classified under various types both anatomically and functionally, here in this research only the grey matter of the brain is considered as it has cumbersome interconnections of neurons[11]. To be more specific with the study the other regions are segmented out using a special algorithm. The MNI template is followed in the study to help in segmentic the functional part of the fMRI images such that only the white matter and the Cerebro Spinal Fluid (CSF) is regressed out. The Broadman reference is used as an anatomical reference to differentiate between regions.

**Normalization**

Normalization is the standardization process in which the data is set to be fit into a globally accepted format. The patients data is proposed to standardize only then the open source algorithm can be applied and checked for its effectiveness in the seizure identification. The healthy controls data are also standardized usualy against the MNI template, in cetain cases Talirach is also used [12]. In our study MNI is preferred and adopted. The standardization is performed and all the pre-processed images are now set to have uniform size, structure and dimensions. Further only the normalized data can be used for the processing of low frequency fluctuations.

**Smoothing**

The fMRI data has good spatial and temporal resolution, the study maily considers the time series hence the temporal resolution is greatly relied on. Here we make use of the spatial data to smoothen itself so that the noise effects are evaded. As the head motion and slice time corrections are already performed, the temporal resolution will be already at
its best efficiency. The earlier Regional algorithm uses the smoothed data for its study whereas in the new enhanced regional clustering is done as a post process [13]. This is to make sure that every voxel is processed for the study with its raw value. The effects of using various filters of different values such as 6mm and 8mm is shown in Figure 5.

Fig. 5: fMRI image smoothing, the effects of smoothing at various FWHM

Filter
In any functional study the data that is processed finds its application mainly concentrated to the frequency range of 0.01 Hz to 0.025 Hz[14]. The fALFF greatly relies on the frequency distribution as the study focuses on the tiny oscillations; the grey matter has its subjects usually operating at the frequency range of 0.01 to 0.073 Hz and in the range 0.073 to 0.25 Hz, the considerable higher frequency values the white matter and its subordinate functionalities can be studied [15]. Further the time study with respect to frequency can also be used in distinguishing the grey matter from white matter.

Region of interest (ROI)
The fMRI study focuses on the identification of the seizure that will help the physician in both the assessing and planning the surgery and to predict the post operative outcome. To ensure that the best results are promised, in addition to the segmentation and filtering the study makes use of ROI mask [16]. The mask is virtually made layer that is made to overlap on the regions of brain which will allow only the grey matter to emerge out such that there is no other part of the brain involved under the study.

3. Enhanced Regional Clustering
The flow of the preprocessing and the processing of the images to get a meaningful and informative data are given as a flowchart.

The data obtained from the fMRI are in raw format and it has to be processed to make it meaningfully, data available format. To get the useful data the raw images are subjected to the Slice timing and head motion correction, Reorientation, Coregistration, Normalization, Segmentation, Smoothing and Filtering.

Fig. 6: a) Enhanced regional clustering results highlighting Right medial temporal region, b) shows IEEG results highlighting right medial region but a large area, d) ReHo results highlighting right precunious and d) FC result highlighting Amygdala

The images that are preprocessed are then taken into processing where the regions of the epileptic seizure are accurately identified. In this procedure the image that is first taken as a whole set, taking the advantage of its matrix nature the image is clustered as one, unlike Regional homogeneity in which the clusters are made as per certain predefined order. This complete clustering is done and their determinant rank is identified using the modified Kendalls coefficients with the consideration of the complete set of voxels in the 3D image considered under the study. The coefficient is utilized for finding the rank of the voxels in the image.

\[ \Omega = \sum (J_i^2 - \bar{n})^2 / K^2(n^3 - n) / (K^2(n^3 - n)) \]

\( \Omega \) is the Kendall Coefficient of Concordance, \( J \) is mean of the Ji and K is the number of time courses and n is the number of ranks. The image obtained is then realized as a 3D image in a software 3D slicer where the sagittal, axial, and coronal axis of the image can be seen. On applying the heat map of intensity on the processed image we can observe the regions with very high correlation corresponds to the diseased region or the region that is the cause for the seizure.
The output is further made accurate by comparing the resultant in two arrangements, initially the right and left region similarity is studied and then a sample 2T test with healthy controls is made. Then the compared results with a threshold of \( p <0.01 \) will yield data that shows the exact location of the seizure. A patient data is in Figure 6 shows the exact location of the epilepsy source.
The output is then compared against the already taken IEEG results to study its accuracy and it is found to be very exact. To validate these results the images are further studied using Regional Homogeneity, fractional Amplitude of Low-frequency Fluctuations and Functional connectivity. The result obtained is tabulated with the other supporting values.
such as Boardman Area number which specifies the region of brain, Left or Right (L/R) of brain; the volume of the highlighted region; its MNI dimensions in the template; the probability, height and volume threshold of the sample 2 T test. The results were found to complement one another and the region identified is very accurate and is also proven from the confidential data in a reputed private hospital. The same result is shown in the Table 1.

| Method | Region                  | Boardman Area | L/R | Volume | Probability | Height Threshold | Volume Threshold |
|--------|-------------------------|----------------|-----|--------|-------------|-----------------|------------------|
| IEEG   | Right Medial Temporal   | 41,42          | R   | 3615   | >0.001      | 3.55181          | 50               |
| ALFF   | Right Temporal          | 41,42          | R   | 2981   | >0.002      | 3.55181          | 50               |
| fALFF  | Right Temporal          | 41,42          | R   | 2651   | >0.003      | 3.55181          | 50               |
| ReHo   | Right Medial Temporal   | 41,42          | R   | 2091   | >0.004      | 3.55181          | 50               |
| ERC    | Right Medial Temporal   | 41,42          | R   | 1614   | >0.004      | 3.55181          | 50               |
| FC     | Amygdala. R             | 42             | R   | 701    | NA          | NA              | NA               |

**Table 1**: Result Comparison Against its Golden Standard

4. Conclusion
Enhanced regional clustering on fMRI proved that the epileptic regions of the brain can be identified with high precision and accuracy. The Enhanced regional clustering makes use of the matrix nature of the 3-Dimensional fMRI image and rather than clustering them as a small cluster as opposed to what is being done in Regional Homogeneity performs a complete study on the both the hemispheres of the brain. To make the processing fast the regions of possibility are masked and the process is applied only on the region of interest which is the region with possibility more neuronal activity. Few exceptions such as the CSF, the breathing pattern change, the cardiovascular disturbance was considered and are included under the mask. The regions that were found to be higher correlation were found to be the regions where the epilepsy originated. The data derived is compared against the control group of 450 data. These results were also validated by the golden standard IEEG on the same patients and were found to be very accurate. The same results were then cross validated using the fractional Amplitude of Low Frequency Fluctuations and Functional Connectivity. The localization of the focus of the exact epileptic seizure is then used as a guide for the surgeon to remove only the damaged region leaving the healthy region intact which will be a permanent fix for all the epileptic patients even to those who cannot be helped with the medications.

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