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Deep Learning with Edge Computing for Localization of Epileptogenicity using Multimodal rs-fMRI and EEG Big Data

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***Abstract*—Epilepsy is a chronic brain disorder characterized by the occurrence of spontaneous seizures of which about 30 percent of patients remain medically intractable and may undergo surgical intervention; despite the latter, some may still fail to attain a seizure-free outcome. Functional changes may precede structural ones in the epileptic brain and may be detectable using existing noninvasive modalities. Functional connectivity analysis through electroencephalography (EEG) and resting state-functional magnetic resonance imaging (rs-fMRI), complemented by diffusion tensor imaging (DTI), has provided such meaningful input in cases of temporal lobe epilepsy (TLE). Recently, the emergence of edge computing has provided competent solutions enabling context-aware and real-time response services for users. By leveraging the potential of autonomic edge computing in epilepsy, we develop and deploy both noninvasive and invasive methods for the monitoring, evaluation and regulation of the epileptic brain, with responsive neurostimulation (RNS; Neuropace). First, an autonomic edge computing framework is proposed for processing of big data as part of a decision support system for surgical candidacy. Second, an optimized model for estimation of the epileptogenic network using independently acquired EEG and rs-fMRI is presented. Third, an unsupervised feature extraction model is developed based on a convolutional deep learning structure for distinguishing interictal epileptic discharge (IED) periods from nonIED periods using electrographic signals from electrocorticography (ECoG). Experimental and simulation results from actual patient data validate the effectiveness of the proposed methods.**

***Index Terms*—Autonomic Computing, Deep Learning, Edge Computing, Epilepsy Seizure Localization, EEG, rs-fMRI, Medical Big Data, Health Monitoring and Treatment.**

I. Introduction

Motivation: One percent of the world's population suffers from epilepsy [1], a chronic disorder characterized by the occurrence of spontaneous seizures. About 30 percent of patients remain medically intractable and may undergo surgical intervention; despite the latter, some may still fail to attain a seizure-free outcome [2], [3]. The brain-computer interface (BCI) allows direct communication between the human brain and a computer providing for data acquisition and analysis leading to the restoration of function. Both noninvasive and invasive BCIs have been developed in recent years. Noninvasive BCIs use multiple electrodes that are spatially distributed over the scalp to capture the brains spontaneous electrical activities based on electroencephalography (EEG). In contrast, invasive BCIs use surgically implanted electrodes for a direct interface with the brain through electrocorticography (ECoG).

Brain Activity: Both EEG and ECoG record the brain's spontaneous electrical activity using multiple electrodes spatially distributed over the scalp or intracranially. It is necessary first to confirm, electrographically, the presence of epileptogenicity and thus a diagnosis of epilepsy. The temporal dynamics of brain activity can be categorized into four states. The interictal or baseline state presents between seizures. The preictal state precedes the seizure or ictal activity. The ictal state identifies the interval during which activity manifests as a seizure. Finally, the postictal state occurs following the ictus. In general, the ictal or seizure state occurs when the brain assumes a synchronized pattern of neuronoglial activity. Clinically, these may manifest clinically in a number of ways ranging from partial seizures with or without loss of consciousness and a localized electrographic expression to generalized seizures that have a widespread expression throughout both cerebral hemispheres. Seizure prediction methodologies must identify the preictal state sufficiently well to differentiate it from other states and with sufficient timing in order to launch an appropriate signal that interrupts the evolution of the ictus.

Medical Big Data: The current and future challenge for BCI centers upon developing methods and systems to remove noise, extract meaningful features and learn from big data [4]. Generally, there are three main steps to develop a system and to make biosignals useful in real-world settings. These include real-time data collection, data processing (e.g., feature extraction and classification) by a computer and biofeedback to apply the desired action. The requirements of a practical

BCI system include methods for signal processing, machine learning, and brain-state prediction in large data sets collected from user populations in real-time and in combination with their health records.Learning applications of big data in the form of real-time acquisition with the background of the electronic healthcare record (EHR) provide for the generation of new knowledge that will aid in predictions of outcome and, therefore, prognosis [5]. This situation calls for the safe storage of a large archive and for high computational resources to process big data. Accordingly, next generation BCI systems must be connected to high-performance computing servers in order to be able to adopt predictive models and to execute computation in real-time for large incoming datasets. Cloud computing and edge computing are new Information and Communications Technology (ICT) that enables ubiquitous and on-demand access to healthcare databases and computational resources through the global Internet.

Autonomic Edge Computing: In many health care systems, cloud computing has been used as a scalable and cost-efficient solution for storing and processing of big data collected from a large number of biosensors. However, such systems face many key challenges regarding location awareness and latency-sensitivity [6]. An emerging solution to overcome these issues is the provision of an extra layer—edge computing [7], [8]—as a smart gateway that bridges end users with remote cloud servers. The realization of edge computing enables various benefits such as low latency, location awareness, geographical distribution and support for online analytics and diagnosis. The recent introduction of a closed loop system for localized ECoG and strategic stimulus delivery (i.e., RNS; Neuropace) has provided greater opportunity to achieve control of an epileptogenic network although further solutions are required to better actuate the system for optimal efficacy and to bring about an improved quality of life for these patients. The goal of autonomic computing is to free the human mind from low level detail, as in a requirement to manually institute a command, and create a system with self-management capabilities. We outline the concept of designing an autonomic edge computing system in which the goal is to regulate the epileptogenic network automatically in order to prevent it from expressing itself clinically.

Challenges: Several challenges exist in developing an autonomic computing system for detection and diagnosis of neurological disorders. Firstly, the differentiation among different brain states such as ictal, preictal, and interictal as well as between normal from abnormal activities is key in implementing self-management system for brain disorders. Secondly, learning from patient data towards self optimization of the autonomic system is paramount in real-time systems. Also, transferring knowledge from experts, neurologists, to autonomic computing systems is non trivial and yet essential for the correct detection and consequently the reduction of the false positive ratio. Thirdly, designing a self mechanism to detect abnormal electrical events and to active a RNS device for providing stimulation to seizure activities is paramount. Fourthly, providing robustness of the system is crucial as we deal with human and patient safety; stability, survivability, and reliability of the autonomic computing system for health care are also critical and challenging. Lastly, using new technologies in neuroimaging and brain mapping produces large amounts of spatially-oriented data over relatively brief durations [9] leading to a medical big data problem. This situation calls for computational methods to extract meaningful results, for safe storage of a large archive, and for high computational resources to process the big data in real time.

Our Goal and Contributions: The goal of this paper is to design, develop, and implement an autonomic computing system for seizure detection using invasive and noninvasive electrographic data. Moreover, we localize the seizure focus and estimate brain network connectivity using resting state-functional magnetic resonance imaging (rs-fMRI) and EEG data analysis.

To address the many existing challenges, we introduce a new method for processing multimodal rs-fMRI and EEG big data for epileptogenic network definition and prediction of seizure (ictal) onset. We developed a deep-learning approach to extract high order features for seizure detection and prediction in epilepsy, leveraging the emerging mobile-edge computing platform. Specifically, our contributions include the development of the following novel methods:

- A mobile edge cloud framework for real-time and ubiquitous processing of medical big data such as EEG, ECoG, and fMRI.
- An optimized model for localization of Epileptogenicity and Estimation of Brain Networks using independently acquired EEG and rs-fMRI data.
- An unsupervised feature extraction model for identification of interictal epileptic discharge (IED) and nonIED time intervals in electrographic data via convolution deep learning and classification of features by an optimized nonlinear SVM.

The proposed system has the ability of pervasive data collection and analysis, which is useful in real-life support for epilepsy patients. To study accuracy and performance, the system is evaluated and compared to other methods on a benchmark epilepsy dataset.

Outline: The remainder of this paper is organized as follows. In Sect. II, we provide a literature review. In Sect. III, we present an autonomic edge computing infrastructure for medical big data processing. In Sect. IV, we present a solution including rs-fMRI analysis, high-level feature extraction by deep learning, time- and frequency-based feature extraction, classification of EEG features, and identification of IED and nonIED time intervals. In Sect. V, we discuss the proof-of-concept prototype of our BCI seizure predictor and show results. Finally, in Sect. VI, we draw the main conclusions.

II. Literature Review

We provide here an overview of previous studies on seizure detection and prediction systems as well as on big data management for epilepsy. In general, existing works have focused on local processing and storage without considering multiple

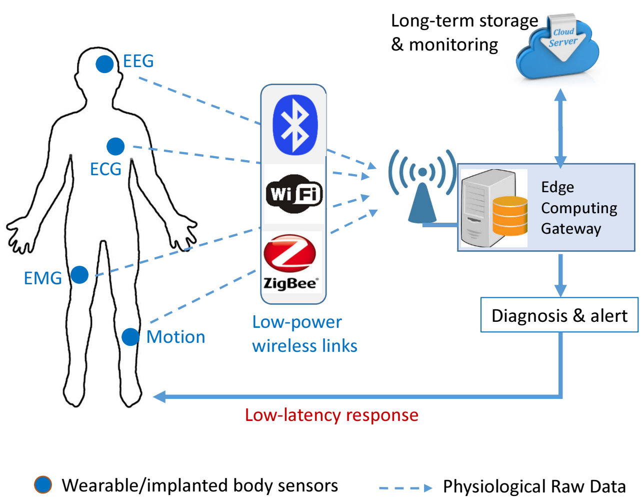

Fig. 1. Illustration of the autonomic edge computing system for health monitoring and treatment.

channels and big patient data. The current work is built upon preliminary findings using a multitier distributed computing structure based on Mobile Device Cloud (MDC) and cloud computing for real-time seizure detection [10]. The deep-learning approach pertaining to BCI has been considered in very few works. Lu et al (2016) manually extracted supervised frequency features from EEG records to train three Restricted Boltzmann Machines (RBM) [11]. These layers were stacked with a softmax regression to form a deep belief network (DBN) for motor imagery classification and adaptive EEG analysis. The DBN can be trained on each EEG channel and the results combined by AdaBoost [12]. This is applied to EEG data correlation analysis and its superiority compared to that of PCA is shown in [13]. In the current work, a deep-learning structure using cloud computing has been applied to address the big data analysis problem in epilepsy. In contrast to existing methods, the proposed method extracts unsupervised features from ECoG patterns to predict ictal activity.

Recently, the application of cloud and edge computing in health care systems have attracted considerable attention in the literature. For example, Rolim et al. (2010) [14] propose a cloud computing solution for collecting patient data in health care institutions whereby the sensors attached to medical equipment collect and send patient data for ubiquitous access. In [15], the authors introduce the use of a smart gateway bridging a wireless sensor network with public communication networks. A personal health monitoring gateway based on smartphones is proposed in [16], in which the gathered data is uploaded to the gateway via a Bluetooth interface before being forwarded to the remote cloud servers. In summary, these systems basically dispense conventional gateways for collecting data from biosensor nodes and forwarding these data to remote servers. In contrast, our work proposes to fully take advantage of the edge computing paradigm and bring the capabilities of processing data for health care services, especially exploiting deep learning of big EEG data in epilepsy.

III. Autonomic Edge Computing Infrastructure

In this paper, we propose to enhance the traditional health care delivery system with the provision of an edge computing infrastructure as illustrated in Fig. 1. The edge computing gateway serves as the middle layer between biosensors, which are wearable or implanted in the human body in conventional systems and a remote cloud computing server. In this context, edge computing extends the cloud computing paradigm to the network edge and overcomes several key challenges faced by cloud computing in health monitoring systems. Firstly, the massive amount of raw data acquired from a multitude of biosensors is preprocessed by the edge computing server before being ultimately transfered to the cloud server for additional processing and/or long term storage; this helps alleviate the burden on the backhaul network and the processing load on the cloud server. Secondly, due to the close proximity to the patient and physicians, the edge gateway can provide real-time services such as those of an alert or neurostimulation mechanism. Additionally, an edge computing gateway is well suited for deployment of monitoring applications which operate unremittingly, requiring uninterrupted data in case of losing connectivity between monitoring systems and the cloud. It should be noted that the edge computing gateway is completely cooperative and interoperable with the existing cloud-based system, while supplementing them in terms of location awareness, real-time response, low latency, scalability and heterogeneity.

As shown in Fig. 1, the proposed autonomic edge computing system for health monitoring and treatment comprises three main layers—sensing, edge computing, and cloud computing as detailed below.

- *Sensing layer*: It comprises multiple biosensors that continuously collect physiological data such as heart rate, motion, electrocardiography (ECG), electromyography (EMG), and EEG. These sensors are wearable or implantable in patients' bodies and are equipped with wireless transmission modules [17] to transmit medical data to the edge gateway using low-power wireless protocols such as BlueTooth, Wifi, and ZigBee.
- *Edge computing gateway*: The edge computing gateway/server is endowed with lightweight computing and storage capabilities and is deployed immediately next to the wireless Access Point (AP) or cellular Base Station (BS) [18]. Differently from traditional AP or BS, which only forward the date, the edge gateway is equipped with advanced monitoring applications and learning algorithms to perform diagnosis in a distributed manner at the institutional level.
- *Cloud computing*: This layer is used to storage long-term medical data of patients and to perform computation-intensive data processing tasks.

The envisioned edge computing infrastructure is applicable for distributed monitoring and processing of various types of physiological data such as EMG, ECG, and EEG. However,

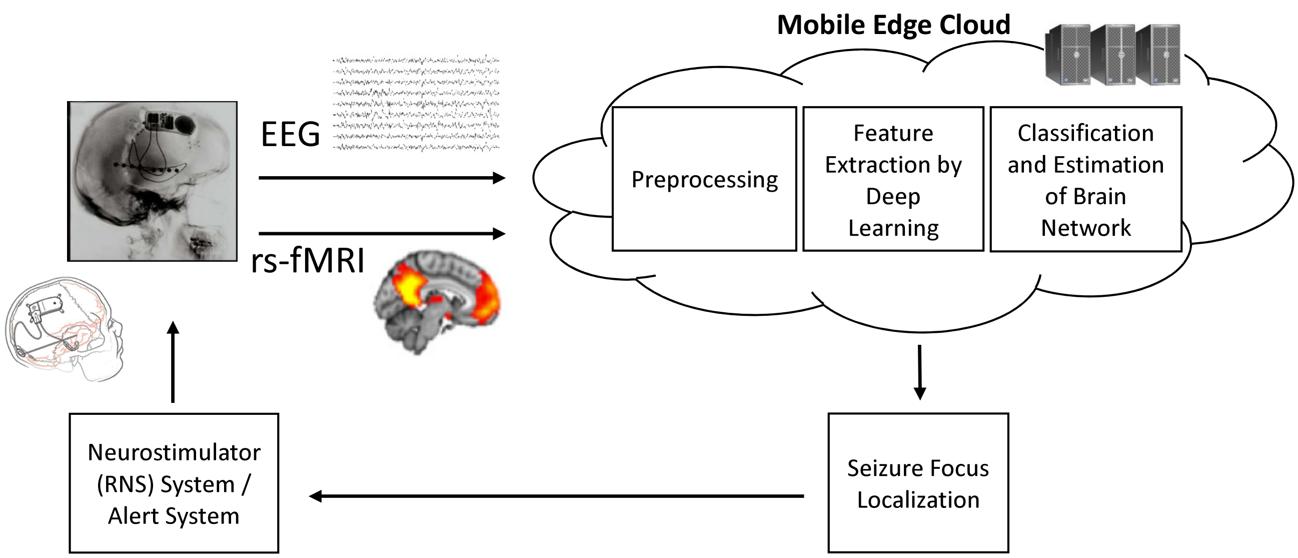

Fig. 2. The proposed autonomic computing for seizure focus localization in epilepsy by multimodal brain data. The goal of autonomic computing is to free the mind from low level detail by creating computing systems with self-management capabilities. We outline the concept of designing an autonomic edge computing system wherein the goal is to regulate an epileptogenic network automatically in order to prevent it from evolving into a clinically manifest seizure.

motivated by the criticality of epilepsy surveillance and treatment, in this paper, we focus on developing autonomic (i.e., capable of self-management) edge computing based framework for processing of electrographic and rs-fMRI data at local level (i.e., hospital, campus, city). The benefits of this approach are centered upon running applications and performing related processing tasks closer to end-users, thus significantly reducing network congestion and latency incurred by transferring data between the edge gateway and the remote cloud on the backhaul networks. Also, the management and sharing of patient data in a privacy-oriented sequestered manner is better effected. Moreover, the idea of developing edge computing systems for healthcare centers may be universalized as each institution uses different imaging protocols with different imaging systems and different strategies implemented in their respective epilepsy units.

IV. Proposed Approach

Functional changes in the brain may precede detectable structural changes and may be detected by existing noninvasive modalities. Functional connectivity analysis through EEG and rs-fMRI, complemented by diffusion tensor imaging (DTI), has provided such meaningful input in cases of temporal lobe epilepsy (TLE) [19]. To this end, the brain is modeled as a connected network of nodes and connectivity matrices are estimated from EEG and rs-fMRI data. The nodes may be selected based on structural or functional parcellation of the brain using model-based or model-independent (data-driven) methods. The entire connectivity matrix or specific connections between any two groups of nodes may be compared between two groups of subjects. Whole brain connectivity analysis can reveal major differences between the two groups and requires more samples and more complicated statistical analysis. In unilateral TLE patients, increased functional connectivity of the default mode network (DMN) to other brain regions has been shown in left TLE along with decreased connectivity in right TLE.

Preprocessing: For preprocessing the EEG data, a fourth-order Butterworth bandpass filter (0.5-150 Hz) is used for cutting frequencies. Then, to remove some unwanted frequencies, a notch filter set at 50 Hz is applied. In the next step, the phase distortion is canceled by using forward and backward filtering. The appropriate wavelet and level of decomposition are chosen based on the input signal and application. Based on our evaluation of common wavelets, we use Daubechies 4 (db4) to find approximation and detail for EEG data. For preprocessing fMRI data, after excluding the first 10 images and with slice-timing correction and realignment, we smoothed the data using a FWHM=4 Gaussian kernel and normalized it to the Echo-Planar Imaging (EPI) template in the MNI space (voxel size =333 mm). Then, we detrended and filtered all volumes (Bandwidth = 0.01-0.08 Hz).

Analysis of rs-fMRI Data: Investigation of specific connections in TLE using seed-based analysis has shown promise and focused on the connectivity of the thalamus [20]and hippocampusThe functional connectivity of the thalamus to the prefrontal cortex, motor and premotor cortex, somatosensory cortex, parieto-occipital region and temporal lobe [21] and that of the hippocampus to the sensorimotor, somatosensory, auditory and visual cortices are altered. Lateralization of TLE using rs-fMRI has shown promise [20] but additional comprehensive studies using both EEG and rs-fMRI, as proposed in this paper, are required to make this practical. Also, identification of epileptogenic networks extending or residing entirely outside the temporal lobe may be achieved by employing the methods developed in this paper.

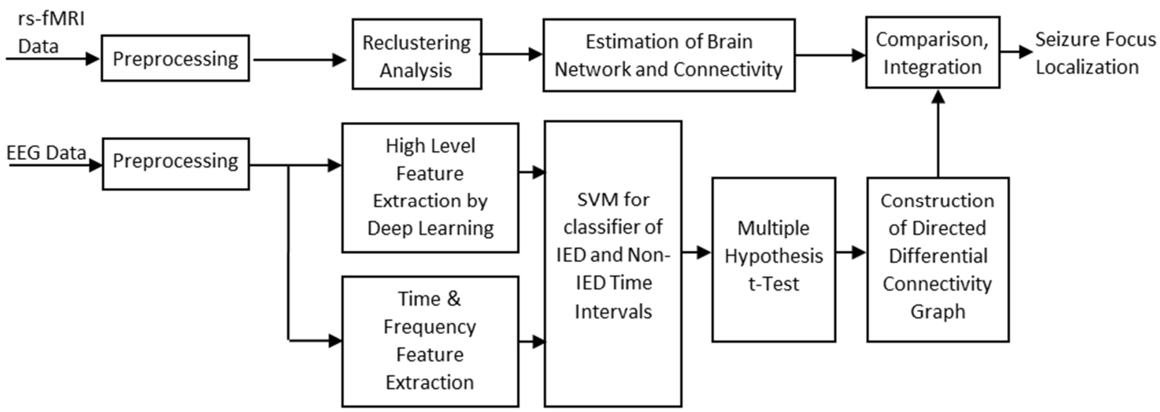

Fig. 3. Flowchart of our model-independent approach for the analysis of independently-acquired EEG and rs-fMRI data to localize the epileptogenic site.

Algorithm 1: Processing of rs-fMRI and EEG data.

```
Input: N-dimensional EEG data, x = [x_1, ··· , x_N]^T
       M-dimensional fMRI data, y = [x_1, ··· , x_M]^T
Output: Seizure Focus Localization
begin
for x = 1 →#N do
    Do preprocessing
    Do reclustering
    Find estimation brain network
end
for y = 1 →#M do
    while y > 1 do
        Extract high level features by CNN deep learning
        Extract time & freq. features by wavelet & ICA
    end
    Do SVM classification
    Do multiple t-test
    Find connectivity graph
end
Do comparison integration
END
```

To find the salient nodes of epileptogenic networks for functional connectivity analysis, spatial clustering of rs-fMRI into potential network connections has been proposed [22]. However, identification of the optimal number remains a challenge. For individual subjects, extraction of a large number of spatially disjoint clusters generates multiple small networks that are spatiotemporally homogeneous but irreproducible across subjects. On the other hand, extraction of a small number of clusters generates spatially large networks that, although spatially reproducible across subjects, are temporally heterogeneous. By leveraging the potential of autonomic edge computing in epilepsy, we further develop and apply the multimodal data analyzing approach to address this challenge (see Fig. 2). We develop and evaluate the following state-of-the-art methods to analyze electrographic data and rs-fMRI data acquired independently for the purpose of localization of the salient sites of an epileptogenic network (which is shown in Fig. 3 along with its pseudocode in Algorithm 2).

After standard preprocessing of rs-fMRI data, we identify and quantify brain networks by applying a reclustering method [23] to find possible functional abnormalities. The data is partitioned into several spatial maps and the associated time series using the reclustering method. Then, the mean time series of each region is found and stored. These mean time series are compared to the IEDs, extracted from the EEG data and convolved with the fMRI HRF, to find the closest (i.e., most similar) mean time series and its associated region. The resulting region will be considered as a potential epileptogenic site. This approach is based on our reclustering method which is a data-driven method and thus called “model-independent.” The results are compared to find optimal connectivity measures and attributes for the localization of the epileptogenic zone.

Analysis of EEG data: An increase in the functional connectivity of the brain during the interictal period has been reported [24].In this paper, we hypothesize that there are differences between the functional brain connectivity in the IED and nonIED periods. To find the differences, a differential connectivity graph (DCG) is constructed. Since the leading IED regions (sources) relate to the epileptogenic zone relative to the propagated IED regions (sinks) [25], we estimate directed DCGs (dDCG) for different frequency bands and characterize them by an information emittance measure. Next, a multiobjective optimization method [26] is applied on the emittance values of all dDCG nodes in all frequency bands to identify the leading IED regions.

Time- and frequency-based feature extraction: Due to the time-varying nature of EEG signals, wavelet transforms are used for for feature extraction and capturing the rhythmic nature of an epileptic seizure. Moreover, wavelets are applied to capture transient features and to localize them in both time and frequency domains. The outputs of filtering and wavelet transform are handled to extract features. Several time and frequency-related features have been extracted including com-

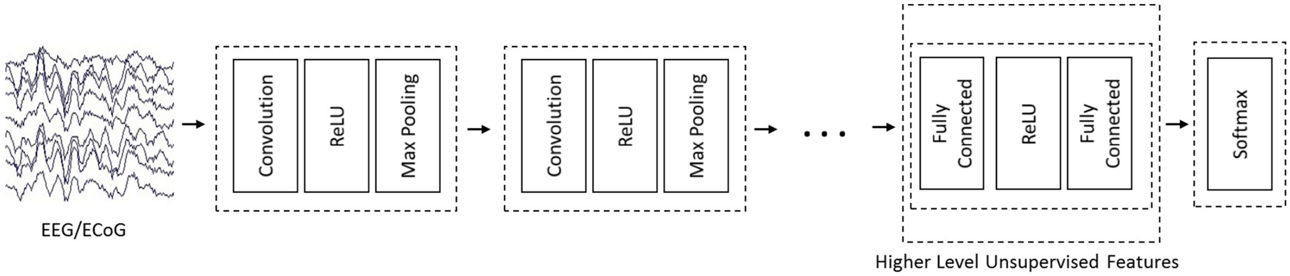

Fig. 4. The CNN consists of a multilayer structure. The input dimensions are defined in the first layer. The intermediate consists of a series of convolutional layers which are interspersed with rectified linear units (ReLU) and max-pooling layers. Features are extracted from the layer immediately before the classification layer since deeper layers combine all the primitive features into a more comprehensive signal representation.

Algorithm 2: CNN Forward and Backward propagation.

Input: M-dimensional data, $\mathbf{x} = [x_1, \cdots, x_N]^T$
Output: Classification result as preictal (1) or nonpreictal (0) signal; $output \rightarrow (0, 1)$
begin
for $l := 1 \rightarrow \#HiddenLayers$ **do**
  for $i := 1 \rightarrow \#RowunitinLayerl$ **do**
    for $j := 1 \rightarrow \#ColumnunitinLayerl$ **do**
      Find the layer activations by,
      $y^l_{ij} = \varphi(x^l_{ij}) + b^l_{ij}$
      Compute next layer inputs
    end
  end
end
Keep the final output as y^l
Calculate error at the output layer.
begin
for $l := \#HiddenLayers \rightarrow 1$ **do**
  Find error partial derivation by Eq. 4.
  Find error at the previous layer.
end
Calculate the gradient of the error by Eq. 3.
END

plexity, mobility, energy, entropy, correlation coefficients, Fast Fourier Transform (FFT), variance, skewness, kurtosis, mean, fractal dimension, frequency band power, peak amplitude, zero crossing, average spectral power, line length, maximal and minimal values, sum absolute value and some others.

High-level feature extraction via deep learning: The extraction of meaningful features and patterns from real-time and continuous EEG data for optimal analysis [27] and data querying is a need to develop an autonomic computing system. Deep-learning structures use an hierarchical multilevel learning approach to extract meaningful abstract representations from raw data [28]. This property empowers deep networks with the capability for higher level and patient-based feature extraction on large scale data [29]. In this study, a Convolutional Neural Network (CNN) is developed for extraction of ictal features from EEG/ECoG data. This class of deep networks is a type of feedforward artificial neural network based on 3D neuronal arrangements, local connectivity between neurons of adjacent layers and shared weight vectors. These properties allow a better generalization with lower memory which are suitable for feature representation in the big data problems associated with epilepsy. A CNN consists of a multilayer structure and is developed for our purpose. The input dimensions are defined in the first layer. The intermediate consist of a series of convolutional layers which are interspersed with rectified linear units (ReLU) and max-pooling layers [30]. Neurons are connected as rectangular grids in each convolutional layer where they have the same weights. In the pooling layer, small rectangular blocks from the convolutional layer are subsampled to find a single output. Finally, the last layer is designed for pattern classification via fully connected layers and the softmax layer (see Fig. 4).

The network is trained by 70% of data. Each of the layers correspond to an input EEG signal but only a few layers are suitable for feature extraction. The first layer of CNN learning filters for basic features. Then, the primitive features are processed by deeper layers to develop higher level features. Features are extracted from the layer immediately before the classification layer since deeper layers combine all the primitive features into a more comprehensive signal representation.

Forward and backward propagation of algorithms are implemented in the CNN to find the output and to optimize the error, respectively. In order to formulate these steps, suppose a N x N square neuronal layer exists in the convolutional layer. By using a $n \times n$ filter, ω, the output is obtained by forward propagation,

$$x^l_{ij} = \psi\left(\sum_{a=0}^{n-1}\sum_{b=0}^{n-1} \omega_{ab} y^{l-1}_{(i+a)(j+b)}\right) \tag{1}$$

where ψ is the nonlinearity weight matrix. In this case, the size of output is (N-n+1) x (N-n+1). In the max-pooling layers, the size is reduced by sparseness. Then $k \times k$ regions are taken and the maximum in the regions is calculated to convert a single value output. Therefore, the size of output is reduced to $\frac{N-n+1}{k} \times \frac{N-n+1}{k}$.

For weight optimization, a back-propagation algorithm is applied to compute the derivative of the loss w.r.t. the network parameters. Given the error function, E, the gradient component for each weight can be found by applying the chain rule,

$$\frac{\partial E}{\partial \omega_{ab}} = \sum_{i=0}^{N-n}\sum_{i=0}^{N-n} \frac{\partial E}{\partial x_{ij}^{l}} \frac{\partial x_{ij}^{l}}{\partial \omega_{ab}} = \sum_{i=0}^{N-n}\sum_{i=0}^{N-n} \frac{\partial E}{\partial x_{ij}^{l}} y_{(i+a)(j+b)}^{l-1} \tag{2}$$

by which the gradient is computed,

$$\frac{\partial E}{\partial x_{ij}^{l}} = \frac{\partial E}{\partial y_{ij}^{l}} \frac{\partial y_{ij}^{l}}{\partial x_{ij}^{l}} = \frac{\partial E}{\partial y_{ij}^{l}} \frac{\partial}{\partial x_{ij}^{l}} (\psi(x_{ij}^{l})) \tag{3}$$

To find the weights of the convolutional layer, the error is back-propagated to the previous layer by the chain rule. Therefore, $\frac{\partial E}{\partial y_{ij}^{l-1}}$ is found by,

$$\sum_{a=0}^{n-1}\sum_{b=0}^{n-1} \frac{\partial E}{\partial x_{(i-a)(j-b)}^{l}} \frac{\partial x_{(i-a)(j-b)}^{l}}{\partial y_{ij}^{l-1}} = \sum_{a=0}^{n-1}\sum_{b=0}^{n-1} \frac{\partial E}{\partial x_{(i-a)(j-b)}^{l}} \omega_{ab} \tag{4}$$

The pseudocode of the forward and backward propagation is shown in Algorithm 2.

Processing the extracted features: A nonlinear SVM with a GRBF kernel is used for classification of the extracted features [31]. To improve the results, the Gaussian kernel parameters are optimized by maximizing a classical class separability criterion as the trace of the scatter ratio. Then, a quasi Newton algorithm is used by exploiting a recently proposed criterion of decomposition of the objective followed by demixing sparse signals [32].

A proposed approach searches for statistically significant connections among a large number of IED and nonIED time intervals. It selects the connections that change significantly between the IED and nonIED states. This approach decreases the effect of common information between the two states like background activity. Using a permutation-based multiple testing method [33], we estimate the distribution of a test statistic from different IED and nonIED time intervals under the null hypothesis and use the result to choose statistically significant connections.

We start with the construction of a DCG which requires identification of IED and nonIED intervals and computation of a coupling measure. Identification of IED and nonIED time intervals is initially done manually by a collaborating epileptologist. Later, the manual results are used to develop an automatic method for this identification. An IED period may include one single IED or a burst of IEDs. A nonIED period is a time interval without any IED or abnormal event. For the coupling measure, we compare linear, nonlinear and directed coupling measures, including wavelet correlation coefficient, phase synchrony and transfer entropy and choose the most informative measure for the project. For preprocessing and feature extraction (i.e., to separate the signal (relevant information) from noise and background (irrelevant information)), we use the wavelet transform, which has been shown to be optimal for analyzing nonstationary EEG signals. A DCG for each of the frequency bands (i.e., wavelet scales) is constructed. Multiple hypothesis t-tests are applied to choose the wavelet bands that are most relevant and thus generate discriminating DCG between the IED and nonIED states.

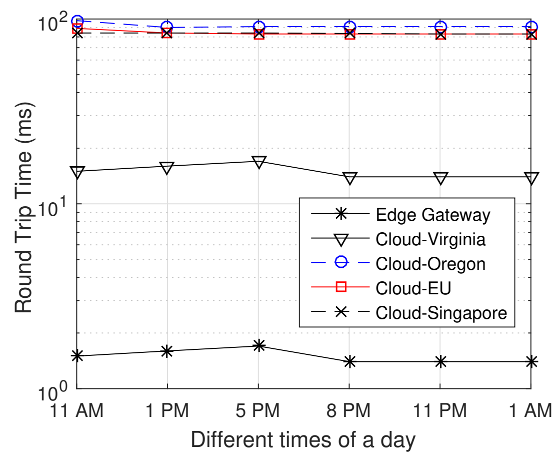

Fig. 5. Round Trip Time (RTT) between a local machine to the edge gateway and to different remote cloud servers (Amazon EC2).

Next, to construct a dDCG, we apply the method of [34] to estimate the drive-response relationship between the signals observed at the nodes of the constructed DCG. To identify the epileptogenic zone, we must classify the nodes of the constructed dDCG to the source and sink groups. To this end, we will use an index called local information (LI) to measure the amount of information that passes through a node. This measure will depend on: (1) incoming and outgoing connections; and (2) the amount of information carried by each connection, which will be calculated using the lagged Mutual Information (MI) between the signal pairs observed at the two ends of the connection.

V. Results

We present here the performance of edge computing for processing medical data. We used a clinical dataset of fMRI and EEG to evaluate the performance of the proposed methods as an autonomic system for epilepsy health care.

Dataset: The ECoG dataset of eight epilepsy patients with temporal and extratemporal epilepsy has been used, which was jointly developed by the U. of Pennsylvania and the Mayo Clinic and sponsored by the American Epilepsy Society [35]. Moreover, we studied functional connectivity among regions of the default mode network (DMN) using rs-fMRI data of five epilepsy patients and five subjects without epilepsy. The rs-fMRI data were collected from subjects on a 3T GE scanner at Henry Ford Hospital in Detroit, MI [36]. A series of 160 scans were acquired with TR = 2 sec, TE = 30 msec, 34 slices, 64×64 matrix and $3.4 \times 3.4 \times 3.5$ 3mm voxel resolution.

Latency: With the intention of presenting benefits of edge computing towards a healthcare system, latencies of transmitting EEG data from a local machine to the gateway and to remote cloud servers are compared. In particular, we repeatedly sent 64B EEG segments from a local machine

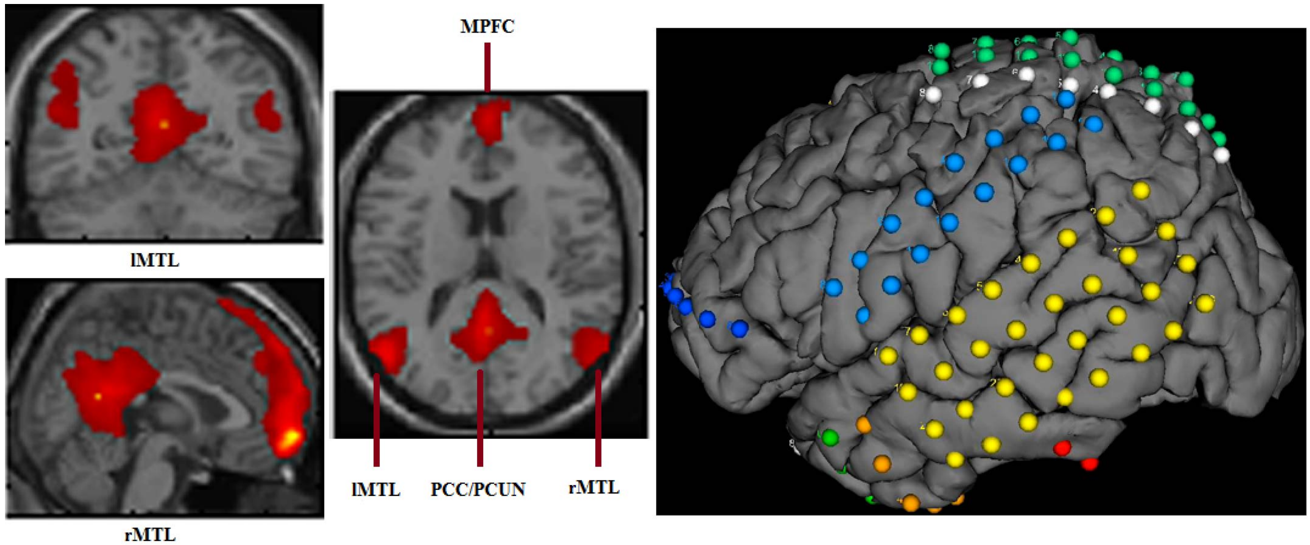

Fig. 6. Regions of the Default Mode Network (DMN) identified by ICA from rs-fMRI of a group of normal subjects: Medial Prefrontal Cortex (MPFC); Posterior Cingulate Cortex/ Precuneus (PCC/PCUN); left Mesial Temporal Lobe (lMTL); right Mesial Temporal Lobe (rMTL) [Database from our group at Henry Ford Hospital] . Right: a recent case from our group at Spectrum Heath, Grand Rapids, MI that underwent wide placement of electrodes over the left hemisphere during a phase II investigation to determine the site of epileptogenicity. We were able to identify the sites of epileptic disturbance and implant a closed loop device with two electrode arrays placed in the locations that were found to be epileptogenic [Database from our group at Spectrum Health].

to a gateway machine located in the same campus, and to different Amazon EC2 servers at different geographical locations (Virginia, Oregon, Singapore, and Ireland). The Round Trip Time (RTT) was recorded during the period of 10 days using the ping command. The average latencies are reported in Fig. 5. It can be seen that the RTT between the local machine and the gateway is always of 10 fold lower than that from the local machine to the closet cloud server in Virginia. This demonstrates the significant benefits of the edge computing paradigm in terms of transmission latency. In addition, the edge computing gateway helps reduce the amount of data transited over the network to reach the cloud servers. As a consequence, the operational cost and the congestion level in the network are reduced.

Since ictal activity with ECoG commonly occurs in $3-25$ Hz, the detail coefficients have been investigated to find this frequency range. First, we consider sampling frequency of the data (500 Hz). By the Nyquist criteria, the maximum frequency of data is obtained at 250 Hz. Finally, by coefficient representation in each scale, the frequency range of $3-30$ Hz is covered in scales of 4, 5, and 6.

To identify regions of the DMN, we applied spatial group ICA (GICA) [37] to the rs-fMRI data of subjects without epilepsy. To do this, we used the infomax algorithm in the GIFT software (version 1.3e) to get 20 independent components for each normal subject, from which we selected the DMN regions. Then, we applied the one sample t-test (p-value < 0.05, FDR corrected) on the five DMN maps to extract the DMN template. We identified four ROIs in the template: medial prefrontal cortex (mPFC), posterior cingulate cortex/precuneus (PCC) and bilateral mesial temporal lobes (mTLs), see Fig. 6. Then, we extracted ROI signals (i.e., mean of the time series) for the 10 subjects. Next, we calculated the Pearson correlation coefficients between each pair of the mean time series of the four ROIs as a measure of functional connectivity. Finally, we applied the two sample t-test on the results to find significant differences (p-value < 0.05) in functional connectivity between the two groups. The significant differences are shown in red in Fig. 7.

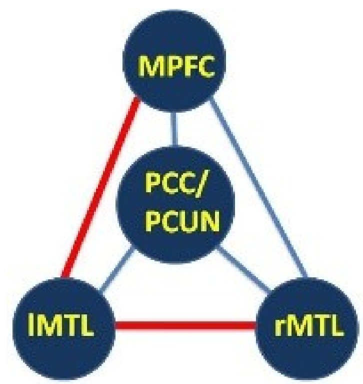

Fig. 7. Connectivity among the regions of DMN where the bold (red) lines show the connections that we found to be statistically significantly lower in TLE patients relative to normal subjects.

To lateralize (i.e., determine the abnormal side [38]) the TLE patients using functional connectivity, we preprocessed the rs-fMRI data of the patients using the FSL software. In the process, we eliminated the first five volumes due to magnetization equilibrium and then performed brain extraction,

TABLE I
LATERALIZATION OF TLE PATIENTS VIA FUNCTIONAL CONNECTIVITY OF THE HIPPOCAMPUS TO THE CONTRALATERAL HEMISPHERE FOR LEFT TLE (FCRL: FC OF R-HIPPOCAMPUS TO L-HEMISPHERE, FCLR: FC OF L-HIPPOCAMPUS TO R-HEMISPHERE)

	Case #	FCRL	FCLR	Diff. (%)
LEFT TLE	1	0.098	0.072	30.3
LEFT TLE	2	0.051	0.046	10.5
LEFT TLE	3	0.045	0.039	15.8
LEFT TLE	4	0.064	0.050	24.8

TABLE II
LATERALIZATION OF TLE PATIENTS VIA FUNCTIONAL CONNECTIVITY OF THE HIPPOCAMPUS TO THE CONTRALATERAL HEMISPHERE FOR RIGHT TLE.

	Case #	FCRL	FCLR	Diff. (%)
RIGHT TLE	5	0.089	0.195	-74.8
RIGHT TLE	6	0.078	0.106	-29.6
RIGHT TLE	7	0.205	0.240	-15.8
RIGHT TLE	8	0.079	0.092	-15.2
RIGHT TLE	9	0.058	0.073	-22.6

motion correction, slice timing, temporal high-pass filtering and spatial smoothing (FWHM = 5 mm). Next, we registered the rs-fMRI data to the B0 images. We used 82 anatomical regions generated by the FreeSurfer software to calculate the functional connectivity matrix for each subject. We calculated and tested the Network Based Statistic (NBS) features but did not find a significant network at the significance level of 0.05. Then, seed-based connectivity analysis for the thalamus and hippocampus is performed. For the limited number of patients (5 R-TLE, 4 L-TLE) who were available for analysis, we found that the number of functional connections of thalamus-to-cortex increased in R-TLE patients compared to normal subjects but decreased for the hippocampus in both R-TLE and L-TLE patients. We also found that the asymmetry of the ipsilateral functional connectivity between thalamus and hippocampus lateralized eight out of nine patients, while the functional connectivity of the right and left hippocampi to the contralateral hemispheres correctly lateralized all patients. Performance of the proposed methods for lateralization of TLE patients are shown in Tables I and II. Table III displays the results of a standard analysis of variance (ANOVA) on the extracted features from EEG dataset for normal and seizure subjects by quartile. The difference between group means and their associated procedures are shown in this table.

TABLE III
SOURCE OF VARIABILITY, SUM OF SQUARES (SS) OF EACH SOURCE, DEGREES OF FREEDOM (DF) OF A SOURCE, MEAN SQUARE (MS) AS THE RATIO SS/DF, RATIO OF THE MEAN SQUARES AS F-STATISTIC, AND P-VALUE DERIVED FROM THE CUMULATIVE DISTRIBUTION FUNCTION (CDF) OF F ARE SHOWN AS THE STANDARD ANOVA.

Group	Source	SS	df	MS	F-statistic	p-value
Normal	Columns	2.89e+09	8	3.62e+08	11.45	1.85e-14
	Error	1.11e+10	351	3.16e+07		
	Total	1.39e+10	359			
Seizure	Columns	1.96e+10	8	2.45e+09	21.92	4.64e-27
	Error	3.92e+10	351	1.11e+08		
	Total	5.88e+10	359			

VI. DISCUSSION

To understand the task at hand, it is useful to review the current investigation aspects involved in elucidating the patient's epilepsy. In those patients declared to have an epileptogenicity that can be further investigated to establish its location in the brain, a number of standard neuroimaging, functional and electroencephalographic studies are undertaken. These include magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), positron emission tomography (PET), inpatient scalp EEG and video monitoring (phase I), sodium amobarbital study and a neuropsychological profile. In select cases, a variety of further MR postprocessing applications and magnetoencephalography (MEG) are applied. Several quantitative neuroimaging metrics have been applied to provide greater precision and reproducibitlity in defining putative sites of epileptogenicity particularly as it applies to the most common area of involvement, the mesial temporal lobe. These are correlated with EEG data to render an initial assumption of the site of epileptogenicity and these may be reported with varying degrees of certainty.

Based upon this preliminary assessment, definitive therapy may be decided in the form of resective surgery or entirely discounted on the basis of multifocality suggesting greater than two sites of independent epileptogenicity. When uncertainty exists regarding the location of a particular focality or a need exists to establish the elequence of cerebral function in the vicinity of a putative site, then intracranial electrographic investigation (i.e., phase II) is required in the form of extraoperative electrocorticography (eECoG). This requires the intracranial placement of surface and/or depth electrode arrays in specific locations of the brain to better understand the distribution of the epileoptogenic network and a further admission to the Epilepsy Monitoring Unit (EMU). The results will often declare the approach to be taken therapeutically.

A means of therapeutic interaction with an area of epileptogenicity, that does not entail removal of a portion of the brain, first requires adequate detection of ictal onset. The use of computers to help physicians in the acquisition, management, storage, and reporting of brain (i.e., EEG) signals is well established. To this end, there are computer-aided detection applications that use a BCI. In order for a autonomic computing system to work effectively, computational algorithms must reliably identify periods of increased probability of an impending ictal occurrence in order to abort its development. Such preictal periods may be of variable duration and may not afford suitable latency to provide current methodologies with sufficient time for signal deployment to achieve control in all circumstances. The development of an autonomic method for detection and epileptogenicity localizing would optimize seizure control and bring about an improved quality of life.

In our future work, we will strive to improve and expand our methods by using past patient medical records in order to make more knowledgable decisions. We also plan to study many other neurological disorders other than epilepsy such as sleep disorders, coma, encephalopathies and brain necrosis to develop a complete and comprehensive neurological disorder system. This system will use other vital biosignals aside from EEG and will require processing a variety of models to estimate different neurological diseases in real-time. Also, we will improve on the autonomic loop by considering the responsive neurostimulation signal. We plan to work on applying an appropriate stimulation signal to abort and impending seizure as the second stage of the autonomic computing system for managing the brains of epilepsy patients.

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