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Survey for Segmentation and analysis of f-MRI images to detect brain activities

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Abstract

Brain is the most important organ in the human body, which controls the vital processes and functional studies. Functional Magnetic Resonance Imaging (fMRI) calculates the small changes in blood flow that occur due to brain activity. To examine the brain's functional anatomy, or to determine which parts of the brain are handling critical functions, to evaluate the after effects of stroke or other disease, or to guide the brain treatment, the fMRI can be generally used. fMRI's are more detailed in their images as compared to Computerized tomography (CT) scan. The images obtained from fMRI are processed using image processing techniques and then learning algorithms are applied to precisely locate, segregate and categorize various brain regions depending upon their level of activity. Analysis of fMRI is beneficial to detect and to cure various syndromes like, Post Traumatic Syndrome Disorder (PTSD), for pre-surgical mapping, to guide a neurosurgeon to spare brain tissues that, if injured, would cause new clinical deficits or limit good recovery. It has had a major impact in cognitive neuroscience. This paper outlines the survey of various studies performed using fMRI images to detect brain activities in numerous application of clinical sciences.

Keywords: brain activity, deep neural network, fMRI, PTSD,

1. Introduction

Neuroimaging, or brain scanning, includes the use of various techniques to either directly or indirectly image the structure, function, or pharmacology of the brain. Neuroimaging has two categories named, structural imaging and functional imaging. Structural imaging deals with the structure of the brain and the diagnosis of large scale intracranial disease (tumor), as well as injury. Functional imaging is used to diagnose metabolic diseases and lesions on a finer scale (such as Alzheimer's disease), and also for neurological and cognitive-psychology research. Functional imaging allows the brain's information processing to be visualized directly, because activity in the involved area of the brain increases metabolism and "lights up" on the scan. Magnetic Resonance imaging (MRI) scan uses echo waves to discriminate among grey matter, white matter, and cerebrospinal fluid. Functional Magnetic Resonance imaging (fMRI) scans are a series of MRIs measuring brain function via a computer's combination of multiple images taken less than a second apart. Specifically, fMRI measures signal changes in the brain that are due to changing neural activity. In an fMRI, a patient can perform mental task and the area of action can be detected through blood flow from one part of the brain to another by taking pictures less than a second apart and

showing where the brain brighten. fMRI's makes it achievable to show when an event or series of events designed to evoke spontaneous reaction to sensory, emotional, or spiritual stimuli occur and how brain area change with experience, and which areas of the brain perform in unison. These fMRIs are use in extensive areas of psychological phenomena, like telling lies, playing musical instruments, dreaming, furious, etc.

Patients with post traumatic syndrome disorder (PTSD), struggled with mental disorder with age as small as child till elderly person. In PTSD, patients feel afraid, stressed and anxious even when they are not in danger. They also encounter problems like, concentration, attention or memory. Various parts of the brain are assigned to the various activities of human (physical, emotional, sensory, etc.). This helps to assess which area of the brain is more active for patients with PTSD. A lot of studies were observed for classifying brain activities based on the deep learning techniques. Some of the techniques studied were, CCNN (connectome- convolutional neural network), VAE's (Variational auto encoder) coupled with GANs (Generative adversarial network), Statistical parametric Mapping (SPM), Independent component analysis (ICA), etc.

This paper reviews the study of numerous techniques used to analyse fMRI images previously researched, and application of those techniques in particular, focusing mainly on brain

activities.

2. Survey details

There are techniques which focus at associating the particular cognitive, behavioral or perceptual state to specific patterns or regional brain activity, called as Multivariate methods or brain decoding or mind reading. Methods like SVM, Gaussian processes classifiers were applied to fMRI images to predict from individual's brain activity, the pattern of perceived objects, mental state related to memory retrieval or even hidden intentions [2]. Complex and imbalanced fMRI data sets appeared due to the number, the sequence and duration of mental state that are unpredictable generated by an individual or patient. Study [2] explains the decoding of spontaneous brain activity from fMRI using Gaussian processes to track brain reactivation. As the spontaneous brain activity cannot be linked to external or internal stimulus, they make it very strenuous condition to decode. Some of the difficult data sets such as, predicting subjective pain intensity, uses GP classifier which uses kernel machine learning, where experimental design completely controlled the nature, timing and duration of trials, and isolate experimental conditions temporarily. The paper [2] shows the study of developed method in which, memory test have been performed on volunteers in order to behaviorally assess the accuracy of both the spatial and content knowledge obtained by volunteers. Then the fMRI images were captured and processed using 3T- head only scanner, then at the same time were realigned and unwrapped for the subject movements in scanner and then smoothed using Gaussian function with 4mm FWHM kernel.

The fMRI analysis performed in [2] first proceed with signal extraction in which, the whole time series of all voxels were extracted. To regress out the movement effects and low frequency drifts, Generalizes linear model (GLM) was used. For further feature selection, both univariate and multivariate techniques were considered, which uses GLM and SVM respectively. To classify the model further, Gaussian process (GP) classification was performed using the expectation propagation approximation of the posterior mode explained in [1]. To obtained multiclass accuracy measure for each subject, an Error-correcting output code approach was considered. It has been observed from the results that, the classification correlated significantly with behavioral data. It was the performance of the subject for spontaneous brain activity, which correlated significantly with behavior and performance. The paper concludes that, a significant correlation between the proportions of spontaneous brain activity linked to the memory task and the subject's performance to memorize the task features suggests that reactivations during post-experience rest are linked to the memorization of the conducted experiment.

Brain state analysis of visual activities using fMRI have been described in [3]. To measure the brain state, fMRI uses Blood Oxygen Level Dependent (BOLD) signal. It's better to observe difference between two states as direct neural activity can't be measured in fMRI. This study [3] targeted 3 brain regions viz., visual cortex, which controls the sight and visual

images, temporal lobe which is involved in short term memory and frontal lobe which is involved in movement activities. During the experiment, difference between the brain states is found during visual task (associated with visual cortex). During the response for True/False category, difference is found in temporal region and frontal region. Temporal region is activated in thinking and recognition of category while frontal region is activated during response (movement). The paper [3] performed the experiment with 2 individuals, who undergoes to perform two tasks i.e. visual and response based task. 3.0 Tesla Philips machine were used to collect data from individual. For data preprocessing, Statistical Parametric Mapping (SPM8) has been used. Preprocessing involves realignment, slice time correction, coregistration, segmentation, normalization and smoothing. First order autoregressive model is used which is then followed by high pass filter. GLM model was used to estimate model parameters to model the BOLD response. T-test was used to see the difference between different states.

Results obtained in [3] significantly shows that, the activities were recorded during visual task which is in primary visual cortex, the activities were recorded in temporal and frontal during response based task. Both memory and movement are involved in response based task and short term memory is associated with temporal region and movement is associated with frontal region cortex. F-test and T-test are usually used to define the contrast between different states. When there are set of predictors, f-test is used. And when there is specific combination of predictors, t-test is used. This study applied T-test to find the difference between the two states and used beta values to evaluate the classification accuracy between two states. Uncorrelated p-value i.e. overall probability (<0.001) is used to calculate the significant voxels in the brain.

For carrying out some complicated tasks, the subjects pass through the sequence of hidden brain states. Paper [4] elaborate the study to discriminate the brain states from fMRI images using Fuzzy support vector machines. This paper focuses on classifying n-class brain states from fMRI data using fuzzy SVM. fMRI integrates neuroscience, informatics science and computational science and help develop approaches needed to understand human brain [4]. Paper proposes a method to automatically classify n-class instantaneous brain state, using fuzzy SVM, which solve the unclassifiable regions in n-class state classification using SVM by defining a membership function [5].

The preprocessing here undergoes in temporal and spatial preprocessing to achieve same acquisition time for each voxel and images with same size. Here, statistical parametric mapping (SPM5) is used. Next step in preprocessing is slice timing, which corrects the differences in slice acquisition times. To remove artefacts in fMRI time series, realignment is done, which uses least square approach and rigid body spatial transformation. Spatial normalization is a requisite step when comparing among multiple subjects. The algorithm, which uses this method is explained in the atlas of Talarach and Tournoux (1988), which works by minimizing the sum of square difference between the image which is to be normalized, and a

linear combination of template images [4]. Furthermore images are need to be co-registered to decrease the difference between subjects, as realignment and normalization are not sufficiently decrease the difference. Paper [4] uses characters in Brodmann's areas of Talarach as features for feature extraction method. Brief steps are follows [4]:

1. Finding out the most active voxels in several Brodmann's areas of level4 under the basic models in SPM5 and save their co-ordinates.
2. Scan fMRI image and search the voxels according to the co-ordinates saved.
3. Respectively average all voxels in the spherical region whose center is corresponding saved voxel and whose radius is predefined constant. These results of a single image are formed one feature vector.
4. If the image is not the last image, go to step 2, else end.

Popularly used learning machine for two class classification problems is SVM, which is an approximate implementation of the structural risk minimization principle and creates a classifier with minimized Vapnik-Chervinenkis (VC) dimension [4]. SVM learns from set of high dimensional example vectors and their associated classes. SVM creates a decision boundary (hyperplane) that can differentiate n-dimensional space into classes thus, effortlessly categorizing future data. Hyperplane equation for linear case is, $D_i(x) = W^T x + b = 0$

If it is not linearly separable, then it is must to map the input training vector into a high-dimension feature space using kernel function, and then creating hyperplane. Fuzzy SVM is a one-against-one method which converts the n-class problem into $n(n-1)/2$ two class problem. The data set of Chinese character vs. English character is considered to classify multiple brain states from fMRI data using fuzzy SVM. The images are processed and transformed to normalized coordinates, on the grounds of activities of voxel and index of Brodmann's area. Then after extracting features, input vectors are given to train the classifier of fuzzy SVM. The paper results both the single subject and multiple subject brain classification is achievable.

To understand the human visual processing system, there are two elementary aspects viz. neural encoding and neural decoding. The brain responses have been predicted according to the presented external stimuli, which is done by encoding models. Whereas decoding model predicts the external visual stimuli information by analyzing the evoked brain signals [6]. Most of the study focuses on methods that are based on linear modelling, brain activity pattern recognition or visual stimuli identification. But the areas of accurate reconstruction of perceived images from measured human brain activities are still untouched. Paper [6] proposes a method of novel deep generative multi view model for the accurate visual images reconstruction from the human brain activities measured by fMRI. Statistical relationship between visual stimuli and the

evoked fMRI has been obtained using 2 view specific generators with a shared latent space [6]. The method acquires the deep neural network architecture for visual image generation and design a sparse Bayesian linear model for fMRI activity generation. An efficient mean-field Variational inference method is used to train the model. Due to the disadvantages of traditional visual image reconstruction approaches, they yield disappointing results. To overcome the pitfall of previous studies, deep learning methods, like, deep neural network (DNN) revolting various fields of machine learning.

The hierarchical layers of DNN can resemble feed forward visual representation in human brain visual system. In correspondence with the output of DNN layers, neural activation in human visual cortex shows correspondence. Paper [6] proposes a deep generative multiview model (DGMM) to reconstruct perceived images from human brain activity. Here, deep generative model is applied to visual images and sparse linear generative model to fMRI activity patterns. The proposed model is trained by using an efficient mean-field Variational inference method and then the DGMM can accurately reconstruct the visual images by Bayesian inference. The paper compares various methods like Miyawaki, BCCA, DCCAE-A, DCCAE-S, De-CNN with DGMM. Results show that the DGMM method produces better reconstruction than the other compared methods, mainly on the handwritten digits and characters data set. This study evaluates person's correlation coefficient, mean squared error, structural similarity index, and accuracy- SVM/CNN. Overall the result of DGMM are of high quality.

Functional MRI (fMRI) is sensitized to the paramagnetic properties of deoxyhaemoglobin which concentration locally fluctuates in strong correlation with the physiological events of the brain activity [7]. The paper [7] proposes a method called SPM-GLM uses a conventional statistical inference methodology based on the t-statistics, where it assumes a rather rigid shape on the BOLD Hemodynamic response function (HRF), constant for the whole region of interest. SPM-MAP algorithm is designed in a Bayesian framework is presented in this paper. The brain activated regions and the underlying HRF in an adaptive and local basis have been jointly detected by the algorithm. SPM-MAP algorithm has been validated using Monte Carlo tests with synthetic data and comparisons with the SPM-GLM are also performed [7]. fMRI images underwent to preprocessing unit which has explanatory variables. The main explanatory variables used in GLM allocate temporal variance in the data with strong correlation with the paradigm stimulus. There is considerably irregularity in in HRF shape, which leads to reduced sensitivity when local HRF is different from the template one. This is one of the disadvantage of the method. Also, SPM-GLM method is based on the p-value tuned by medical doctors which introduces a subjective factor on the final results. These limitations have been overcome in this paper by designing an algorithm in Bayesian framework based on the Maximum A Posteriori (MAP) criterion. To minimize the detection error probability, this algorithm combines the activity detection problem and the local HRF estimation problem, to provide best results with available data. [7] Monte Carlo tests

with synthetic data are performed, for comparison purposes with the SPM-GLM method and also for absolute assessment in order to statistically categorize the overall error probability.

[7] The data from fMRI have been preprocessed with the standard procedure implemented in the Brain Voyager software, to decrease the distortion due to motion or other phase changes over time and spatial smoothing. Then data is been statistically processed further by the Brain voyager SPM-GLM and SPM-MAP algorithm. The paper shows that the SPM-MAP outperforms the SPM-GLM tested on Monte Carlo, for almost every tested conditions.

Treatment tool to neurological disorders uses non-invasive neuromodulation technique such as Transcranial direct current stimulation (tDCS). Paper [8] studies the dynamic influence of ongoing brain stimulations on resting state fMRI connectivity. Simultaneous acquisition of neuroimaging data together with the brain stimulation allow an examination of the brain dynamic changes during the process [8]. tDCS technique has been applied to facilitate neuroplasticity and proved to show prominent effect for stroke rehabilitation, depression and other neural disorders. fMRI captures the brain activity on impulse. But some important facts might get overlooked if looking into brain activity after the stimulation ends. To study brain reorganization during the stimulation, concurrent tDCS and fMRI was applied to healthy subject. Dynamic functional connectivity and a Bayesian network were adopted to demonstrate information flow in the process.

For experimental setup, healthy subject (23 year old) has given the direct current through anode and cathode. 1mA for 20 minutes with 30s ramp up and ramp down periods. A 7 min pre-stimulation block of resting state fMRI has been acquired and set as a baseline. Then the stimulation started for 21 minutes with three blocks of simultaneous 7 minute resting state fMRI acquisition. Immediately after stimulation, another 7 minutes block of resting state fMRI data was acquired. The acquired data of images underwent for the preprocessing. The complete brain reconstructed from the images was segmented with FreeSurfer. Analysis of functional neuroimages software were used for fMRI data analyzing which is then followed by resting state fMRI analysis. The process is been followed by slice time correction and spatial normalization of images registered to Talarach standard space and Gaussian kernel smoothing were applied. Motion censoring, nuisance regression and bandpass filtering are then performed simultaneously [8].

Pearson correlation matrix of pre-stimulation block was used to investigate functional connectivity changes (FC), and used as a baseline for computing the differences between the baseline and the blocks during and after the stimulation. Changed correlation values of one region with all other regions were summed up to represent the positive/negative FC for demonstration purpose. During 1st 7 minute stimulation, F did not notably increase and turned out to decline in some regions, implying that the functional connectivity (FC) changes would behave differently at different time points during the stimulation. During the stimulation, either the direct influence

within the right hemisphere or between hemispheres tends to increase compared to the baseline and post-stimulation. Some direct influence between inter-hemispheric regions reversed during and after stimulation. Paper concludes that, during early stage of stimulation, the whole brain functional connectivity tended to decrease and afterwards the FC increased gradually and achieved the highest after stimulation ended. Which indicates that the brain may respond differently to the exposure time of the external stimulation, making it important to decide the stimulation duration for specific treatment purposes. The study gives insight to the casual relationship between regions during the process provided the information flow in brain processing.

Paper [9] proposes an efficient data mining algorithm for augmenting voxel activation detection, best performed specially with task specific information, which is primarily temporal. Due to low temporal resolution, typically in scales of seconds, fMRI put at a disadvantage. Paper [9] proposes an algorithm to enhance structural brain connectivity, a spatial based analysis, with temporal information. Data set has been collected from multiple trails and preprocessed using statistical parametric mapping (SPM). Further, a neurophysiological explanation of the activated brain regions according to the voxel labeling of AAL2, a standard brain atlas of SPM, is provided. The paper concludes that, although the brain region locations are fixed, their cooperation is task specific and, therefore, any change in brain activity during the motor task had to be described in temporal terms. Sample mean and sample variance were computed to discover patterns in time series pairs.

Paper [10] studies the research on functional brain networks topological properties by real-time fMRI emotion self-regulation training. It has been demonstrated by various studies that, multiple brain regions would activate during execution of cognitive task. Self-regulation brain activity of human can be assist by real-time functional MRI neurofeedback (rtfMRI-NF). To investigate the problem of unclear neural mechanism about rtfMRI-NF, paper combined the graph theory with resting state fMRI to explore the topological properties of functional brain networks. Topological properties like, integration, segregation, and centrality of the obtained networks are used as features to input to the further classifier. Here, subjects were provided with the ongoing functional connectivity information which was related to emotion regulation. Results show that, rtfMRI-NF training could improve the small-world properties and nodal degree in the temporal lobe, frontal lobe and limbic system. Results in paper suggested that rtfMRI-NF training was associated with alters in topological properties of functional brain networks.

Resting state fMRI is widely used methodology to study brain connectivity. Mostly the studies assume that resting state fMRI time series are stationary. But the ongoing studies show that they are in fact dynamically evolving. Paper [11] describes the work related to the resting state dynamics. Here, hidden Markov model is applied to the resting state fMRI data and derive model parameters reflecting the states. Also, the dynamic parcellations and of thalamus, leading the state specific

parcellation and their merged results, both of which revealed new insights about the thalamic function and connectivity. Techniques such as, co-activation patterns (CAPs) and spatial independent component analysis (ICA) have not completely utilized the information contained in the temporal order of rfMRI time series, treating each time point as independent. Also, in sliding window approach, contamination and interference between states occur due to fixed length sliding window, which leads to mixing of signal from multiple states in the same window. Also, other technique ICA has limitation of assumption of temporal independence.

The brain is constantly switching from one metastable state to another. The hidden Markov model (HMM) can be the alternative approach, which can describe the latent state switching process of the brain as a Markov chain with different transition probabilities between states. It takes into account the temporal order of data and is not restricted by a fore mentioned data [11]. HMM has been working as a sequential modelling tool and was applied to electrophysiological data and detected 4 brain states of neuronal firing patterns in rodents subjected to different kinds of stimuli. Here, hidden Markov random field was applied in fMRI to detect binary state switching on voxel level. Also, the paper presents a method to determine the number of brain states based on the reproducibility of the algorithm. The method further performs a state specific parcellation of the thalamus based on its connection to the cortex and examine the state specific parcellations and combined parcellation.

In paper [11], the switching process of the brain state was modelled as a Markov chain (GHMM), with the brain state represented by a multivariate Gaussian distribution. The Baum-Welch algorithm was employed to solve the optimization problem and the parameters from the fMRI are estimated. It is then followed by the Viterbi algorithm, to decode the optimal brain state sequence. Also, the posterior probability of each brain state at all the points has been calculated. In present paper, parcellation also focused on the connectivity of thalamic voxels with 5 cortical region of interest in each hemisphere. The thalamus was extracted using the Harvard-Oxford subcortical structure atlas and voxels in ventricles or white matter regions were removed [11]. rsfMRI data is also preprocessed and went through the steps of rigid body motion correction, cross-modal registration, spatial transformation, denoising with the ICA based algorithm and regression out nuisance signals and then the bandpass filtering and spatial smoothing. A sliding window approach was used to divide thalamus and cortex fMRI signals into windowed time series. [11] Thalamo-cortical connectivity matrices were generated for each of these windows, temporally concatenated across subjects, and fed into a normalized spectral clustering algorithm to derive thalamo-cortical connectivity states at the group level, resulting in 9 states. Normalized spectral classifier was applied to for each state for thalamus parcellation. The paper [11] concludes that, result of parcellations reveal rich connectivity and dynamic insight of the thalamus and demonstrate a powerful parcellation tool that matches better with histology.

Data driven methods treat fMRI data in the context of the blind source separation (BSS) problem. Multivariate approaches like, principal component analysis (PCA), independent component analysis (ICA) and independent vector analysis (IVA) have been propose in [15] in regard to a BSS problem. For fMRI data, nonnegative matrix factorization (NMF) have been applied in single trial first level individual analysis and second level group analysis. The paper [15] proposes constrained alternating least squares nonnegative matrix factorization (cALS/NMF) algorithm to enhance original ALS/NMF in detecting task related brain activation from single subject's fMRI data without any prior information. Paper suggests that the cALS/NMF fits fMRI data better and performs more flexibility in detecting brain activation from single subject's fMRI data. [11] Proposed a constrained ALS/NMF algorithm which has two constraints of maximizing uncorrelation and Tikhonov L2-norm added in original Euclidean distance cost function, together with a novel training paradigm combined by modified updating rules and OBS algorithm. The experimental results on both simulated data and real fMRI data show that cALS/NMF fits fMRI data well without any prior information, which indicates that the cALS/NMF may be more suitable for detecting the task related neuronal activity from fMRI data than the original ALS/NMF.

Discussion

Various techniques have been studied over the period to study the brain activities in variation applications and disorders like, PTSD, Alzheimer's, short term memory loss, pre-surgical mapping, head injuries, etc. it has been observed that fMRI are popularly used in almost every techniques mentioned above. Time series data of fMRI's are preprocessed as per requirement of the application and then filtered and smoothed out for further classification and processes. PCA, ICA, SVM, GHMM, deep neural network, etc, are widely used methods to train and study brain activities using fMRI images.

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