Journal of Computing & Biomedical Informatics
ISSN: 710-1606
Volume 07 Issue 02
2024

Research Article
https://doi.org/10.56979/702/2024

Revolutionizing Schizophrenia Diagnosis: A Transfer Learning Approach to Accurate Classification

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Received: June 11, 2024 **Accepted:** August 08, 2024 **Published:** September 01, 2024

Abstract: Schizophrenia is one of the most serious mental disorders that has been both widely researched and extensively feared. It is among those mental illnesses which are relatively less unveiled to the world but its effects upon people living with it are undoubtedly profound. Significance of identification of schizophrenia is of vital importance because it has become a critical and challenging problem. In the past decade, different artificial intelligence techniques have been introduced to assist mental health providers, but no satisfactory results have been obtained for identification of schizophrenia and there is no front-end application to which doctors are interacted and to use these techniques or algorithms knowledge of programming required. Furthermore, Neuroimaging technique like functional magnetic resonance imaging (FMRI) is not able to perform adequate temporal sampling due to slow bold response. In this research work, pre-defined fMRI regions specifically related to the schizophrenia are used for mapping. Schizophrenia disease has been classified through transfer learning algorithm Alex Net. In order to evaluate algorithm results, we used the standard measures accuracy, sensitivity, specificity, prevalence, likelihood ratio positive, and likelihood ratio negative. This project provides front end window form designed using Tkinter python module where doctors upload user's details and FMRI 4D image and window form first convert into 2d images and then take specific slice to classify is image is positive or negative and store result in database.

Keywords: Schizophrenia; Transfer Learning; Machine Learning; Neural Networks; Convolutional Neural Networks; Alex Net.

1. Introduction

Schizophrenia is a severe mental disorder that influences the way a person reason, feel and act. It is however manifested by such signs and symptoms as hallucinations, delusions, distorted thought patterns and processes, and bizarre feelings [1-3]. It therefore comes as no surprise that schizophrenia is one of the most disabling mental illnesses and affects the lives of those afflicted with it in a huge way [1].

The definite cause of schizophrenia up to date has not been fully determined, but it is thought to be the interplay of genetic, environmental, and neurochemical factors [1] [4]. So, for example, the tendency to schizophrenic disorders is inherited: those who have close relatives with schizophrenia have a higher risk of developing the disease themselves [4]. Poor nutrition during pregnancy; if the mother has a viral infection, her child is more likely to develop schizophrenia; or lack of brain chemical balance; for instance a natural level of dopamine and glutamate in the brain are off [1] [4].

The symptoms of schizophrenia can be divided into two categories: positive symptoms and negative symptoms [4] [3]. Specific examples of positive symptoms include auditory, visual, tactile or olfactory hallucinations and schizophreniform ideas of reference, paranoid or bizarre persecutory delusions and thought disorder. Hallucinations therefore refer to the events that occur in the senses wherein the perceiving subject cannot contact the supposed actual object or source in the external physical environment: for example, hearing voices or seeing cats that are not real [4] [3]. An example of a psychotic feature is a delusion, which is a firmly held belief outside of the person's culture that doesn't make sense to others and is not caused by ordinary life stresses and does not change when presented with information that contradicts the belief, for instance, the idea that one is being watched or followed by a higher power [3]. The consequences of disordered thinking include a person's inability to classify his or her thought process and come up with a coherent rationality between each given notion [4].

This paper's negative symptoms comprise apathy, affective blunting, and functional imprescriptibly, including initiating and maintaining social activities [4] [3]. Negative symptom is defined as people with reduced or absent emotional responses and motivation and can present with slowed movement, and lack of responsiveness, lack of drive, or inability to finish tasks, or even loss of interest in activities that were once enjoyed [4] [3].

Schizophrenia can also be diagnosed by a qualified psychologist, but usually, this process is carried out by a psychiatrist who having checked a patient, examines their symptoms and previous illnesses [3] [5]. Like many other mental illnesses, there is no definitive test for schizophrenia, which means that the diagnosis is usually made symptomatically, based on the patient's history, and the exclusion of other possible causes of the same symptoms [3] [5].

Schizophrenia treatment always targets the use of drugs combined with counseling. First generation antipsychotic drugs are the most often administered drugs for schizophrenia illness. These medications assist in lessening the signs and effects of this disorder through lessening the impact of dopamine, a neuro transmitter in the brain. Cognitive behavior therapy seems to be effective in managing certain psychotic symptoms and in improving functioning of patients with schizophrenia.

In conclusion, schizophrenia is a severe mental illness that has a peculiarity to alter the mental processes of an individual in terms of thinking, feeling and even acting. The illness is said to have a variety of symptoms such as hallucinations, delusions, disordered thinking and abnormal feelings. It had not been determined the cause of schizophrenia but it involves genetic, environmental and neurochemical factors. Schizophrenia requires medications and sessions with a psychiatrist, psychologist or a social worker; it doesn't mean one with the disorder cannot have a normal happy life like everyone else.

2. Literature Review

[6] They used Canonical Multiple Sentence Correlation Analysis (MCCA) to combine data from resting fMRI, EEG and sMRI to unravel the abnormalities underlying patients with schizophrenia and also to covariate between the modalities [7] [8]. They proposed an ensemble characteristic selection strategy in which SVM-RFE acts as the core and takes advantage of the strengths of several methods, leading to the discovery of the most differentiating group characteristics for each individual modality and modal combination. The accuracy achieved is less than 90%.

[9] Investigates the resting state of magnetic resonance imaging in 48 patients with schizophrenia and no other medication and 31 healthy subjects using ReHo, an index of the regional synchronization [10]. Non-stop local connectivity or synchronization also indicates the regional integration to the information processing. Then, receiver char charve curt eristic curves and vector machines are employed to analyze how regional variability affects Control compared to the patient's control [11]. The obtained results are the accuracy of 90,14%, sensitivity of 88,24% and specificity of 91,89%.

[12] take functional magnetic resonance imaging (fMRI) data for schizophrenia as an example, to extract effective time series from preprocessed fMRI data, and perform correlation analysis on regions of interest, using transfer learning and VGG16 net, and the functional connection between schizophrenia and healthy controls is classified [13] [14]. Experimental results show that the classification accuracy of fMRI based on VGG16 is up to 84.3%.

[15] They detects input variables extracted from electroencephalography (EEG) and structural magnetic resonance imaging (MRI) and then classify disease from dementia separately on both type of variables extracted from EEG and MRI [17]. For the classification, artificial neural network (ANN) is used that included auto encoding [18]. They also combine EEG and fMRI experiment simultaneously in a room. ANN also perform on the variables extracted from EEG + MRI. The ANN auto encoder showed classification accuracies 80%, 85%, and 89% using EEG, MRI, and EEG + MRI features, respectively. [15]

has established a comprehensive DAN's network with multiple fMRI atlases that discriminate against schizophrenic patients in healthy control over a large sample of multiple sites. A variety of input variables have been used to obtain the most accurate results and to improve methodological results such as abnormalities, GM gray matter variations and white matter WM in the brain function of FC frontiers and networks or all active connections. They achieved 85% upper extremity function and 81.8% cortical stiffness.

[16] fMRI and sMRI data were used for a new analysis method called multimodal imaging and multilevel characterization with multi-classifier, here referred as M3 for delineating SZs and HCs. They employed maximum uncertainty linear discriminate analysis (MLDA-) based classification, and multi-classifier. To estimate the performance classifier leave-one-out cross-validation (LOOCV) has been used. Their method achieved an accuracy of classification of 83. 49%; sensitivity 68. 69%; specificity of 93. 75%; and AUC of 0. 849, respectively.

3. System Design and Methodology

This research works concerns task is to categorize Schizophrenia patients while operating the graphical user interface which has been designed and developed using Tkinter. This GUI is designed for the doctors' purpose, so it is to import the patient records and fMRI scans. The fMRI scans obtained are then in the form of 4D but they are then sampled into 2D formats and are saved in a particular folder. The application then will choose out some slices from the folder for classification by the algorithm [17] [18]. The AlexNet model pre-trained on the ImageNet database is employed in the background for the classification purpose. Also, the data entered by the doctor during the classification of the patient such as the symptoms of the patient forms the basis for statistical analysis for the classification of the patient [19].

This data of the respective patient is then pre-processed and subjected to above devised classification model which predicts whether the patient is positive for Schizophrenia or not; this classification result along with the patient data is stored in a MySQL database [20]. To add to that the GUI enables the doctors to view the images as well as the results on the screen. Also important, the doctors can either modify some of the previous records stored concerning a specific patient, or totally eliminate that patient's record from the database [21].

The identification of Schizophrenia patients based on their fMRI scans and symptoms may be challenging and the present project envision to simplify the process for doctors. The procedure improves because one does not have to rely on massive human intervention that could be time-consuming, in addition, it utilizes pre-trained models and automizes fMRI scans slicing [22]. The fact that data is stored in a database to be updated with new changes helps the doctors in case they need to monitor certain patient information or progress of a patient's treatment.

Tkinter has been used in the construction of the graphical user interface; this means that the project can be run on any operating system. MySQL DBMS is chosen to be used as a database management system; it is resistant and can be easily scaled in the context of the project [23]. For instance, the classification done by AlexNet gives very good accuracy and does not require the use of a model that has been trained from scratch [24].

In conclusion the paper gives a solution to the problem of classification of Schizophrenia patients using fMRI and patient symptoms. The gui of the software is easy to use and self explains, the fMRI scans are automatically split into entries, the models which are used are pre-trained, and it is possible for doctors to update the patient data into a database which makes the whole solution efficient and effective. The compatibility of Tkinter and MySQL and the ability of both platforms to expand equally are advantages of the program. The findings and presentations of this project can be useful for doctors and researchers in the field of Schizophrenia.

3.1. FMRI Data Description

The examination was affirmed by the Institutional Review Board (IRB) of King Khalid University, hospital. The group of Member included: healthy controls (control; n =10); and schizophrenia (schizophrenia; n = 10) all those have 400 scans. Participant ages reached between 33.14 ± 9.96 (mean ± SD) in years. Participants have been recruited through the homegrown psychotic clinics or hospitals, and the control group was selected from the health recruitment of a hospital volunteers. Patients and controls participants were all cases, for at least two weeks they were clinically stable.

3.2. Data Pre-Processing

For pre-processing of fMRI data of schizophrenia and healthy control, we used MATLAB (2017) and Statistical Parameter Mapping (SPM 12) software. In SPM12 there are two parts for processing the data. The first part is spatial preprocessing and the second part is parameter estimation. Screening the functional data, we used the pre-processing phase of SPM12. Some steps for basic pre-processing are Realignment, Spatial Normalization, and Spatial Smoothing [25] [33].

3.3. Realignment

When an object moves his head during brain scanning it will disturb (give wrong information) activation of the brain. Therefore, the purpose of realignment is given to correct the location of activation of the object in the brain. The main purpose of realignment is to set all the images in a way in which they lie in the same position in the brain (Zafar, 2016). This head alteration is defined by 3 conversions in the "x, y, z" direction and 3 rotations around the "x, y, z" axes. All images are realigned to a reference image (reference image would be a mean image or any image which one wishes to use as representative). The diagram of realignment is shown in (Figure-3.1).

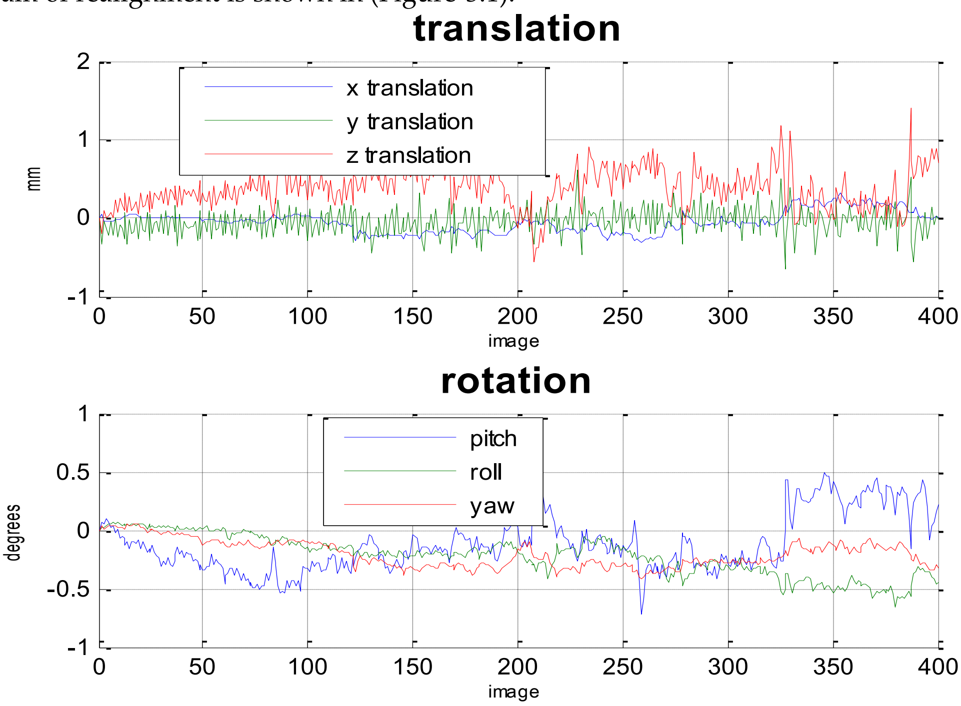

Figure 1. Realignment

In the above figure, we show the translation and rotation limits. The translation range lies between -0.2 to 1 and the rotation range mostly lies -0.5 to +0.5. We can see in the above figure correctly realign because the value of realignment lies between -0.5 to +0.5.

3.4. Spatial Normalization

Spatial normalization is an image recording technique. Brain size varies shift from individual to person.in this step, we normalized the image and transform it in a way that it matched with the template image then apply the parameters of fMRI images [26] [36]. Normalization rotations the one's brain in the rumor runs to a characteristic MNI/EPI format brain, so we can compare useful start crossway over people. Image of normalization, the result is given under in (Figure 2).

In the above figure, EPI template image is on the left side and our image is on the right side. These scans are resliced to a new size.

3.5. Spatial Smoothing

The main purpose of smoothing is to manage functional structural inconsistency that is not rewarded by spatial normalization and improve or recover the signal-to-noise ratio. Further smoothing increases the statistical power. Spatial smoothing (SS) develops flag to demand proportion. Smoothing depends on the Gaussian curve in SPM [27] [37]. After realignment and normalization images are smoothed with a 7x7x7 mm Gaussian filter. The limits of the scan become blurring and the grey areas show the correlation within the regions.

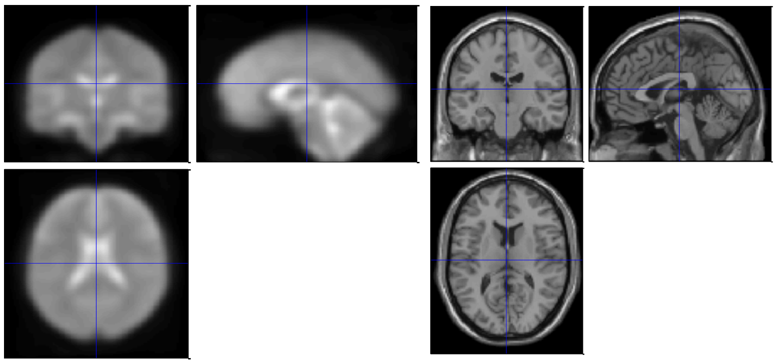

Figure 2. Results of SPM-12

3.6. Parameters Estimation

After preprocessing, we used to specify at 1st level for the analysis of the data. Specifying 1st level follow some steps like after specifying the directory all the 400 scans will be selected units of design will be scanned and inter scans interval is 2 [28]. In this specification, we will give a condition as we know that our data is resting-state data so only a single condition will be used. In this condition, we have used on set 0:20:40:400 with the duration 10.

3.7. Extraction of Data

After specifying the model, the next step is estimation and result. All subjects who are participating in experimental differ that way contrasts are used. Two types of contrast are used t-test and f-test for estimating beta images in this experiment contrast [29] is used for the activation of schizophrenia and healthy control. Next, we define threshold p (0.05, 0.01, and 0.001) value and extent value 0.

The above figure 3.4 shows the activation of the patient in glass brain view during resting-state fMRI experiment. Dark colors in "glass brain" represent the smaller or negative numbers and light colors show the larger numbers. Grey and black area of "glass brain" showing the activated area of SCZ patients.

The above figure 3.5 shows the activation of healthy control in glass brain view during resting-state fMRI experiment. Dark colors in "glass brain" represent the smaller or negative numbers and light colors show the larger numbers. Grey and black area of "glass brain" healthy control brains while resting-state fMRI experiment.

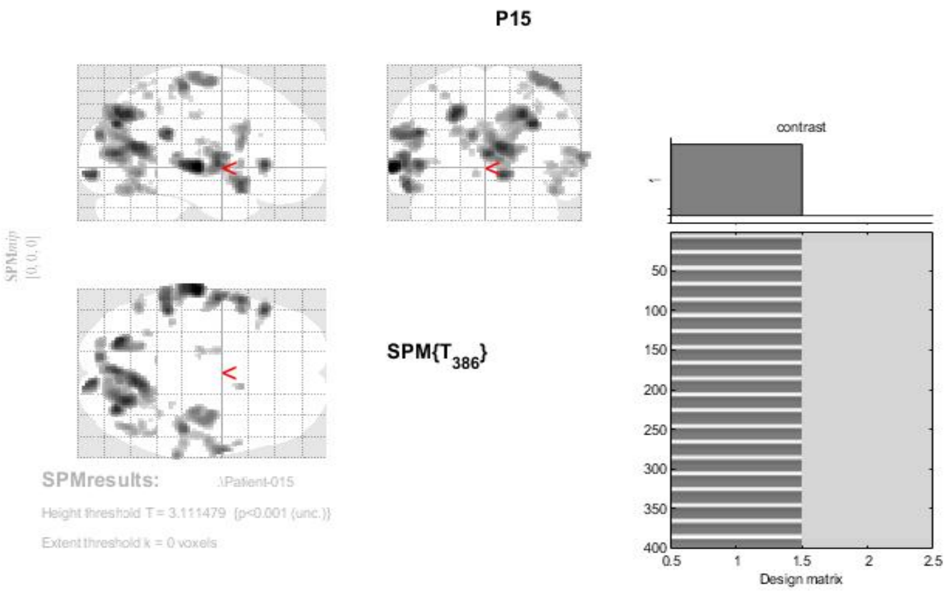

Figure 3. Glass Brain View Shows

The above figure displays the Activation of control and SZ patients in anatomical overlays. Color bar shows of activated area and t-value. Dark color has minimum and Light has a maximum value. This image has a much better view of the activated area of the brain. From the color bar, we can see that healthy control have a more activated area of brain regions as compared to schizophrenia patients.

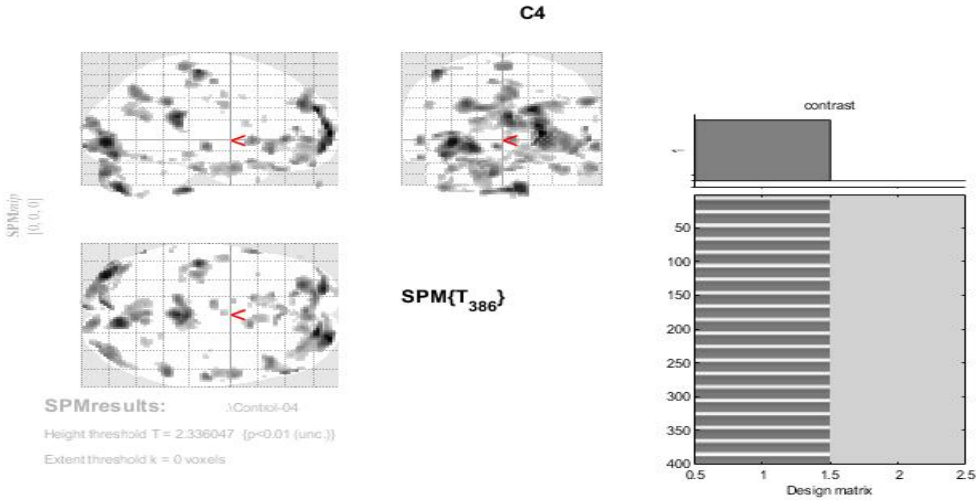

Figure 4. Activation in Patient (Result of SPM-12)

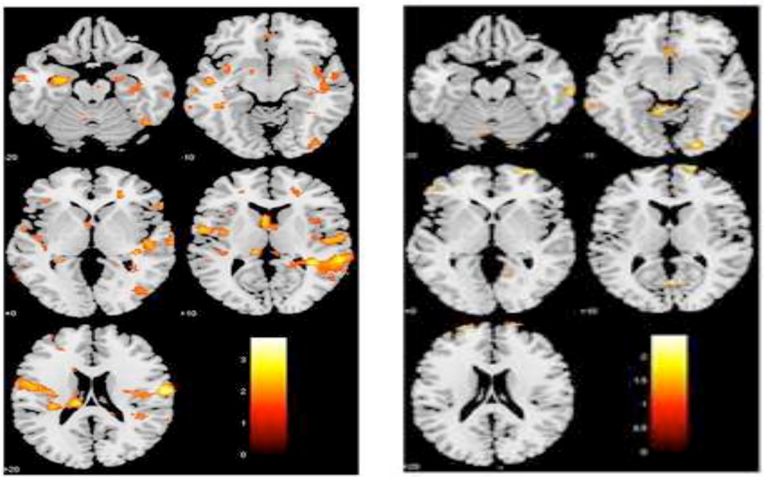

Figure 5. Activation in Control and Patient

4. Algorithm

AlexNet is a type of deep convolutional neural network that was named and presented by Alex Krizhevsky in collaboration with Ilya Sutskever and Geoffrey Hinton in 2012. It was the victorious model in the Image Net Large Scale Visual Recognition Challenge (ILSVRC) of the year 2012. AlexNet is one of the first models that can be attributed to the use of deep convolutional neural networks for the problems in the sphere of computer vision [29].

AlexNet has been designed with five convolutional layers and three fully connected layers besides an input and an output layer. It employs ReLU activation function, max pooling to manage the over fitting and dropout for the same reason [30]. The structure of AlexNet has been employed as the basis of many other computer vision applications, and it has made a considerable contribution to the development of deep learning.

4.1. Input Layer

The input layer in AlexNet is the starting point of the described net; the layer which receives the input data, which, in the case of AlexNet, are images. Hence, the input layer does not alter any of the data but rather collects the data and then forwards the same further to the next layer in the net [31]. The size of the input layer in a neural network depends with the size of the input data; in this scenario, the images.

For instance, if the images are 256 x 256 pixels, then the input layer neurons would be of the order of 256 x 256 x 3 since the images are in three colors of Red, Green and Blue [32]. The result of the input layer is passed to the other layer in the network that is most probably a convolution layer through which feature extraction is conducted on the input.

4.2. Convolution Layer

Convolutional layer is a type of layer that is used in various types of such architectures as Convolutional Neural Network for images identification and computer vision. The main function of a convolutional layer is to identify features in any given data; or in other terms to identify patterns in the data.

A convolutional layer takes an image for instance as the input data and subjects it to a mathematical process referred to as convolution [33] [37]. The operation is calculated by passing a small filter or kernel, also referred as a weight, over the image and taking the dot product of the filter values with the pixel values in the receptive field of the filter. This dot product is then used to produce a new feature map which actually corresponds to a feature map of the original input which has been filtered.

There are various ways in which the filters can be employed on an input data to obtain the features and all the filters give out a feature map. Filters can also be learnt during training using back propagation and gradient descent routines. After convolutional layers are activation functions, pooling layers, and batch normalization layers used. Stating all these layers one on top of another and repeating them multiple times is done to form a deep convolutional neural network.

4.3. Fully Connected Layer

A fully connected layer or also known as a dense layer is a form of layer that is utilized in deep neural networks. Contrary to the convolutional layers, which are designed to work with the spatial structure of the input data, the fully connected layers use the input data as a vector and perform simple matrix operation.

Fully connected layer which may take the output of the previous layer which could be the convolutional layer output, pooling layer output, or the output of another fully connected layer performs the dot product of the weight between the input data. The result is then passed through an activation function such as ReLU or sigmoid function in order to get the output of the fully connected layer.

The fully connected layers are employed in the next levels of the deep neural network for the purpose of making forecasts based on such features. The final fully connected layer of the network usually contains the neurons in the equal number to the quantity of classes in the classification problem and outputs the probability distribution over the classes using the SoftMax activation function. In this manner, the class that has the maximum probability is employed in decision- making as the final prediction of the network.

4.4. Output Layer

It is the last layer of a deep neural network and has the function of giving the final prediction. The output layer consists of taking the output of the previous layer, which could be a fully connected layer or another layer, and working on it to give the final prediction of the class.

Thus, the number of neurons in the output layer depends on the type of the performed task. For instance, in a binary classification problem, the output layer most often contains one neuron only and applies the logistic sigmoid function in order to output probability estimates for each class. For example, in a multi-class classification, the output layer of the neural network model contains as many neurons as the number of classes, and the SoftMax activation function is adopted to calculate the probabilities for each class.

The output of the output layer is compared to the ground truth labels during training and the difference is used to update the weights of the network with the help of back propagation and an optimizer namely stochastic gradient descent or Adam. The main purpose of training is to minimize the difference between the outputs of the network to the actual labels, which enhances the performance of the network on the task being done.

4.5. Output Layer

AlexNet is the technique employed in this project; it is a type of deep convolutional neural network popularized in 2012. AlexNet, is one of the first networks for deep learning in visioning, and has played a role in the later developments of deep learning algorithms in this sector. The purpose of the present work is the usage of AlexNet for the classification of schizophrenia in patients according to the functional magnetic resonance imaging (FMRI).

AlexNet has a structure of 8 layers of which, 5 are convolution layers, 3 are fully connected layers and one output layer. The first layer of the network is the convolutional layer in which the set of filters is convoluted on the image input. They are applied in order to find some specific characteristics or regularities in the input data. The second layer is pooling layers, and its job involves down sampling of the feature maps that have been produced by the convolution layer. This goes a long way in the reduction of the dimensionality of the data as well as in doing away with over fitting. The two subsequent layers are the convolutional and pooling layers that work in the similar way as done for the first two layers.

The last three layers are classified layers, which are fully connected layers for the classification activity. In the final layer of output, the input data is converted for output classifications, and they are probabilistic in nature. AlexNet architecture is built in a manner that allows the model to work with big volumes of image data and provides the feature spaces that are most discriminative.

In this work, the architecture of AlexNet is used and modified for the classification of schizophrenia patient using their fMRI data. The network is learned on the basis of the data pertaining to the patients of schizophrenia and healthy controls. The input data for the network are fMRI data of the patients, where fMRI reflects the functional state of the patients' brain with respect to their cognitive tasks. The target class of the network is also binary, with two classes of control and patient.

The network is optimized by stochastic gradient descent (SGD) and the loss function is the cross-entropy function. Network accuracy is determined normally through commonplace interpretation accuracies which include; accuracy, sensitivity, specificity, prevalence, likelihood ratio of positive and likelihood ratio of negative.

The conclusion of the study shows that the analysis of the patient's condition by using the AlexNet architecture is feasible for the classifying the schizophrenic patients with the help of their FMRI images. The connectivity between the schizophrenia patient and the healthy control subjects in the network is also observed to be significant in terms of accuracy of the network. The project includes front end window form that is enables the doctors to upload the patients' details and FMRI 4D images using Tkinter Python module. The window form first converts the images into 2D images then selects a certain slice for the classification of either positive or negative then the result is stored in the respective database.

All in all, the given project implies that AlexNet can be used for classification of patients with schizophrenia based on their FMRI. In this case the results show that the network is in a position to be able to differentiate patients with schizophrenia and healthy control subjects. It being a project in mental health, this can be of great benefit to the field and can also be further expanded and implemented in other mental health illnesses.

5. Results

5.1. Slicing Nifti Images

Slicing of 4D NIFTI images into 2D PNG images involves the first step of getting the path to the directory of the NIFTI images. This can be done using a function such as askdirectory () from a graphical user interface toolkit such as Tkinter. After obtaining the path to the folder of the NIFTI file the program goes through all the images in the folder of the NIFTI format and loads the image using file using nibabel. Load () from the Nibabel package.

In case of each of the NIFTI images, a particular slice or volume is then chosen, and then transformed into a 2D matrix of the grayscale intensities of the image. The 2D array is further normalized so that the variations in the intensity levels are well defined within a certain interval range such as 0 – 255. The user is then asked to specify where to save the PNG images by another function such as askdirectory (). By normalizing the above obtained 2D array, it can be stored in the location stipulated as the PNG image format by the aid of proper library such as OpenCV or pillow. This is done for all NIFTI images in the folder and the end results are a set of 2D PNG images that can be considered as slices or volumes of the original 4D NIFTI images.

5.2. Train Model

Segmentation of 4D NIFTI images into 2D PNG images entails first determining the path to the directory containing the NIFTI images. This means that slicing of 4D NIFTI images is only achievable if one acquires the path that leads to the directory of the NIFTI images. This can be done with a function for example askdirectory () from a gui toolkit such as Tkinter. Once the function gets the path to the folder of the NIFTI file, it goes through all the images in the folder of the NIFTI format then it loads the image using file using nibabel. for which I used the function load () from the Nibabel package.

For each of the NIFTI images a specific slice or volume is selected and then converted into a two-dimensional matrix of the gray scale intensity of the image. Further normalizations are performed on the 2D array so that contrast in intensity values is clearly defined in terms of the range of intervals such as 0 – 255. The user is then asked where to save the PNG images by other function for instance askdirectory (). The above obtained 2D array can be normalized and it can be stored in the location described that is PNG image format with the help of proper library like OpenCV or pillow. This is done for all the NIFTI images in the folder and the final result is in terms of a series of 2D PNG images which can be regarded as slices/volumes of the original 4D NIFTI image sequences.

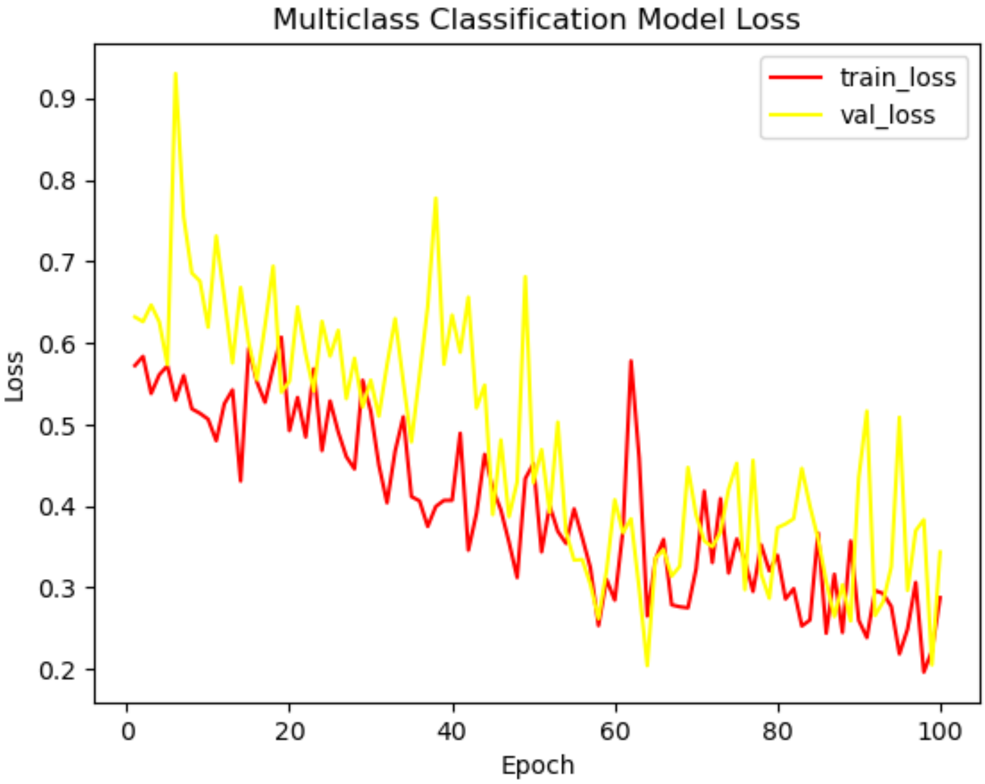

Figure 6. Model Lose Graph

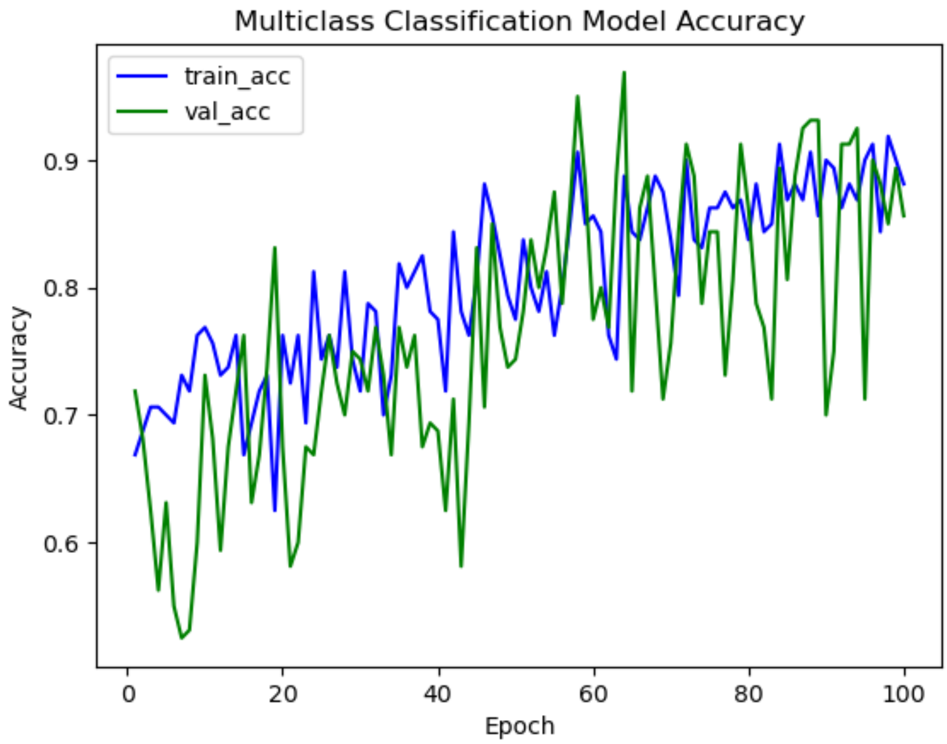

Figure 7. Model Accuracy Graph

The training process resulted in an accuracy of 88%, which means that the AlexNet model was able to correctly classify 88% of the images in the test dataset.

6. Conclusions

This research work has sought to solve the problem regarding the diverse diagnosis of schizophrenia by developing transfer learning algorithms and FMRI data. It was evident from the finding of this study that 88% confidence level, it is possible to enhance the transfer learning algorithms such as Alex Net to classify the patients suffering from schizophrenia through their fMRI data. The front-end window form which was developed using the Tkinter python module offers a friendly environment for the mental health providers to input and analyse patient's data for diagnosis. The performance of the algorithm was compared with the standard performance metrics including the accuracy %, likelihood ratio positive and likelihood ratio negative to prove that the algorithm possesses the ability to enhance the quick and accurate diagnosis of the diseases. The conclusion drawn from this project therefore bear implications on the management of persons with schizophrenia and the general applicability of the artificial intelligence techniques in mental health practice. But more work needs to be done to develop and study these methods to understand to the fullest how they can be applied to this area.

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