Control or Autism - Classification using Convolutional Neural Networks on Functional MRI

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***Abstract*—Autism spectrum disorders (ASDs) because of it's permanent nature, high prevalence, substantial heterogeneity, and complexity contributes to a redoubtable challenge to the field of neuroscience and psychiatry. Thus in order to minimize the requirement of Large-scale multidisciplinary efforts, there is a dire need for the development of a reliable and efficient model that gives results at par with the ones offered by the doctors based on symptomatology. Many significant works have been propagated for classification of ASD, carried out over the Resting-State functional MRI (RS-fMRI) data. A novel convolutional neural network architecture has been developed for substantially analyzing the similarity in brain neural connectivities of the two classes, i.e. autism and control that outperforms existing Machine Learning/Deep Learning methods and produces state-of-the-art (SOTA) results. We have been able to attain an accuracy of 0.76 ± 0.039, precision of 0.7863 ± 0.037, and specificity of 0.8169 ± 0.047 using ten-fold Cross-validation policy on the pre-processed version of RS-fMRI data from the ABIDE-I database.**

***Index Terms*—Autism Spectrum Disorder, Resting-State Functional MRI, Functional Connectivity Matrix, Rectangular Kernels, Evolving Normalisation-Activation**

I. Introduction

In the current scenario, the diagnosis of mental or neurological disorders is difficult as monitoring a set of prodromes forms the pure basis for the diagnosis. Reasons like resembling symptoms and lack of quantitative tests make it a complicated process. Among a large number of such identified disorders, Autism Spectrum Disorder or ASD is a condition of brain development that affects patient ability to perceive and socialize with others as they show repetitive behaviours and limited patterns [1]. A person who has ASD, a developmental disorder starts to show the first of his symptoms in early childhood while it lasts throughout his life. Structural abnormalities in many parts of the brain disrupt connection and the communication of neurons among themselves, which form the cause of this disorder. Facts and figures state that one in every sixty-eight children get affected by ASD with boys being nearly five times more incline to be diagnosed with it than the girls making it one of the fastest-growing developmental disorders in the United States [2]. Brain scans used for diagnosing medical issues are of two types i.e. computed tomography (CT) [3] and magnetic resonance imaging (MRI) based on the medium used for generating the image. CT Scans use X-Ray radiations [4], whereas MRIs uses a strong magnetic field for the same. MRI scans can be further classified as structural and functional where the former create static images of the body's internal anatomy and later generates dynamic images for detecting metabolic activities of the corresponding organ. As it is found that ASD influences the global brain network by blemishing the functional connectivity between multiple regions of the brain. So the proposed method uses RS-fMRI images to classify ASD and control subjects as it is a fast, efficient, and non-invasive technique that evaluates neural patterns. Functional Magnetic Resonance Imaging (fMRI) detects the active parts of the brain by measuring the change in the flow of the blood of the corresponding part, as the neuronal activation and cerebral blood flow are coupled. It is also known as blood-oxygen-level-dependent fMRI (BOLD fMRI) [5]. Autism spectrum disorders (ASDs) contribute to a redoubtable challenge to the field of neuroscience as well as psychiatry due to their permanent nature, high, prevalence, substantial heterogeneity and complexity. Large-scale multidisciplinary efforts are required to face such a problem. Looking at the intensity of the problem posed by this disorder worldwide, We need a model which is reliable and accurate enough to match up to the level of doctors. With the significant advancements in the field of Machine Learning and Neural networks [6], we can come up with a solution which is reliable enough to parallel the result of classification between a normal and an autistic brain given by the doctors. The objective of this research is to effectively carry out the classification between control and autistic brain samples. The technique of anticipating the category/class of input data samples by estimating a mapping function is termed as classification. The selected dataset for

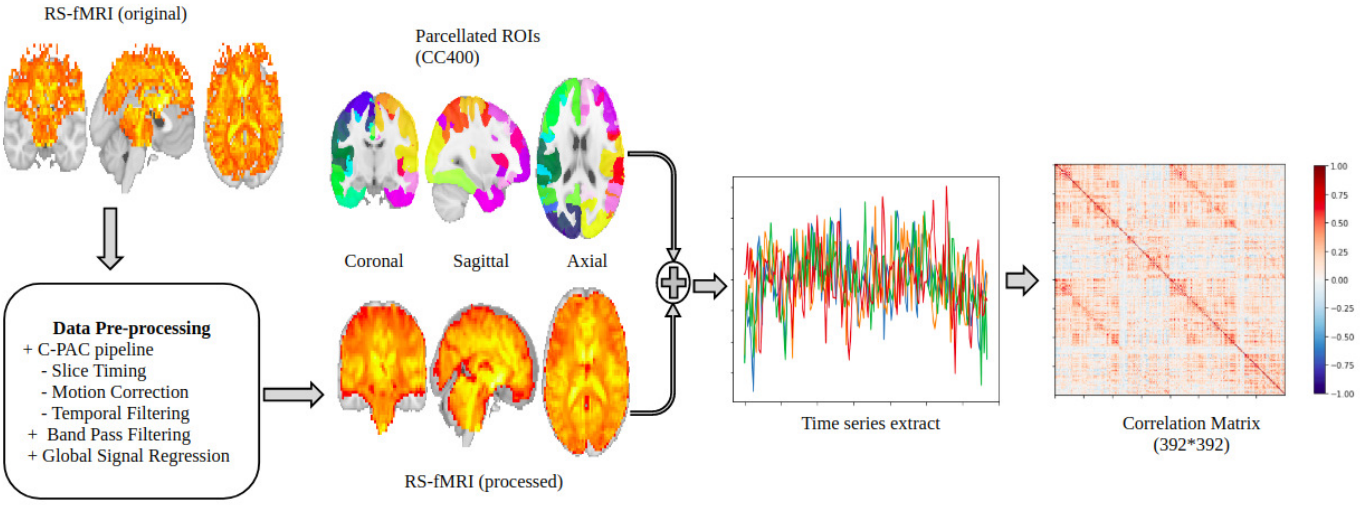

Fig. 1: Data Pre-Processing

the intended work is the fMRI data from the ABIDE dataset. We also intend to propose the model with higher accuracy than the already existing ones.

II. Related Works

An appreciable amount of study confirms that the field of classification of autism spectrum disorder uses Resting-State functional MRI data (RS-fMRI) and Machine Learning/Deep Learning algorithms to process the same [7]. To achieve the objective researchers develop the algorithms which help in finding the similarity in brain neural connectivity of autism and control subjects for the appropriate classification. Abraham et al. [8] proposed an architecture in which predefined brain structural atlases are further improved through four strategies namely K-Means, Ward's clustering, Independent Component Analysis (ICA) and Multi-Subject Dictionary Learning (MSDL). The corresponding data-driven atlases are used to extract time series data and connectivity features. This technique achieves an accuracy of 0.67 by using l_2 & l_1 regression on Support Vector Classification (SVC) algorithm and ridge regression with l_2 penalisation on brain connectivity matrix. Dvornek et al. [9] uses Recurrent Neural Networks (RNN) for classifying RS-fMRI time series into healthy or autistic. In the proposed model, they have achieved the highest accuracy of 0.685 using Long Short Term Memory (LSTM) cells with 32 hidden nodes and a dropout (keep probability rate = 0.5) for regularisation. Parisot et al. [10] leverages graph theory to represent patients or control subjects as nodes and similarity among them as edge weights. They have used Graph Convolutional Networks (GCN) to achieve an accuracy score of 0.7040 in classifying autism and healthy individuals. Aghdam et al. [11] came out with a framework that uses a stack of restricted Boltzmann machines with fully connected layers to form Deep Belief Network (DBN). In this research, authors operated on the data comprising both the RS-fMRI and Structural-MRI(s-MRI) images yielding high sensitivity of 0.84 with 0.6556, 0.3296 as accuracy and specificity, respectively in the classification of autism. Heinsfeld et al. [12] converted functional adjacency matrix (symmetric matrix) into one-dimensional features with unique values. They utilized two auto-encoders to extract lower dimensional features and further to train fully connected layers for classifying autism from typical control individuals. Its accuracy, sensitivity and specificity were 0.7, 0.74 and 0.63, respectively. Niu et al. [13] for classifying autistic patients applied Support vector machine which yielded 0.693 ± 0.059, 0.713 ± 0.059, 0.696 ± 0.072, 0.673 ± 0.113 as accuracy, sensitivity, precision and specificity respectively.They proposed a model Multi-channel Deep Attention Neural Networks (DANN). They combined multiple attention units with densely connected layers, which gave better results than the normal Multi-channel Deep Neural Networks (DNN) model. Their results are reported as 0.732 ± 0.024, 0.745 ± 0.115, 0.730 ± 0.053 , 0.717 ± 0.101 being the accuracy, sensitivity, precision and specificity respectively. Sherkatghanad et al. [14] used convolution networks accompanying rectangular sized filters, max pooling, and dropout operations to classify control and sufferers with an accuracy of 0.7020, sensitivity as 0.77 and specificity as 0.61. In the past, deep learning algorithms using fully connected layers and square sized kernels for convolutional neural networks performed better than machine learning algorithms. One of the recent success [14] utilized rectangular sized kernels which served as our motivation for the current work. We further modified the architecture [14] and minimized the trainable parameters which substantially analyzed correlation among connectomes and consequently outperformed the existing methods.

III. Dataset

Deep learning models require immense amounts of data for training. Collection and processing of medical images is a tedious and arduous task because of a small number of input data as these diseases are rare and sometimes due to privacy

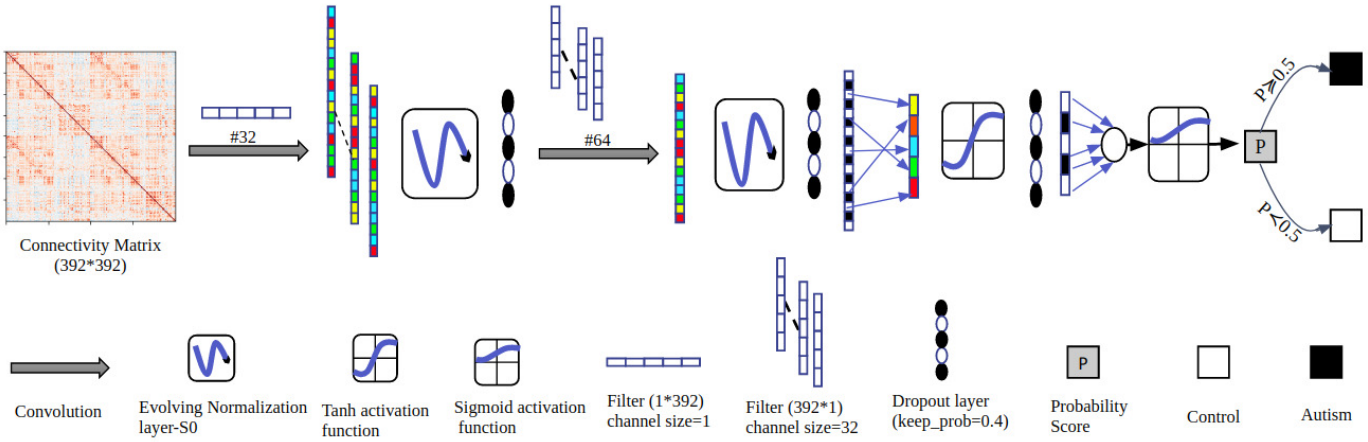

Fig. 2: Network Architecture

issues of the patients. In order to overcome these problems, multi-site worldwide collaborated and gathered phenotypic data and neuroimages obtained from 1,112 patients and created an open-source dataset, namely Autism Brain Imaging Data Exchange (ABIDE) [15]. ABIDE I Preprocessed dataset has been used in our proposed method. It consists of phenotypic and Resting-State fMRI data of 505 ASD and 530 controls patients. We have used RS-fMRI data since ASD impacts the functional connectivity between multiple regions of the brain; these types of data is beneficial for understanding the neural bases of ASD.

A. *Preproccesing*

We have used Connectomes(CPAC) configurable pipeline, band-pass filtering, and global signal regression as strategies to preprocess ABIDE-I RS-fMRI data. The pipelining corrects slice timing, realigns motion artefacts, normalizes voxel signal intensity, and removes the unwanted variation due to heartbeat, respiration, and scanner drift (low frequency) from the functional data. Further, Band-pass filtering (0.01 - 0.1 Hz) [15] was applied to preserve oscillations in functional MRI data between a specific frequency range for better signal to noise ratio, detect actual activation from a Region Of Interest (ROI) in the brain. Global signal regression refers to excluding the global mean signal generated from each voxel of the brain [16]. It enhances both the specificity of positive correlations [17] and anatomical neural connectivity. To obtain specific ROIs, we utilized Craddock 400 [18] (CC400) brain parcellation atlas procedure with ROIs equal to 392, which works a mask for preprocessed RS-fMRI data. Using these, we extract time-series data and further form a functional connectivity matrix using person correlation coefficient between each multivariate time series data. This process is summarised in Figure 1.

IV. Network Architecture

Time series multivariate data gets transformed into a functional connectivity matrix of 392 x 392 dimensions, where each row and column denotes a region of interest (ROI), and each cell represents Pearson correlation coefficient along the corresponding row and column ROIs (ranges from 1 to -1). The matrix so formed is a symmetric matrix with 1 representing the highest correlation between ROIs and vice versa. For attaining higher performance in the classification of Autism Spectrum Disorder using functional connectivity matrix, we have designed a novel architecture based on convolutional neural networks. For Classifying images through Convolutional Neural Networks (CNN), generally small symmetric square size filters (3 x 3 or 5 x 5) is used for extracting valuable features which include information from the neighbouring square pixels [6]. Whereas classifying adjacency brain connectivity matrix in which each cell correlates with every other cell, traditional small symmetric square size filters will not be sufficient. Although through rectangular kernels (with receptive fields being equal to the number of ROIs), we can extract useful content related to correlation per ROI, which serves as an intuitive reason for its improved yielding. We propose an architecture where convolution is applied in two stages, the first row by row (1 x 392 filter), then along with columns (392 x 1 filter) which maps to two hidden dense layers with the final output as a single neuron differentiating control and autism subjects. Initial convolutional layer takes a matrix of 392 x 392 dimension as an input and applies convolution operation using 1 x 392 dimensional 32 filters; thus, these filters can extract 32 unique features per ROI. To further lessen the dimensionality, we convolve the first layer output by 64 filters of 392 height and one as its width & comprising of 32 channels(i.e. 32 x 392 x 1), resultant 64 units feature vector translates to 32 neurons and consequently maps to a single neuron through fully connected dense layers. The recent success of Evolving Normalization-Activation layers [19] in improving convolutional neural networks performance on classification objectives have inspired us to apply in our network instead of using batch normalization along with ReLU as non-linearity. These layers add a slight amount of stochasticity and help in smoothing the optimizing loss curve which speeds up the training time through its normalizing part, CNN

can map its input to output effectivity using its non-linearity function. EvoNorm-S0 is a sample-based (batch independent) evolving normalization-activation function similar (but equal) to Swish activation in the numerator and standard deviation of group normalization in the denominator. Mathematically,

$$\text{EvoNorm} - S0 = \frac{x\sigma(\mathrm{v}_1 \mathrm{x})}{\sqrt{s^2_{w,h,c/g}(x)}}\gamma + \beta \tag{1}$$

In the above equation 1, $s^2_{w,h,c/g}(x)$ refers to group variance, whereas $\beta, \gamma, \mathrm{v}_1$ are learnable parameters and x is an input. It is scale-invariant to x which means it becomes either constant zero or $\frac{\mathrm{x}}{\sqrt{s^2_{w,h,c/g}(x)}}$ when the magnitude of x becomes sufficiently large, the value depends upon the sign of v_1. It is visualised in Figure 3. We use the Tanh activation function for adding non-linearity in the first fully connected layer while the The sigmoid function operates in the last dense layer of the network. If the probability score (Sigmoid's output) is less than 0.5, then the model classifies subject as control otherwise as autism sufferer. Since the dataset was small, a dropout with a keeping probability of 0.4 was applied after each layer output (except the last layer) to regularize the model for achieving better generalization. Our Model's framework is depicted in Figure 2 and its corresponding parameters information is provided in Table I.

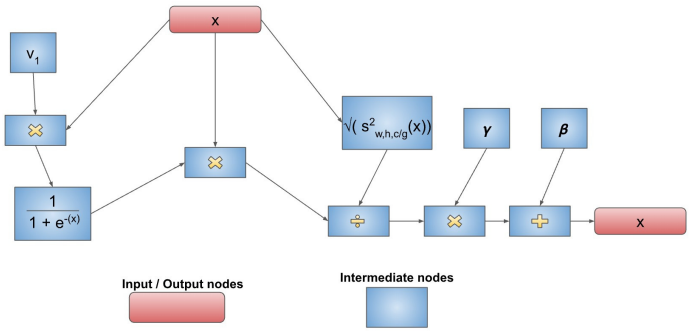

Fig. 3: Evo Norm Act

V. Experimental Setup

A. Implementation Details

Model trains on Resting-State Functional MRI data from the open-source ABIDE association. Pytorch as a framework along with Nvidia Quadro P5000 GPU (16GB virtual RAM) was used to train the model. For classifying Typical Control (TC) and Autism Spectrum Disorder (ASD) patients, we opt for Binary Cross Entropy function as a network's loss function, Adam as its optimizer accompanying a batch size of 32 and performed ten-fold cross-validation on a dataset of size 1035, which includes 931 subjects for training and 104 subjects for validation per fold. As a part of Repeatability, we perform three repeats for getting a better estimation of the evaluation parameters used in the model. Model's input was a brain connectivity matrix (392 x 392) with a single channel and its output was a probability score classifying TC & ASD subjects.

TABLE I: Model summary of the proposed CNN architecture

Layer - #	Output shape	Parameters
Conv2d - 1	[-1, 32, 392, 1]	12,576
EvoNorm2dS0 - 2	[-1, 32, 392, 1]	3
Dropout - 3	[-1, 32, 392, 1]	0
Conv2d - 4	[-1, 64, 1, 1]	802,880
EvoNorm2dS0 - 5	[-1, 64, 1, 1]	3
Dropout - 6	[-1, 64, 1, 1]	0
Linear - 7	[-1, 32]	2,080
Tanh - 8	[-1, 32]	0
Dropout - 9	[-1, 32]	0
Linear - 10	[-1, 1]	33
Total Parameters		**817,575**
Total Trainable Parameters		**817,575**
Total Non-Trainable Parameters		**0**

B. Evaluation Criteria

Confusion-Matrix, Accuracy, Precision, Sensitivity and Specificity is computed using ground truth and predicted labels, whereas receiver operating characteristics by ground truth labels and predicted output probabilities. We tested these parameters for each fold from the validation dataset. Terminologies for the above metrics are:

- Confusion matrix: It is a matrix of 2x2 (binary classification) whose cells represent True Negative (TN), False Positive (FP), False Negative (FN) and True Positive (TP) values, shown in Figure 4.

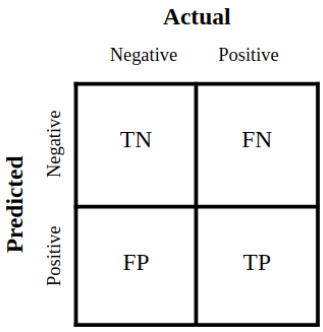

Fig. 4: Confusion matrix

- Accuracy - Amount of correct predictions from the total observed data, calculated by equation 2.

$$Accuracy = \frac{tp + tn}{tp + tn + fp + fn} \tag{2}$$

- Precision: The part of positive predictions, which is actually positive, given by equation 3.

$$Precision = \frac{tp}{tp + fp} \tag{3}$$

TABLE II: Comparing performance values of various models (some entries are: $mean \pm standard\ deviation$)

Reference	Method	Accuracy	Sensitivity	Precision	Specificity
Abraham et al. [8]	SVC-l1 and SVC-l2 Networks	0.67	—	—	—
Dvornek et al. [9]	LSTM32	0.685	—	—	—
Parisot et al. [10]	Graph Convolutional Networks (GCN)	0.7040	—	—	—
Aghdam et al. [11]	Deep belief Network (DBN)	0.6556	**0.84**	—	0.3296
Heinsfeld et al. [12]	Deep Neural Networks (DNN) and transfer learning	0.7	0.74	—	0.63
Niu et al. [13]	SVM	0.693 ± 0.059	0.713 ± 0.059	0.696 ± 0.072	0.673 ± 0.113
Niu et al. [13]	Multichannel DNN	0.707 ± 0.027	0.673 ± 0.088	0.740 ± 0.106	0.700 ± 0.067
Niu et al. [13]	Multichannel DANN	0.732 ± 0.024	0.745 ± 0.115	0.730 ± 0.053	0.717 ± 0.101
Sherkatghanad et al. [14]	CNN	0.7020	0.77	—	0.61
Current work	CNN	$\mathbf{0.76 \pm 0.039}$	0.7004 ± 0.092	$\mathbf{0.7863 \pm 0.037}$	$\mathbf{0.8169 \pm 0.047}$

- Sensitivity: The part of actual positive, which the model correctly predicts, defined by equation 4.

$$Sensitivity = \frac{tp}{tp + fn} \tag{4}$$

- Specificity: The part of actual negative, which the model correctly predicts, calculated by equation 5.

$$Specificity = \frac{tn}{tn + fp} \tag{5}$$

- Receiver Operating Characteristics: It is a curve between True Positive Rate (TPR, y-axis) and False Positive Rate (FPR, x-axis), area under this plot refers to AUC and higher the AUC (tending to one) better the model classifies the dataset, as illustrated in Figure 5.

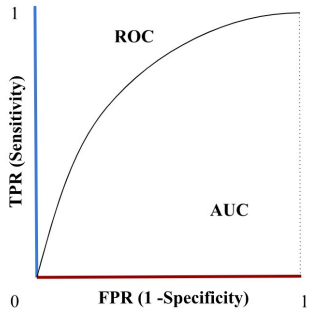

Fig. 5: Receiver Operating Characteristics

VI. Results

We have conducted ten-fold cross-validation on the pre-processed RS-fMRI ABIDE dataset. Results are reported by confusion matrix in Figure 7, receiver operating characteristics in Figure 6 and other testing parameters for each fold as represented in Table III. A unique confusion is computed by summing the confusion matrices of each fold, representing a metric for the whole dataset. Model's accuracy, sensitivity, precision and specificity has been compared with the existing techniques using Machine Learning / Deep Learning within the Domain of RS-fMRI data using the ABIDE Consortium database under ten-fold cross-validation policy, depicted in Table II.

TABLE III: Summary of evaluation metrics using our Model

Fold #	Accuracy	Sensitivity	Precision	Specificity
1	**0.8269**	0.8039	0.8367	0.8490
2	0.8173	**0.8823**	0.7758	0.7571
3	0.7211	0.6078	0.775	0.8301
4	0.7596	0.7647	0.75	0.7547
5	0.7980	0.7058	**0.8571**	**0.8867**
6	0.7184	0.68	0.7234	0.7547
7	0.7572	0.72	0.7659	0.7924
8	0.7087	0.56	0.7778	0.8490
9	0.7475	0.62	0.8157	0.8679
10	0.7475	0.66	0.7857	0.8301
Mean	0.7602	0.7004	7863	0.8169

VII. Conclusion

In the current work, a novel architecture using CNN has been proposed for classifying autism and control patients using RS-fMRI data which outperforms existing Machine Learning/Deep Learning methods and produces state-of-the-art results in terms of accuracy (0.76 ± 0.039), precision (0.7863 ± 0.037) and specificity (0.8169 ± 0.047) using a ten-fold Cross-validation policy. The preprocessed version of RS-fMRI data from the ABIDE-I database was used to train the model. The model, along with high dropout and fewer number of trainable parameters, was able to generalize well despite being trained on a small dataset. Rectangular kernels with a receptive field equal to the total number of regions of

interest (included in RS-fMRI) can extract valuable features as compared to small symmetric filters. The Evo-Norm layer not only sped up the optimization aim but also was scale invariant to the input. Aggregating the techniques as mentioned above, a robust classifier was build for classifying control and autism subjects. Sparse quantity and the bias present in data confined our model's performance which seems to be the only limitation at the moment. Thus as a part of future work, Data augmentation process and better regularization techniques can be used for RS-fMRI data to enhance the above-stated results further. Moreover, 3-D convolutional neural networks can also be utilized for classifying healthy subjects and autism patients through Structural MRI Images.

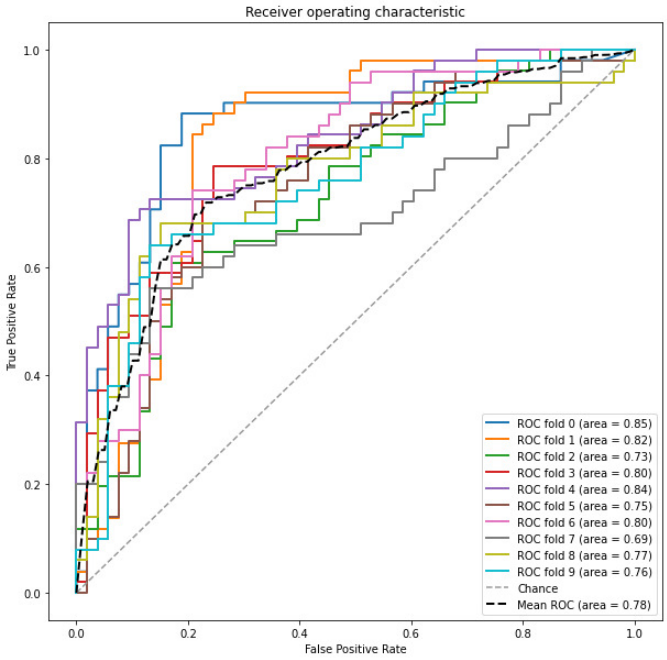

Fig. 6: ROC Curves for each fold

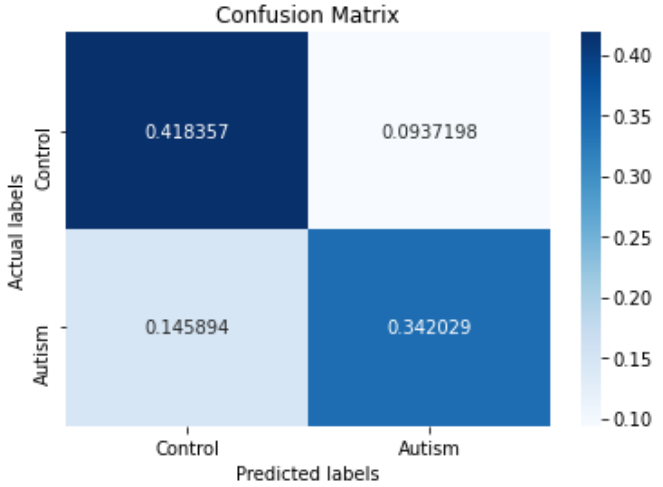

Fig. 7: Confusion Matrix for Whole Dataset

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