

Analysis of Machine Learning and Deep Learning Models to Classify ASD Using fMRI

Dr. Kavitha Jayaram¹, Namya Shrinidhi Sharma², Pooja Basker², Sagarika S.², Sridevi V. Aithal²

¹Associate Professor, Computer Science and Engineering, BNM Institute of Technology, Bengaluru, Karnataka, India

²Computer Science and Engineering, BNM Institute of Technology, Bengaluru, Karnataka, India

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ABSTRACT

Diagnosis of autism spectrum disorders (ASD) is a complex task, the solution of which usually depends on the experience of the physicians due to the lack of specific quantitative biomarkers. Machine learning and Deep Learning approaches are increasingly being used as a diagnostic tool for ASD classification, with the potential to improve discrimination validity among ASD and typically developing (TD) individuals. This paper describes the use of feature selection and two classification techniques to successfully distinguish between individuals with ASD and individuals without ASD, using data from a large resting-state functional magnetic resonance imaging (rs-fMRI) database.

Keywords: ASD, fMRI, Functional Connectivity, Machine Learning, Deep Learning

I. INTRODUCTION

Autism spectrum disorder (ASD) is a disorder that affects a person's social and communication abilities as well as their interests and repetitive behaviours. According to recent research, it is estimated that worldwide about one in 160 children is affected by ASD. Early diagnosis of ASD is critical for the implementation of early intervention and providing a proper treatment plan. The symptom-based diagnosis of ASD generally requires a lot of behavioural assessments under the guidance of a highly experienced multidisciplinary team.

One of the promising candidates for data-driven diagnosis is resting-state functional connectivity MRI (rs-fc MRI) data. Previous research has found that people with autism have abnormal brain connectivity.

Despite extensive research evidence that ASD is a disorder of brain connectivity, it lacks a distributed framework for brain abnormalities. It is still unclear whether brain abnormalities are associated with specific brain regions of ASD.

In this study, we implemented a data-driven approach to classify ASD patients and typically developing (TD) participants by using the rs-fMRI features extracted from Blood Oxygen Level Data (BOLD) in the regions of the brain. The goal of this paper is to apply and analysing machine learning algorithms and deep learning algorithms to classify ASD patients and TD participants using the rs-fMRI data from a large multisite data repository ABIDE (Autism Brain Imaging Data Exchange) and identify the important brain connectivity features.

II. LITERATURE SURVEY

A. Functional Connectivity

Karampasi A. et al. [1] used the ABIDE Preprocessed Dataset along with CC200 atlas. Feature extraction was done using functional connectivity, along with Divergence and Haralick Texture. Five feature selection algorithms were used to select the optimal parameters - Recursive Feature Elimination with Correlation Bias Reduction (RFE-CBR) using both linear and Gaussian kernel, Local Learning Based Clustering FS (LLCFS), Infinite FS (InffS), minimal Redundancy-Maximal-Relevance (mRMR) and Laplacian Score (employing the Feature Selection Library Toolbox). Features selected from each of these algorithms were fed into the classification algorithms - Support Vector Machines (SVM) with linear and Gaussian kernels, k-Nearest Neighbours (kNN), Linear Analysis (LDA) and Ensemble Trees Discriminant. Highest accuracy of 72.5% was obtained with SVM (Linear) when FS is done using RFE-CBR (Linear).

Chaitra N. et al. [2] used the ABIDE Preprocessed dataset along with CC200 atlas. Data Processing Assistant for Resting-State MRI (DPARSF) software was used for pre-processing of resting-state fMRI. Blind deconvolution was carried out to reduce non-neural variability because of hemodynamic response function (HRF). Feature extraction is done using functional connectivity using Pearson's Correlation and complex network analysis. T-test was performed for feature selection. Data after functional connectivity alone, complex network analysis (graph measures) alone and both together were fed into Recursive Cluster Elimination Support Vector Machine (RCE-SVM) classification algorithm. It was seen that combined connectivity and graph measures gave a better accuracy of 70.01% when compared to the rest (67.31% for connectivity and 64.47% for graph measures). Not only this, but they were also able to find the differences in brain connectivity between a control and a patient.

X.Yang et al. [3] used ABIDE Preprocessed dataset and tested the classification algorithms on all atlases - AAL, Dosenbach, EZ, HOA, TT, CC200 and CC400. Feature extraction is done using functional connectivity between 2 regions of the brain. This correlation value ranges between -1 and 1. After feature extraction, the data of each atlas was fed to classification algorithms - Support Vector Machines (SVM), Logistic Regression (LR), Ridge and Random Forrest (RF). It was found that the Ridge classifier along with CC400 produced the best accuracy of 71.98%.

B. Machine Learning

In the past few years, an increasing number of neuroscience research studies have used machine learning models like Naive-Bayes and Decision Tree[4], Support Vector Machines[5] - [8] and deep learning approaches like Convolutional Neural Network[10] and mathematical approaches like Graph theoretical measures[12] to implement data-driven diagnosis of ASD, which would lead to more effective treatment outcomes.

Parikh, et al. [5] Applied linear and non-linear Support Vector Machines (SVM), Random Forest (RF), k-Nearest-Neighbour (KNN) algorithms to diagnose autism in individuals, based on ABIDE I pre-processed data. In SVM, each personal characteristic data (PCD) feature was normalized into a [0, 1] scale to prevent any feature from dominating the optimization of SVM models. For the decision tree model, the CART algorithm was applied (Breiman, L., et al. Classification and Regression Trees, 1984) to create decision trees. For the random forest model, the number of trees were optimized by searching the empirical values [50, 60, 70, 80, 90, 100]. The number of trees was selected when the AUC was the best on the training data.

Wang, et al. [6] defined 35 spheres with the MNI coordinates of these regions as the centre and 5 mm as

the radius. Time courses were extracted from each of the 35 spheres and averaged within each region. Pearson's correlation coefficients (r) were computed between these average time courses. Individuals' r values were normalized to z values using Fisher's z transformation. The SVM and XGB were applied to identify these features, separately. GridSearch CV strategy was used to search for the optimal parameters for the three classifiers. The SVM achieved a mean classification accuracy of 90.60% Applied SVM-RFECV to the obtained data to compare the performance of SVM-RFECV (90.6%) with XGB (72.56%).

C. Deep Learning

Meszlényi, et al. [9] described a convolutional neural network architecture for functional connectome classification called connectome-convolutional neural network (CCNN). The results on resting state fMRI (functional magnetic resonance imaging) network-based classification and a publicly available dataset for amnesic mild cognitive impairment classification demonstrate that the CCNN model can efficiently distinguish between subject groups. The connectome-convolutional network is capable to combine information from diverse functional connectivity metrics and that models using a combination of different connectivity descriptors are able to outperform classifiers using only one metric is also shown. From this flexibility follows that the proposed CCNN model can be easily adapted to a wide range of connectome-based classification or regression tasks, by varying which connectivity descriptor combinations are used to train the network.

F. Ke, et al. [11] investigated the structural and strategic bases of ASD using 14 different types of models, including convolutional and recurrent neural networks. Using an open-source autism dataset consisting of more than 1000 MRI scan images and a high-resolution structural MRI dataset, the paper demonstrated how deep neural networks could be used

as tools for diagnosing and analyzing psychiatric disorders. Training 3D convolutional neural networks to visualize combinations of brain regions is achieved, thus representing the most referred-to regions used by the model whilst classifying the images. Recurrent neural networks to classify the sequence of brain regions efficiently were also implemented. We found emphatic structural and strategic evidence on which the model heavily relies during the classification process.

III.METHODS AND MATERIAL

This paper is a data-driven analysis to classify subjects as neurotypical or autistic, with the data being obtained from ABIDE under a specific ROI atlas. Here, we use Craddock 200 (CC200). The time-series data undergoes further pre-processing to deem it suitable for the next steps.

The functional correlation between the regions of interest (ROI) is calculated, after which the matrix undergoes a dimensionality reduction. This ensures that only significant correlations are retained. The resulting dataset is fed to RCE-SVM and CNN models. The results obtained are collected and compared for analysis.

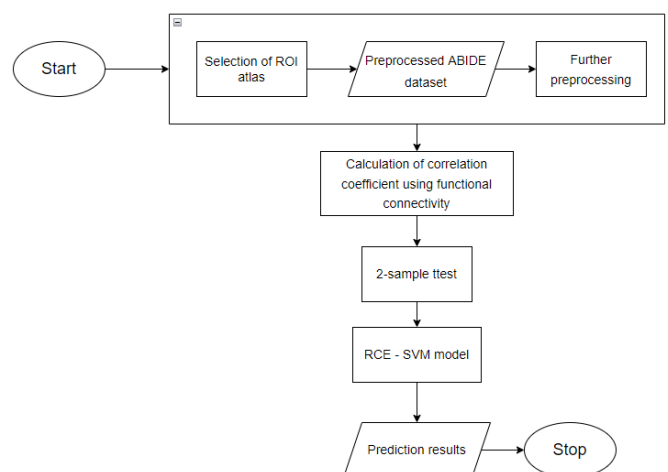


Fig. 1. Methodology

I. Dataset

The ABIDE consortium of 16 imaging sites has aggregated data from 539 individuals with ASD and 573 individuals without ASD, sharing the data openly so that researchers can learn more about the differences between these groups. These 11112 datasets are composed of structural and resting state functional MRI data along with an extensive array of phenotypic information.

ABIDE data can be used in various formats. There a number of atlases available, such as CC200, C400 and AAL which map out the human brain into several sections, each following a different set of areas, partitions and labelling. The data extracted from the ABIDE dataset first undergoes pre-processing to remove any unwanted information such as noise, outliers, incorrect values and values in inconsistent formats. There are various pipelines that can be used to filter the data, such as CCS, CPAC, etc. This data is then processed to extract features. The algorithms used to extract the features determine which have a higher correlation to ASD symptoms. These features are then used, while the irrelevant ones are discarded. The finalized features are then fed as input to the classification algorithms.

The paper is a data-driven analysis to classify subjects as neuro-typical or autistic, with the data being obtained from ABIDE under a specific ROI atlas. Here, we use Craddock 200 (CC200). The processed dataset used in the paper was segregated on the basis of the university from which the time-series data was obtained. We have made use of data from four universities, namely Caltech, UCLA, Yale and CMU. The time-series data is stored in the form of 1D files per patient in each college, as shown below:

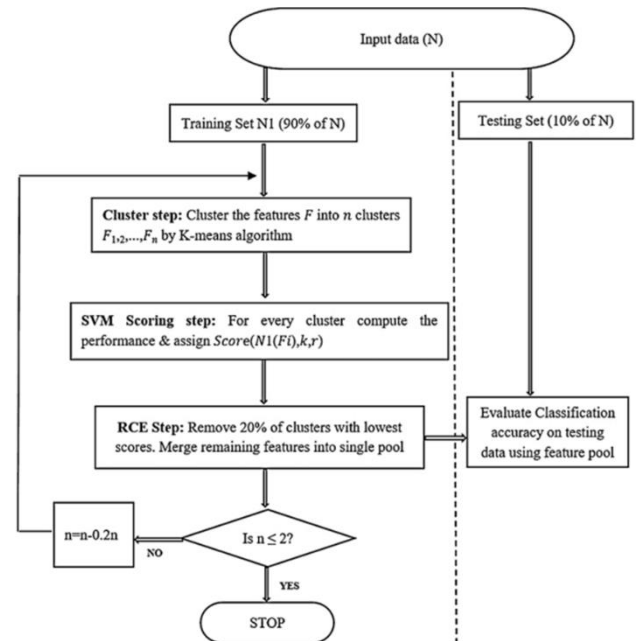
ROIS_cc200	CMU_a_0050653_rois_cc200.1D	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12
Caltech_0051491_rois_cc200...	1	-22.528225	-9.658229	-8.58878	0.764776								
Caltech_0051492_rois_cc200...	2	-18.691798	-22.752668	-2.308194	-1.731526								
Caltech_0051493_rois_cc200...	3	-16.308761	-28.892603	3.776652	-1.189408								
CMU_a_0050649_rois_cc200.1D	4	-15.79153	-23.678346	2.195081	2.512485								
CMU_a_0050653_rois_cc200.1D	5	-11.085301	-9.476474	-8.64767	10.101422								
CMU_b_0050651_rois_cc200.1D	6	0.787822	6.543935	-21.472713	21.921497								
CMU_b_0050657_rois_cc200.1D	7	13.730187	16.503708	-25.375607	33.321258								
CMU_b_0050669_rois_cc200.1D	8	18.278797	16.248162	-15.12768	34.275791								
KKJ_0050772_rois_cc200.1D	9	12.109015	8.313014	4.050718	18.035408								
KKI_0050773_rois_cc200.1D	10	2.738198	0.621843	21.029855	-9.234075								
KKI_0050774_rois_cc200.1D	11	-0.162027	0.234703	28.468229	-30.96479								
KKI_0050775_rois_cc200.1D	12	6.583639	7.030798	28.307167	-35.328318								
KKI_0050776_rois_cc200.1D	13	18.888333	14.250751	27.971969	-26.93732								
KKI_0050777_rois_cc200.1D	14	30.848527	16.283794	31.775102	-20.811446								
KKI_0050777_rois_cc200.1D	15	38.662698	14.89931	36.72085	-24.888948								
KKI_0050777_rois_cc200.1D	16												

Fig. 2. Time series data

The time-series data undergoes further pre-processing to deem it suitable for the next steps.

II. Data Preprocessing

Time series data taken from ABIDE’s public S3



bucket on AWS data undergoes pre-processing where it undergoes slice timing correction, motion realignment, normalization, nuisance removal and standardization.

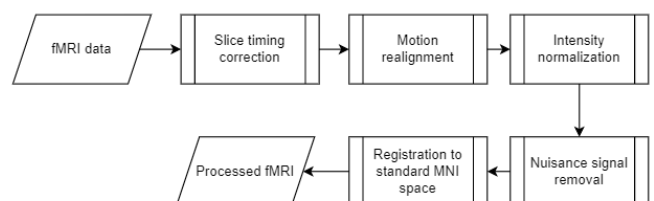


Fig. 3. Data Preprocessing

III. Feature Extraction

The correlation of the different regions of the brain are calculated using functional or effective connectivity. This is done for each subject.

IV. Feature Selection

The goal of feature selection is to remove noisy, redundant or irrelevant features from the data while minimizing the information loss. Feature selection can often be an advantageous pre-processing step for training supervised learning algorithms. Feature selection can be performed in a supervised or unsupervised fashion. The T-test estimates the true difference between two group means using the ratio of the difference in group means over the pooled standard error of both groups. It can only be used when comparing the means of two groups. T-Tests is used to perform feature selection.

V. Learning and Classification

1) Recursive Cluster Elimination Support vector machines (RCE-SVM): The SVM is one of the most commonly used classification and regression algorithms in rs-fMRI studies. The support vector machine finds an optimal separating hyperplane between classes to maximize the margin. The RCE-SVM tool facilitates the easy assessment of the performance of every individual cluster of functional connectivity groups. This helps to identify those clusters that offer the least significance in classification of the data. These clusters are excluded from the analysis, with clusters showing higher performance in the classification retained. After each elimination, the data is re-clustered to form new clusters. These clusters may be stronger than the previous clusters.

Fig. 4. Flow of RCE-SVM [14]

2) Deep neural networks: A CNN uses a system much like a multilayer perceptron that has been designed for reduced processing requirements. The layers of a CNN consist of an input layer, an output layer and a hidden layer that includes multiple convolutional layers, pooling layers, fully connected layers and normalization layers. Generally, CNN's have multiple layers that process and extract features from data. Firstly, convolution layer which has several filters to perform the convolution operation. It is followed by Rectified Linear Unit (ReLU) to perform operations on data elements, the rectified feature map output is then fed into the pooling layer which is a is a down-sampling operation that reduces the dimensions of the feature map. The pooling layer then converts the resulting two-dimensional arrays from the pooled feature map into a single, long, continuous, linear vector by flattening it.

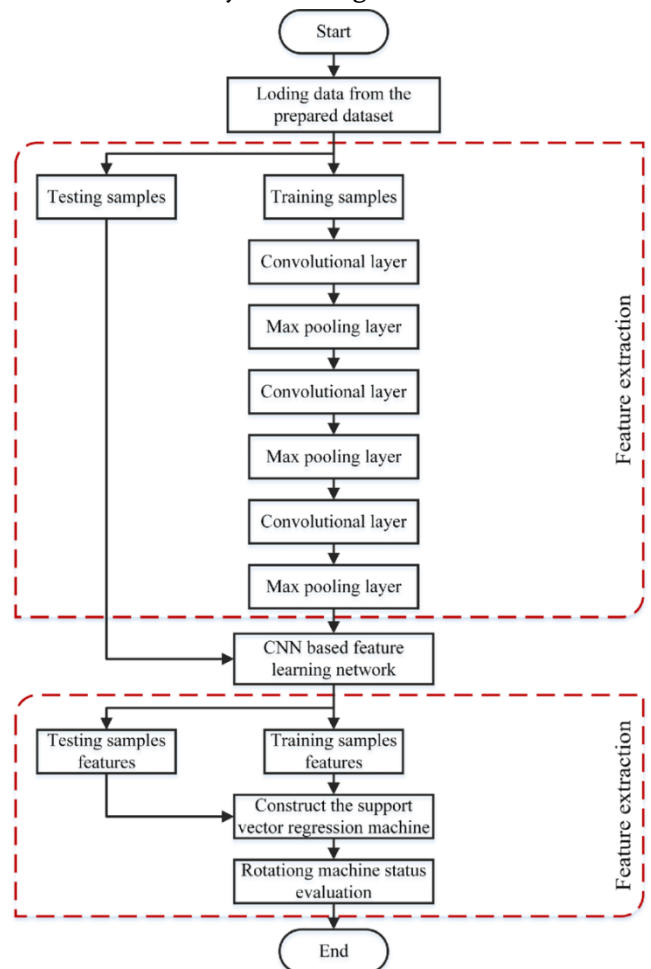


Fig. 5. Flow of CNN [13]

IV.IMPLEMENTATION

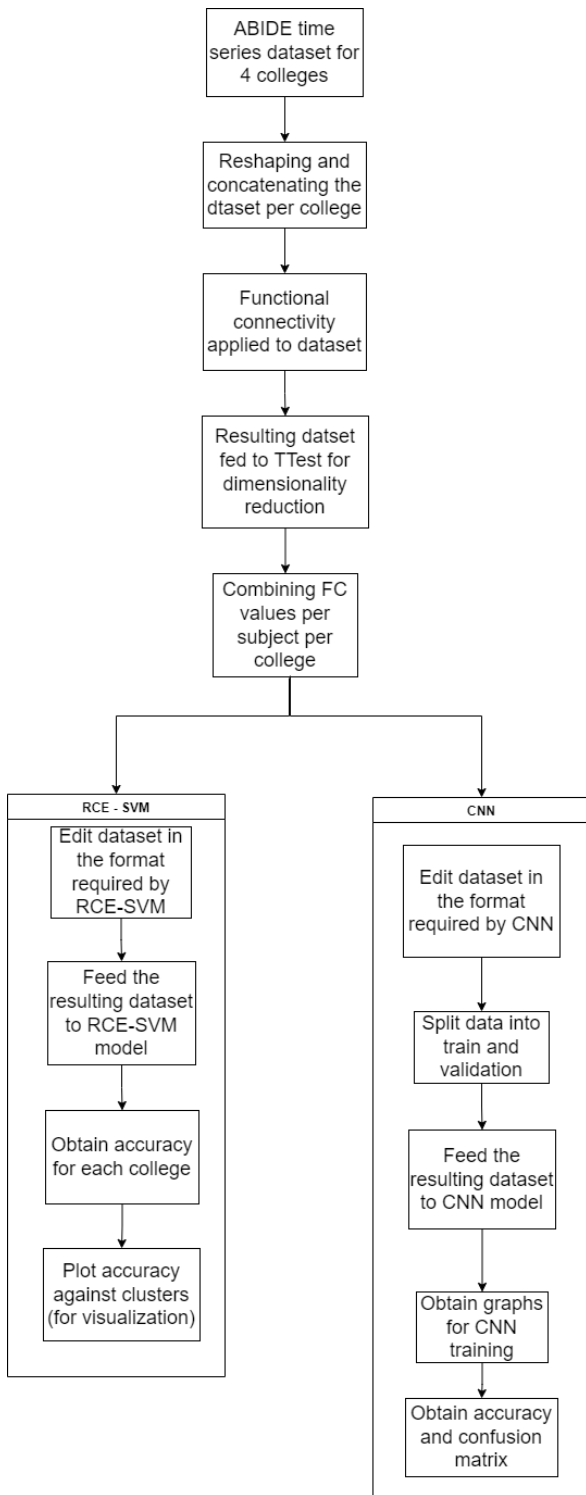


Fig. 6. Flow of the implementation

The system is designed and developed on MATLAB (MATrix LABoratory), which is a programming and computing platform that is used extensively by scientists, research students and engineers to analyse and build systems. It is often used for technical computing and visualization. Many functions, such as matrix manipulation, function plotting, graphs are used, along with supplementary programs that help to simulate graphics, neural networks, embedded systems, etc.

First, we downloaded the ABIDE time series dataset for four colleges – Yale, UCLA, CMU and Caltech. Each college had multiple subjects. Every subject’s time-series data is stored in one file. We performed reshaping and concatenation of the data in such a manner (flat 1D files to 3D) that it can be fed to the functional connectivity algorithm. Resulting dataset of functional connectivity between multiple regions of the brain is fed to the t-test algorithm for dimensionality reduction.

We then combined the functional connectivity data for each subject per college into one excel file which will be converted to mat file and fed to both CNN and RCE-SVM.

For RCE-SVM: After obtaining the accuracy for each college, we plot the accuracy against the number of clusters for visualization.

For CNN: We split the data into train and validation (the amount of split varies each time) and obtain the accuracy and confusion matrix for each split.

```

MATLAB R2012a
File Edit Debug Desktop Window Help
Shortcuts How to Add What's New
Command Window
#Iteration:600

Start the Learning...
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (8/8) (classification)
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (11/11) (classification)
Accuracy = 100% (8/8) (classification)
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (9/9) (classification)
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Accuracy = 100% (9/9) (classification)
Accuracy = 100% (11/11) (classification)
Accuracy = 88.8889% (8/9) (classification)
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (8/8) (classification)
Accuracy = 100% (9/9) (classification)
Accuracy = 100% (9/9) (classification)

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Fig. 7. RCE-SVM in progress

V. RESULTS

We investigated how machine learning and deep learning models can be applied to identifying individuals with a complex psychiatric disorder such as ASD. We primarily used the RCE-SVM algorithm and CNN as analysis and diagnosis tools, building them with various architectures.

RCE-SVM

In Fig 7, we displayed the classification of RCE-SVM in progress. The input data an Excel file format (.xlsx) is split into training and validation in a ratio of 60-40 (according to the k-fold value of 6). The accuracy obtained on the input data collected from patients across various universities, such as UCLA, CMU, Caltech and Yale are presented below. Each university has a set of patients segregated into two classes - control (CNT), who are neurotypical individuals, and autistic (ASD), who are individuals suffering from Autism Spectrum Disorder. The results for each of these universities implementing RCE-SVM is given below:

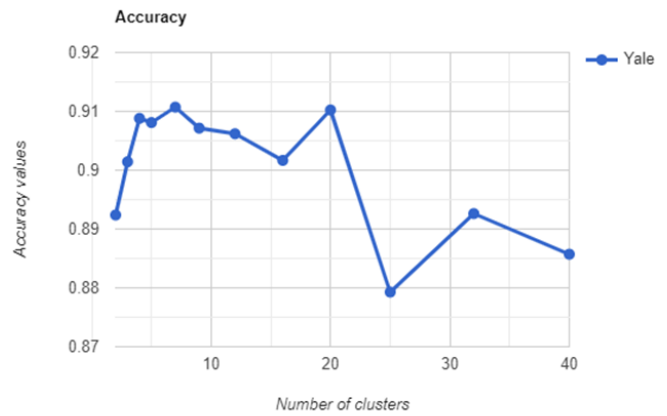


Fig. 8. RCE-SVM results for Yale

In Figure 8, RCE-SVM for Yale is seen to perform best on the data when the number of clusters are 20, with a steep improvement in accuracy. It finalizes its accuracy at 87.93% at a cluster level of 2.

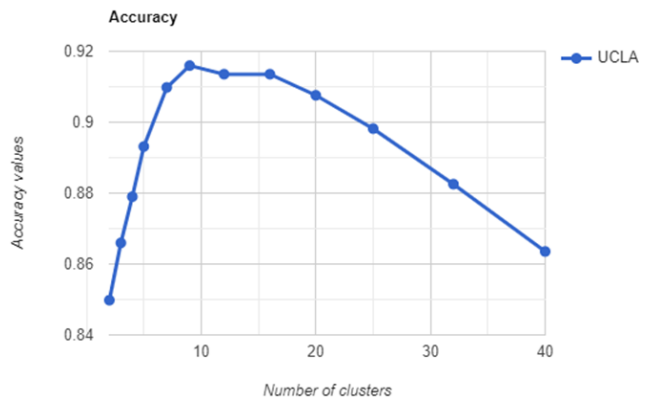


Fig. 9. RCE-SVM results for UCLA

In Figure 9, RCE-SVM for UCLA performs best on the data when the number of clusters are 8, and sees a rapid decline with a further decrease in clusters. It finalises its accuracy at 84.98% at a cluster level of 2.

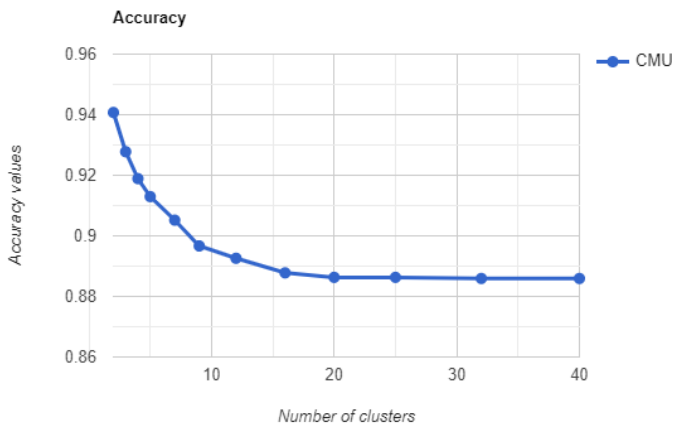


Fig. 10. RCE-SVM results for CMU

In Figure 10, RCE-SVM for CMU is seen to have a steady improvement in accuracy as the number of clusters decrease. It performs best on the data when the number of clusters are 2, facing no decline in accuracy as the algorithm proceeds further. It achieves its final accuracy at 94.07% at a cluster level of 2.

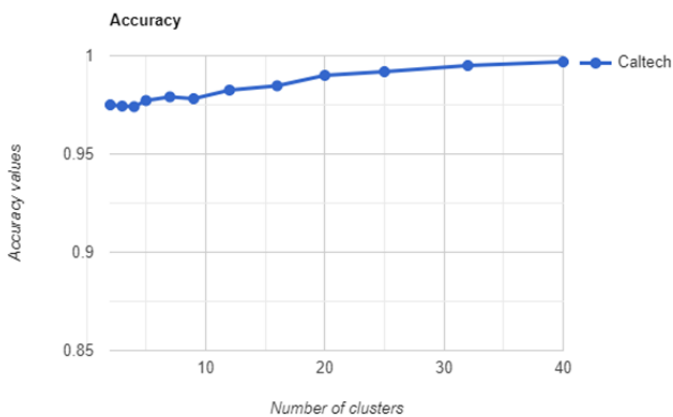


Fig. 11. RCE-SVM results for Caltech

In Figure 11, RCE-SVM for Caltech is seen to have a steady decline in accuracy as the number of clusters decrease. It performs best on the data when the number of clusters are 40, facing a slight decline in accuracy as the algorithm proceeds further. It achieves its final accuracy at 97.50% at a cluster level of 2.

CNN

The training progress, validation results and confusion charts are illustrated for the data retrieved

from mentioned universities. In the implementation, part of the data is split for modelling, testing and training and the experimentation involves three different cases for each of the individual university data collection. For every university, 30% of the data for training and 70% for validation, similarly 50% for training with 50% for validation and 70% for training with 30% for validation.

Caltech

Train-Validation split: 70-30

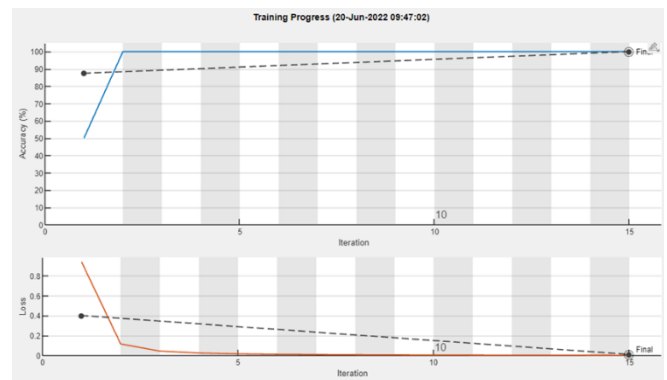


Fig. 12. CNN results for Caltech 70-30

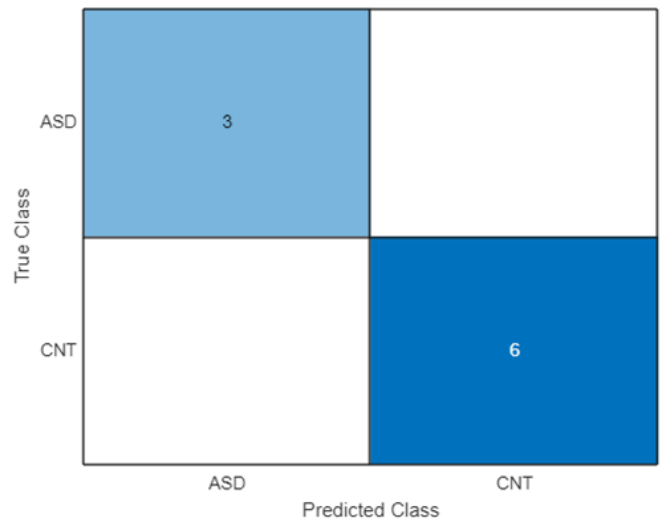


Fig. 13. CNN confusion matrix for Caltech 70-30

Results	
Validation accuracy:	100.00%
Training finished:	Max epochs completed
Training Time	
Start time:	20-Jun-2022 09:47:02
Elapsed time:	28 sec
Training Cycle	
Epoch:	15 of 15
Iteration:	15 of 15
Iterations per epoch:	1
Maximum iterations:	15
Validation	
Frequency:	50 iterations
Other Information	
Hardware resource:	Single CPU
Learning rate schedule:	Constant
Learning rate:	0.001

Fig. 14. CNN validation results for Caltech 70-30

For data collection retrieved from Caltech University, the data is split into 70% for training and 30% for validation and the training progress and validation results are displayed in Figure 11 and Figure 13 in which we can observe that accuracy is increasing after each epoch(iteration). Figure ## shows confusion chart where parameter representing patients suffering from Autism is ASD and CNT represents control that is neurotypical individuals. The confusion matrix displays the total number of observations in each cell. The rows of the confusion matrix correspond to the true class, and the columns correspond to the predicted class. Diagonal and off-diagonal cells correspond to correctly and incorrectly classified observations, respectively. The accuracy obtained using our proposed 1D CNN is 100% for this case.

Comparatively, we have fed the Caltech data to the network with 30 -70 and 50 - 50 training and validation split leading to 95.45% and 100% accuracy. Similarly, for data retrieved from patients across universities like Yale, UCLA and CMU, the training and validation split levels are experimented and the resulting training - validation progress, confusion charts, and the accuracies are recorded.

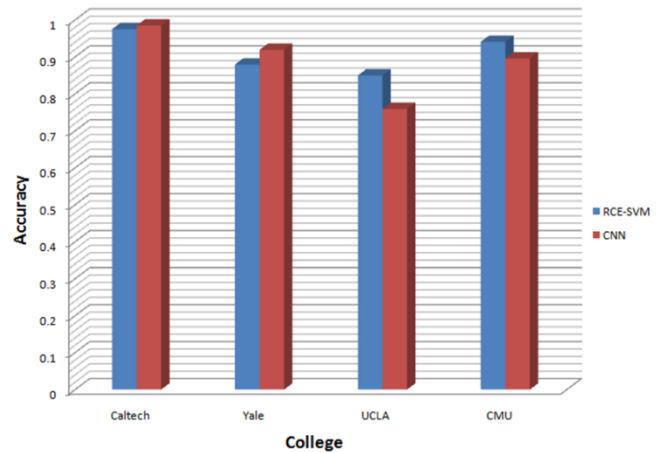


Fig. 15. Comparison of Accuracy for CNN vs RCE-SVM

COLLEGE	ACCURACY
Caltech	0.975
Yale	0.8793
UCLA	0.8498
CMU	0.9407

Fig. 16. Consolidated results for RCE-SVM

COLLEGE	TRAIN	VALIDATION	ACCURACY
Caltech	0.3	0.7	0.9545
	0.5	0.5	1.00
	0.7	0.3	1.00
Yale	0.3	0.7	0.8996
	0.5	0.5	0.8571
	0.7	0.3	1.00
UCLA	0.3	0.7	0.6667
	0.5	0.5	0.7143
	0.7	0.3	0.8966
CMU	0.3	0.7	0.8889
	0.5	0.5	0.9231
	0.7	0.3	0.875

Fig. 17. Consolidated results for CNN

Figure 15 and Figure 16 specify the obtained accuracies for the universities Caltech, Yale, UCLA and CMU patients data for experimentation done using RCE-SVM and CNN. We compared classification performances of both RCE-SVM and CNN for simulated data of every college and the accuracies are graphically represented in the below figure, having blue bar and red bar representing machine learning model, RCE-SVM and proposed deep learning model, CNN respectively.

VI. CONCLUSION

As seen from the results, the outputs from the deep learning model (CNN) are slightly better than the results obtained from the machine learning model (RCE-SVM). This can be attributed to the fact that deep learning model out performs other techniques when the data size i.e., the number of features, is large. The number of features for each college is 2000+. Thus, deep learning gives a slightly better output. In the paper we have considered 4 colleges separately. There is a lack of understanding of how the functional connectivity data relates to ASD. In such situations, deep learning techniques outshine others as they will draw conclusions when the relationship between the label and features isn't apparent.

VII. FUTURE ENHANCEMENTS

As a future enhancement, we can perform effective connectivity on the time-series data instead of functional connectivity and compare the two methods of feature selection. Apart from this, the scope of this paper extends only to 4 colleges, but in the future a combined dataset can be fed to the deep learning and machine learning models and observed.

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