TransLearning ASD: Detection of Autism Spectrum Disorder Using Domain Adaptation and Transfer Learning-Based Approach on RS-FMRI Data

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Autism Spectrum Disorder abbreviated as ASD, is a complex neuro-developmental disease specifically linked to nervous system that influences patients' communicationand social behavior. Traditional clinical techniques used for the discovery of ASD fall short of definite and early ASD diagnosis. Consequently, biomarkers have been introduced in the field of ASD diagnosis and particularly, resting-state functional Magnetic Resonance Imaging (rs-fMRI) has posed as a valuable biomarker. Researchers have focused on utilizing the vast span of Artificial Intelligence techniques in combination with rs-fMRI, to build an effective framework for ASD detection. However, these systems have not been able to generalize to a larger set of patients, because of theheterogeneity in the available f-MRI dataset for ASD. Motivated from the aforementioned discussion, this study performs a comprehensive literature review of the existing systems covering a period of 2019-2021, thereby identifying several research gaps. To overcome the effect of existing implications, this paper expounds a TransLearning ASD framework which will achieve normalization of the heterogeneous fMRI data using domain adaptation followed by transfer learning technique for effective ASD prediction and to overcome the model generalization problem

Keywords: Machine Learning, Deep learning, ABIDE, ASD, Functional MRI, Domain Adaptation, Transfer Learning etc.

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1. Introduction

Autism Spectrum Disorder is a neuro-developmental condition that influences the way a person perceives and communicates with others. The disorder causes problems with social interaction and communication. According to the Centre for Disease Control and Prevention's (CDC) Autism and Developmental Disorders Monitoring Network (ADDM) approximates that about 1 in 44 children have been diagnosed with Autism SpectrumDisorder (ASD). Moreover, ASD has been reported to occur in all cultural, ethnic and socioeconomic groups. Clinical behavior and symptoms form the base of most of long-established diagnosis of ASD, which is carried out using interview-based methods. These methods can be accomplished successfully only after the symptoms show to a particular extent in the affected children. According to a study, ASD symptoms at the age of 2 years can strongly predict its diagnosis by the age of 4 years[1]. Another study's results show that ASD diagnosis before the age of 2.5 years can be instrumental in significant improvement in social symptoms, later on[2]. Thus, even if ASD is incurable, early diagnosis can be highly beneficial for the affected.

To circumvent the shortcomings of traditional clinical methods, Machine Learning and Deep Learning is being introduced in the field of Neuro-imaging so that the exact diagnosis of ASD can be performed effectively. Researchers have turned to machine learning over traditional statistical methods for data analysis due to the high prevalence rate and heterogeneous nature of ASD. Machine Learning techniques have been employed on various biomarkers in the field of ASD diagnosis of which Resting State Functional Magnetic Resonance Imaging (rs-fMRI) has come out as a potential biomarker[3], [4], [5]. Resting state functional magnetic resonance imaging is a non-invasive brain imaging technique which uses blood-oxygenation-level dependent (BOLD) as a neurophysiologic indicator to measure brain activity. The main drawback of using ML techniques is that they do not take into account the heterogeneity in the f-MRI dataset (Demographics, Age, Scan Parameters) and therefore, fail to develop a generalized model for ASD detection. More recently, Transfer Learning techniques have come into picture, which can be instrumental for normalizing the multi-site data obtained from different sources and bringing it to an equivalent level which can aid an early ASD diagnostic process.

The structure of the paper is as follows: Autism Spectrum Disorder (ASD) has been explained in brief in Introduction part in Section 1. Section 2 describes a range of techniques presented by various researchers for ASD detection. Comparative and relative analysis of the ASD techniques is illustrated in Section 3, followed by the limitations in existing systems in Section 4. A new framework TransLearning_ASD for detection of ASD using domain adaptation and transfer learning on rs-fMRI data is proposed in Section 5. Finally, Section 6 completes the paper by pointing out some noteworthy statements.

2. Literature Review

- This section presents a concise outline of the existing systems which have employed AI techniques namely Machine Learning (ML), Deep Learning (DL) and Transfer Learning (TL) for the detection of ASD.
- Karampasi et al. [3] presented a model which adopted modular features extracted from f-MRI data, namely the Haralick texture features and the Kullback-Leibler divergence in collaboration with FC and demographics, to classify ASD and TD. RFE with correlation bias reduction was used for feature selection which were fed to several ML models. SVM with linear kernel outperformed the rest with an accuracy of 72.5% on a group of 399 ASD and 472 TC.
- In the work of Ahmed et al. [6], deep learning-based features extracted from f-MRI data using Restricted Boltzmann Machine (RBM) and fed as input to SVM classifier to achieve an accuracy of 83.00% on a dataset comprising 79 ASD and 105 TC subjects.
- Y. Liu et al. [4] utilized Extra-Trees algorithm for feature selection from rs-fMRI data of CC200 atlas of the brain. With cross-validation strategy using SVM classifier their proposed method achieved a mean classification accuracy of 72.2%.

- Zhao et al.[5] developed a novel high-order dynamic-FC networks based central-moment method to extract temporal-invariance properties inherent in either low- or high-order D-FCNs. Using SVM as a classifier, they were able to achieve 83% accuracy with their model.
- Chaitra et al. [7] computed a set of complex brain network features were computed from the FC network using graph techniques. Using Recursive Cluster Elimination, the features were selected and provided to SVM classifier to achieve an accuracy of 70.1%.
- Song et al. [8] conducted their study on a f-MRI data of a ABIDE cohort of 119 ASD and 116 TC obtained from multiple sites. By using only community pattern quality metrics as features, they trained KNN and a LDA ML models, subsequently achieving better accuracy with LDA (85.16% maximum accuracy for in-site data and 74.86% maximum accuracy for multisite data).
- In a study by Kazeminejad and Sotero[9], the preprocessed ABIDE dataset comprising 817 participants was split into five age groups and classification accuracies for each range were obtained in the range of 69%-95%. The model employed graph theoretical metrics of fMRI-based FC to train a SVM classifier.
- Shao et al. [10]propounded a united framework consisting of deep feature selection (DFS) and Graph Convolutional Network(GCN) method to detect ASD. DFS network selected a subset of FC features which are fed to the GCN to achieve an accuracy of 79.5%.
- Huang et al. [11] propounded a graph-based kNN algorithm to find more informative representations of the FC networks in the f-MRI data. The features were fed to a three-layer Deep Belief Network (DBN) model for classification of ASD and TC. The model achieved 76.4% accuracy.
- Sewani and Kashef[12] combined the power of unsupervised Neural Network learning, an Autoencoder for feature selection and Convolutional Neural Networks for classification on a large dataset from ABIDE. Autoencoder was tested along with SVM, RF, KNN and CNN for comparative analysis. CNN outperformed the rest with accuracy of 84.05%.
- Ronicko et al. [13], in their study, compared various ML algorithms namely RF, ORF, SVM, and CNN methods with features that were extracted by the CRF. They examined the f-MRI data of a cohort of 300 ASD and 300 TC by partial and full correlation methods. 1-D CNN outperformed the other algorithms by achieving an accuracy of 70.30%.
- Shi et al. [14] proposed a novel method using domain adaptation for ASD classification, wherein a three-way decision method was established and applied to enhance the pseudo label of the target site from f-MRI features. They used Transfer component analysis for reduction of feature differences in different sites and linear SVM was used for classification to obtain a maximum accuracy of 75.41%.
- Aghdam et al. [15] presented a model for the diagnosis of ASD where they combined classifiers namely mixture of experts and simple Bayes method and also employed transfer learning. Using CNNs and multisite data from ABIDE I as well as ABIDE II repositories they obtained accuracy of 72.73% and 70% respectively. Using a combination of ABIDE I and ABIDE II data, however, the accuracy obtained was 70.45%.

3. Comparative Analysis

3.1 Comparative Analysis of various MRI based ASD detection Techniques: The study of various ASD detection systems using rs-fMRI as a biomarker proposed by researchers has been briefly summarized in Table 1 below.

Table 1: Comparative analysis of existing frameworks for ASD diagnosis using rs-fMRI data.

Autho	Objective	Data set	Sampl Size	Method	Perform ance	Remarks
Shao et al. (2021) [10]	To classify ASD From TC using Deep feature selection and GCN	ABIDE I	403 ASD and 468 TC	GCN	79.50%	Comparison with several other ML models and was performed. Model only suitable for large dataset owing to the DFS network used.

Shi et a (2021) [14]	To employ domain adaptation to enhance the identificatio of ASD from multisite fMRI data	ABII E I	159 ASI and 184 TC	L-SVM	75.41%	In spite of using domain adaptation method, unfiltered original high-dimensional features of fMRI were as input.Future work may focus on fusion of functional brain network topology data and multigranularity rough sets.
Karam asi et a (2020) 3]	To employ modular feature from fMRI data for the detection of ASD.	ABII E I	399 ASI and 472 TC	L-SVM	72.50%	Multiple ML models were compared. Novel features were explored for training the classifiers.
Ahmed et al. (2020) [6]	To classify ASD from TC by extracting features from fMRI using RBMs	ABII E I	79 ASD and 105 TC	SVM	83.00%	Deep Learning approach was used for feature selection. Employs a normalization strategy to decrease the heterogeneity of data.
Y. Liu e al. (2020) [4]	To predict ASD using heterogeneous r fMRI Data from CC200 Atlas.	ABII E I	506 ASI and 548 TC	SVM	72.20%	Model generalizes to larger ASD population. Model used only CC200 atlas, other atlases may not produce same results.
Zhao et al. (2020) 5]	To diagnose ASI using central-moment feature extracted from low- and high-order dynamic r FC Networks	ABII E I	45 ASD and 47 TC	L-SVM	83.00%	Small sample size. Aggregation of the 3 methods based on the decision value of SVM might not integrate the complementary information affecting the accuracy.
Chaitra et al. (2020) 7]	To predict ASD by computing complex networ measures from fMRI data	ABII E I	432 ASI and 556 TC	SVM	70.10%	Study doesn't generalize to a larger society. Future work may include larger dataset and other fMRI features to the feature set.
Huang et al. (2020) [11]	To distinguish Autism from control using rs-fMRI and Dee Belief Network	ABII E I	505 ASI and 530 TC	DBN	76.40%	Study also highlights the identification of other possible subtypes within spectrum o Autism. Future work aims on combining the rs-fMRI and s-MRI data.
Sewani and Kashef (2020) [12]	To diagnose ASD using an AE-based Deep Learning Classifier	ABII E I	539 ASI and 573 TC	NN	84.05%	Multi-site multidimensional data was use Future work may include other personal characteristics as features.
Ronick et al. (2020) [13]	To classify ASD using rs-fMRI data based on fu correlation brai FCs.	ABII E I	300 AS and 300 TC	NN	70.30%	Performance of multiple ML models was compared. Future work may focus on comparing the performance of model's partial correlation methods with FSL nets.

Song et al. (2019) [8]	To detect ASD by using rs-fMRI and community pattern quality metrics as features.	ABIDE I	119 ASD and 116 TC	LDA	85.16%	Classification employed a smaller number of features. The same spatial normalization pattern was used for all the subjects despite age differences.
Kazemi ejad and Sotero (2019) [9]	To establish a novel pipeline using graph theory and ML for the diagnosis of ASD.	ABIDE I	28 ASD and 23 TC	SVM	95.00%	Uses a single preprocessing pipeline for easier comparative analysis. Further investigation is reqd. to ensure if data variance through preprocessing has been eliminated.
Aghdam et al. (2019) [15]	To diagnose ASD in young children using rs-fMRI and CNNs	ABIDE I and I	210 ASD and 249 TC	CNN	70.45%	Performs early diagnosis. Requires more computational time and more time to train.

TC: Typical Control, GCN: Graph Convolutional Network, DFS: Deep Feature Selection, L-SVM: Linear Support Vector Machine, RBM: Restricted Boltzmann Machine, CC200: Craddock 200, FC: Functional Connectivity, DBN: Deep Belief Network, s-MRI: Structural Magnetic Resonance, AE: Autoencoder, NN: Neural Network, LDA: Linear Discriminant Analysis, CNN: Convolutional Neural Network.

3.1 Relative comparison of existing MRI based Autism Spectrum Disorder detection techniques:

The following section provides the relative comparison of the existing studies based on various parameters such as percentage usage of AI techniques in ASD diagnosis field, usage rate of classification model etc. in figures 1,2 and 3.

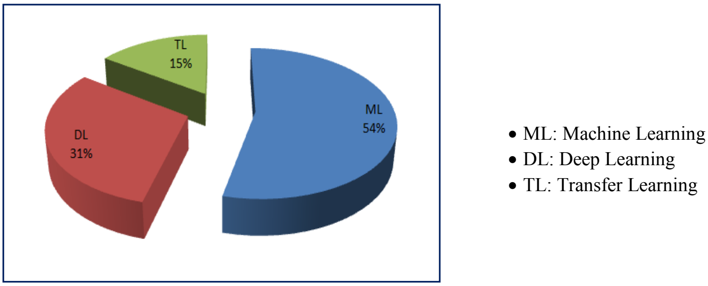

Fig 1. Percentage usage ratio of AI techniques in existing systems.

After analyzing studies that detected ASD using various techniques including ML, DL, and TL, it can be concluded that the ML methods are the most frequently used, followed by DL techniques. Transfer learning was recently introduced because existing ML- and DL-based systems ignored the problem of data heterogeneity. The TL-based model can overcome fluctuations in multiple sites of data and provide the best results with less computational time.

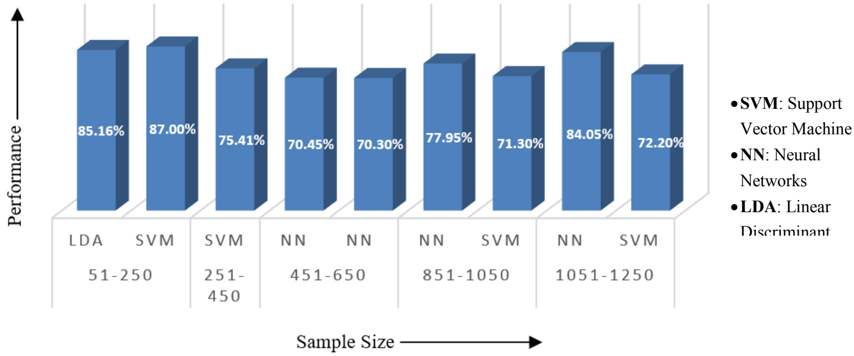

Fig 2: Performance Evaluation of ASD detection systems based on sample size.

It is clearly obvious after analyzing Fig 2, that Machine Learning classifiers such as SVM, show higher accuracy when the sample size of fMRI data is less, whereas the accuracy falls when the sample size increases. On contrary, Neural Networks when engaged with less sample size yield less accuracy. Their performance is enhanced with large sample data.

4. Open Gaps and Challenges

Various challenges involved in the existing ASD detection techniques are:

- **Limitation in the available dataset:**The publicly available dataset for ASD neuro-imaging is still limited and there is a dire need for increasing the f-MRI dataset. Apart from one study [16], no other research has been able to fuse together the dataset from multiple sources.
- **Data Heterogeneity in Multisite data:**In order to decrease the data heterogeneity, studies have eliminated much of the dataset from the dataset ABIDE [17], ultimately limiting the sample size. This results in less prediction capability of the developed framework. Not many studies have formulated novel methods to eliminate the variance in the f-MRI dataset[6], [18], [19]due to age, sex, head motion etc. Methods such as Transfer Learning and Domain Adaptation have been utilized to minimize the effect of data heterogeneity but the efforts are still in infancy as only a few studies have been able to implement these techniques.
- **Severity Estimation:** Most of the studies have only focused on classifying Autism from Typical Control and did not consider the severity of the disorder or ASD subtypes [3], [5].

5. Proposed TransLearning_ASDFramework

As explained in section 1, the latest research on ASD with f-MRI as a biomarker, has indeed provided breakthroughs in preliminary screening, detection and monitoring of ASD. But the main shortcoming of the existing systems is that the studies which employ f-MRI dataset with a limited sample size, often exhibit good classification performance however, when the sample size increases (due to increase in heterogeneity in data), the performance tends to decline. As a consequence, the model fails to generalize to a larger affected cohort. Thus, keeping in a view the aforementioned limitations of the existing methodologies, a novel framework has been proposed in the following section which will employ domain adaptation and transfer learning, will ensure definite diagnosis of ASD and generalize to a larger cohort of patients. The proposed framework has been divided into the following components as shown in Fig 3

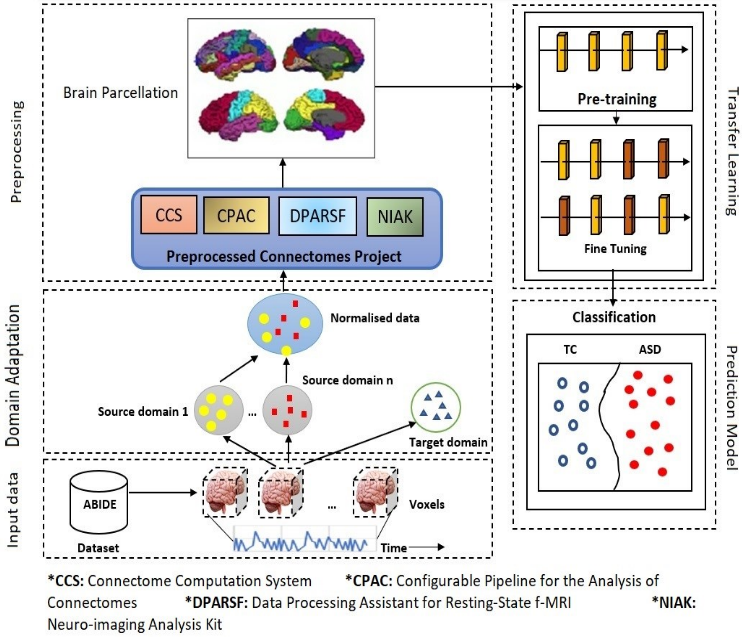

Fig 3: Proposed TransLearning_ASD framework**.**

5.1 Input data: The dataset will be procured from ABIDE repository[20]that has aggregated functional and structural neuro-imaging data collected from 24 international brain imaging laboratories around the world. For this study, only the resting state f-MRI data will be utilized.

5.2 Domain Adaptation: Due to the distribution heterogeneity in the ABIDE dataset from multiple sites, domain adaptation will be employed in this study, that deals with reducing the difference in the data distribution between the source domain and the target domain. As a result, the data after this process will be brought at the same normalized space.

5.3 Data preprocessing: Preprocessing of the functional MRI data will comprise of the following components:

- **PCP:** This study will utilize the pipelines released by the Preprocessed Connectomes Project[21] initiative for preprocessing the fMRI data, namely, Connectome Computation System (CCS), Configurable Pipeline for the Analysis of Connectomes (CPAC), Data Processing Assistant for Resting-State f-MRI (DPARSF), Neuro-Imaging Analysis Kit (NIAK). The preprocessing steps applied by these pipelines vary inonly the algorithms used for the steps, software implementations and the parameters used.

- **Brain Parcellation:** Brain Parcellation is defining distinct partitions in the brain, either areas or networks that comprise multiple discontinuous but closely interacting regions called region of interests (ROIs). The PCP preprocessed dataset provides mean time-series for several sets of ROI atlases.

5.4 Transfer Learning: In this component, the preprocessed data will be fed to a CNN pre-trained on a large dataset. Transfer learning is a technique where a model trained on one task is re-purposed on a second related task. In the proposed model, the preprocessed data will be utilized to perform the task of repurposing or fine tuning, which is carried out by training some layers of the CNN and leaving others frozen.

5.5 Prediction Model: It is known that different approaches can be followed to build the classifier on top of pre-trained convolutional neural network such as L-SVMs or fully connected layers. The train-to-test ratio will be 70%-30%. The model will distinguish between two classes: class 1 will predict ASD and class 2 will predict TC.

6 Conclusion

Afterreviewing the existing literature relating toautomated ASD diagnostic systems employingAI techniques (ML, DL and TL) on rs-fMRI data, it can be concluded that Machine Learning and Deep Learning are the most used technologies for ASD detection, while there is still a lot of scope for the exploration of Transfer Learning techniques.About 54% of the studies employed Machine Learning techniques, 31% employed Deep Learning Techniques and 15% of them made use of Transfer Learning techniques. Although, one study utilized Linear Discriminant Analysis, under Machine Learning, Support Vector Machine with a linear kernel outshone as the favorite choice of researchers for the classification. Under Deep Learning, a variety of neural networks for instance, Restricted Boltzmann Machines, Graph Convolutional Networks etc. were employed. As discussed in section4,the prime shortcoming of the abovementioned studies came out to be the inability of handling the heterogeneity in the fMRI dataset, which resulted in a lesser generalized model.Current literature demonstrated that Domain Adaptation and Transfer Learning could be utilized for proper and effective handling of such type of data. Domain adaptation aims at removing the effects of data distribution/heterogeneity and Transfer Learning helps in efficient learning of the model, which the ML and DL techniques have failed to deliver. Driven from these actualities, this study proposed a novel framework TransLearning_ASD using domain adaptation and transfer learning, for normalizing the effect of heterogeneity in multisite data and building a generalized, effective model for the prediction of ASD, which will be implemented in near future and will pose as a potential aid to research scholars and health practitioners.

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