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A Review on Autism Spectrum Disorder Diagnosis using MRI data

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Abstract: *Autism Spectrum Disorder (ASD) is a multifaceted neurodevelopmental disorder that presents with difficulties in social interaction, communication, and repetitive behavior. Accurate and early diagnosis is vital for effective intervention. Functional Magnetic Resonance Imaging (fMRI) has been an important tool to investigate the neural correlates of ASD. Recent deep learning advancements, especially transformer-based models, have proven useful for processing fMRI data for ASD detection. This review paper offers a general overview of transformer architectures for fMRI-based ASD classification. We address several methodologies, including spatial-temporal transformers, graph transformers, and mixed models combining convolutional neural networks (CNNs) and transformers. Prominent studies, such as the STAR Former model, showcase the success of both spatial and temporal features of BOLD signals being captured by novel modules such as eigenvector centrality-based ROI analysis and multiscale attention mechanisms. Nevertheless, despite these improvements, issues still persist, such as requiring large amounts of data to avoid overfitting and combining multimodal data to increase accuracy. This review will focus on outlining the current state-of-the-art transformer-based methods in fMRI-based ASD detection, identifying their advantages and disadvantages, and providing future directions to improve the field.*

Keywords: *Autism Spectrum Disorder (ASD), Autism Brain Imaging Data Exchange (ABIDE), Deep Learning, Convolutional Neural Networks, Graph Neural Networks, Autoencoder, Multi-Layer Perceptron, Support Vector Machines, Random Forest, Transformers.*

I.INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition marked by significant challenges in social communication, restricted interests, and repetitive behaviors. Authors characterize ASD as a behaviorally distinct syndrome resulting from atypical brain development, highlighting its existence along a continuum where individuals display a broad spectrum of deficits in social interaction, language, and behavior[15].

Recent advancements in neuroimaging have yielded objective metrics that can assist in the identification of ASD. Another study employed resting-state functional magnetic resonance imaging (fMRI) to examine intrinsic brain connectivity in high-functioning individuals with autism in comparison to typically developing controls[16]. While overall brain activation during rest was found to be comparable between the two groups, the study uncovered that individuals with autism demonstrated widespread underconnectivity, particularly between anterior regions (such as the ventral anterior cingulate cortex) and posterior regions (including the posterior cingulate cortex and precuneus). Moreover, the diminished connectivity was observed to correlate with reduced dimensions of the corpus callosum, indicating an anatomical foundation for these functional impairments. This evidence reinforces the perspective that ASD is a disorder of distributed neural systems and underscores the potential of fMRI as a method for identifying neural biomarkers associated with ASD.

II.LITERATURE REVIEW

All the research papers included in this study have utilized the publicly accessible Autism Brain Imaging Data Exchange (ABIDE) dataset. In the subsequent sections, we will first examine the dataset referenced in the literature, followed by an exploration of the diverse methodologies employed for the detection of Autism Spectrum Disorder.

2.1 Dataset

The Autism Brain Imaging Data Exchange (ABIDE) dataset encompasses resting-state functional magnetic resonance imaging (fMRI) and anatomical imaging data from individuals diagnosed with Autism Spectrum Disorder (ASD) as well as typically developing control subjects[1]. This dataset has significantly advanced our comprehension of the neural connectivity related to ASD. It comprises the ABIDE I and ABIDE II collections, which collectively contain over 2,000 datasets sourced from 17 international sites. These datasets offer critical insights into ASD by encompassing a broad age range from 7 to 64 years and by providing both structural and resting-state fMRI data. The preprocessing of the data ensures uniformity across various acquisition protocols and imaging locations. Several reputable preprocessing pipelines, including CPAC, DPARSF, and NIAK, are employed to standardize the data. Researchers can subsequently derive functional connectivity matrices utilizing widely recognized brain

parcellation atlases such as the AAL, HO, or CC200 atlases, facilitating the efficient analysis of extensive fMRI data. Additionally, the dataset contains phenotypic information regarding the subjects, including gender, handedness, and age.

Site	ASD	Control	Age Range	Total
Caltech	19	19	17.0-56.2	38
CMU	14	13	19-40	27
KKI	22	33	8.0-12.8	55
MaxMun	24	33	7-58	57
NYU	79	105	6.5-39.1	184
Olin	20	16	10-24	36
OHSU	13	15	8.0-15.2	28
SDSU	14	22	8.7-17.2	36
SBL	15	15	20-64	30
Stanford	20	20	7.5-12.9	40
Trinity	24	25	12.0-25.9	49
UCLA 1	49	33	8.4-17.9	82
UCLA 2	13	14	9.8-16.5	27
Leuven 1	14	15	18-32	29
Leuven 2	15	20	12.1-16.9	35
UM 1	55	55	8.2-19.2	110
UM 2	13	22	12.8-28.8	35
Pitt	30	27	9.3-35.2	57
USM	58	43	8.8-50.2	101
Yale	28	28	7.0-17.8	56

Fig 2.1: Description of ABIDE Dataset collection and Demographic information[1]

In this study, the ABIDE data underwent preprocessing through standardized protocols aimed at minimizing inter-site variability and improving data quality. This preprocessing was conducted with the assistance of the Neuro Bureau Preprocessing Initiative (NRI), which provides openly accessible preprocessed neuroimaging data and its derivatives. The protocols established by this initiative are designed to ensure consistency and comparability of the data, thereby facilitating rigorous analyses and reproducible research within the neuroimaging domain.

2.2 Methods

A range of machine learning algorithms is employed to predict Autism Spectrum Disorder (ASD) using resting state functional magnetic resonance imaging (fMRI) data. These algorithms are utilized for dimensionality reduction, feature extraction, and addressing classification challenges. The methodologies implemented include Support Vector Machines (SVM), Random Forest (RF), Multilayer Perceptron (MLP), Autoencoder, Convolutional Neural Networks (CNN), and Graph Neural Networks (GNN).

2.3 Support Vector Machines

Support Vector Machines (SVM) have been among the earliest and most popular classifiers for the prediction of autism spectrum disorder (ASD) from fMRI data. The most significant advantage of SVM is its capacity to deal with high-dimensional data, which makes it especially suitable for neuroimaging features such as voxel-wise activation levels or functional connectivity matrices. A seminal work by Plitt et al. employed SVM on resting-state fMRI (rs-fMRI) data taken from the Autism Brain Imaging Data Exchange (ABIDE) dataset. They derived functional connectivity features between brain regions based on Pearson correlation and then trained SVM classifiers to separate ASD from typically developing (TD) individuals[2]. The study reported classification accuracies of 60% to 70%, depending on the specific preprocessing pipeline and feature selection protocols employed. Although the performance was rated as moderate, the interpretability and simplicity of SVM facilitated its wide acceptance as a baseline. However, the performance of SVM models is usually constrained by their reliance on manually crafted features and inability to model nonlinear temporal or spatial relationships inherent to fMRI data. Recent advances include kernelized SVM variants and feature selection strategies based on graph metrics or independent component analysis; however, deep learning models have started to surpass SVMs in large-scale studies.

2.4 Random Forest (RF)

Random Forest (RF) is a popular machine learning method utilized for the classification of Autism Spectrum Disorder (ASD) from functional Magnetic Resonance Imaging (fMRI) data, valued for its ensemble-based method that avoids overfitting and manages high-dimensional and noisy features effectively. Compared to Support Vector Machines (SVM), which are based on a margin-based optimization strategy, RF builds a set of decision trees and aggregates their predictions, thereby providing robustness and interpretability via feature importance scores. Yahata et al. (2016) employed a machine learning pipeline wherein functional connectivity features extracted from resting-state fMRI were utilized to train an RF classifier[3]. They employed sparse canonical correlation analysis to reduce feature dimensionality prior to inputting the data to the RF model. The findings of the study illustrated that some sparse connections in the frontoparietal and default mode networks were strongly predictive of ASD, with cross-validation run classification accuracies greater than 75%. The primary strength of RF is its capacity to emphasize significant functional connections, rendering it simple to detect potential ASD biomarkers. Nevertheless, RF models continue to be dependent on handcrafted features and are unable to learn latent representations from raw or minimally preprocessed fMRI

data. Thus, while beneficial for exploratory analysis and feature ranking, RF methods are now being supplemented or replaced by deep learning architectures in state-of-the-art ASD detection pipelines.

2.5 Multi-Layer Perceptron (MLP)

Multilayer Perceptrons (MLPs), or fully connected neural networks, have been used for fMRI-based detection of ASD with moderate success, particularly in early deep learning research. In contrast to conventional classifiers like SVM or Random Forest, MLPs can learn complex, nonlinear mappings between input features and class labels, which makes them more appropriate for high-dimensional neuroimaging data. Heinsfeld et al. (2018) performed one of the most referenced studies that employed an MLP architecture for the classification of ASD from the ABIDE dataset[6]. They initially extracted functional connectivity features by calculating Pearson correlations between 111 brain regions of the Harvard-Oxford atlas, creating a feature vector of 6,105 distinct pairwise connections. The vectors were then input into an MLP with three hidden layers trained to separate ASD from control participants. Their model had an accuracy of 70.4% and an area under the ROC curve (AUC) of 0.76, outperforming classical methods such as SVM and RF in the same environment. The research proved that even shallow deep learning models, if properly regularized, have the ability to provide better performance than classical methods. But MLPs are not spatially inductively biased and thus are less effective than CNNs or GNNs for structured data such as images or graphs, except when carefully engineered preprocessed features are used. A bio-inspired modification, known as Zealous Particle Swarm Optimization-based Reliable MLP Neural Networks (ZPSO-RMLPNN), has also been proposed, which employs swarm intelligence techniques to optimize weight settings and enhance the model's robustness in managing complex neuroimaging data[7].

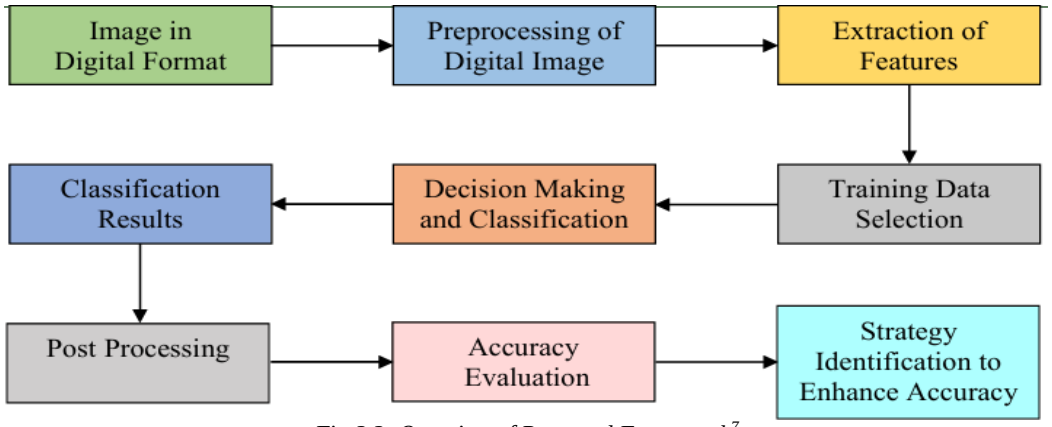

Fig 2.2: Overview of Proposed Framework[7]

2.6 Autoencoder

One study employs a two-stage denoising autoencoder methodology to diminish the dimensionality of resting state fMRI-based functional connectivity data. In the initial stage, the researchers condense the 19,900-dimensional feature vector, derived from the vectorization of a 200×200 functional connectivity matrix, into a 1,000-dimensional space[5]. This process involves introducing 20% noise to the input (utilizing a binomial distribution with n = 1, p = 0.8) and training the autoencoder to minimize reconstruction error, thereby learning features that are robust and resistant to noise. In the subsequent stage, a second autoencoder further reduces the dimensionality from 1,000 to 600 features, this time with an increased corruption rate of 30% (n = 1, p = 0.7). The unsupervised pre-training of these autoencoders is designed to extract pertinent features from the complex connectivity data, and the weights learned by the encoder serve as the initialization for a multilayer perceptron classifier. This classifier begins with a dense input layer corresponding to the original feature size and employs the compressed representations in its hidden layers, culminating in a SoftMax output layer for binary classification (ASD/typical development). The integration of these denoising autoencoders not only mitigates the challenges associated with high dimensionality but also enhances classification accuracy by providing a robust and well-regularized feature extractor that reduces the risk of overfitting.

2.7 Convolutional Neural Networks (CNN)

Convolutional Neural Networks (CNNs) showed great potential for classifying autism spectrum disorder (ASD) from fMRI data by automatically learning complex spatial features from connectivity patterns of brains. Sherkatghanad et al. (2020) designed a CNN model with training on resting-state fMRI data from the ABIDE dataset, where the inputs were taken as 2D connectivity matrices[8]. Their model reached a level of 70.22% accuracy, better than other conventional machine learning approaches and indicating certain brain regions like the precuneus and prefrontal cortex as crucial in ASD discrimination. On the back of this, Qiu and Zhai (2024) suggested a hybrid CNN-SVM framework wherein CNN layers identified spatial features which were subsequently classified using an SVM[9].

This blend harnessed the CNN's representational capability and SVM's stability, obtaining enhanced diagnostic performance of as high as 76% on cross-validation. In another development, Gupta et al. (2024) proposed an ultra- lightweight quantized CNN model trained within a federated learning environment[10]. This configuration maintained data privacy between institutions and enhanced generalizability, obtaining competitive accuracy at heavily reduced model size and computational requirement. These studies together show the changing function of CNNs in ASD detection, particularly when combined with hybrid or decentralized learning paradigms.

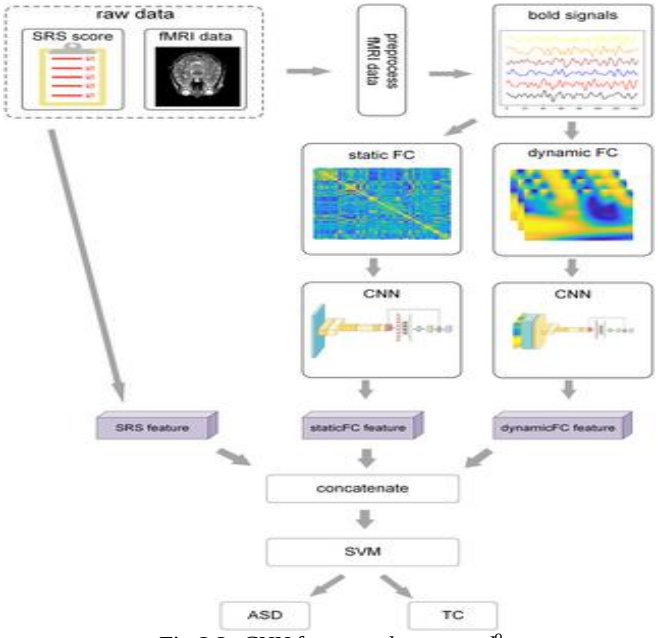

Fig 2.3: CNN framework proposed[9]

2.8 Graph Neural Networks (GNN)

Graph Neural Networks (GNNs) have also proved to be effective for modeling brain connectivity in ASD identification since they are capable of naturally embedding the topological structure of fMRI-based functional networks. Wang et al. (2021) proposed MAGE, a multi-atlas graph convolutional network ensemble that built individual brain graphs from rs-fMRI based on multiple brain atlases[11]. By integrating ensemble learning with graph convolutional layers, MAGE attained improved classification accuracy and generalizability between various connectivity representations to a 76.5% accuracy level on the ABIDE dataset. Building upon this, Liu et al. (2024) introduced a DeepGCN model that used multiple functional connectivity graphs across different brain states and modalities[12]. Their multi-graph model with variable variables successfully represented inter- and intra-subject variability, greatly enhancing classification performance. Likewise, Wang et al. (2024) utilized Graph Attention Networks (GATs) to learn weighted connections between brain regions, highlighting key connections implicated in ASD and improving model interpretability[13]. In parallel, Liu et al. (2023) introduced NF-GAT, which integrated node-level features into the attention mechanism to further improve connectivity-based classification[14]. These GNN-based methods demonstrate the importance of graph topology in the diagnosis of ASD and provide new insights into the neural basis of the disorder.

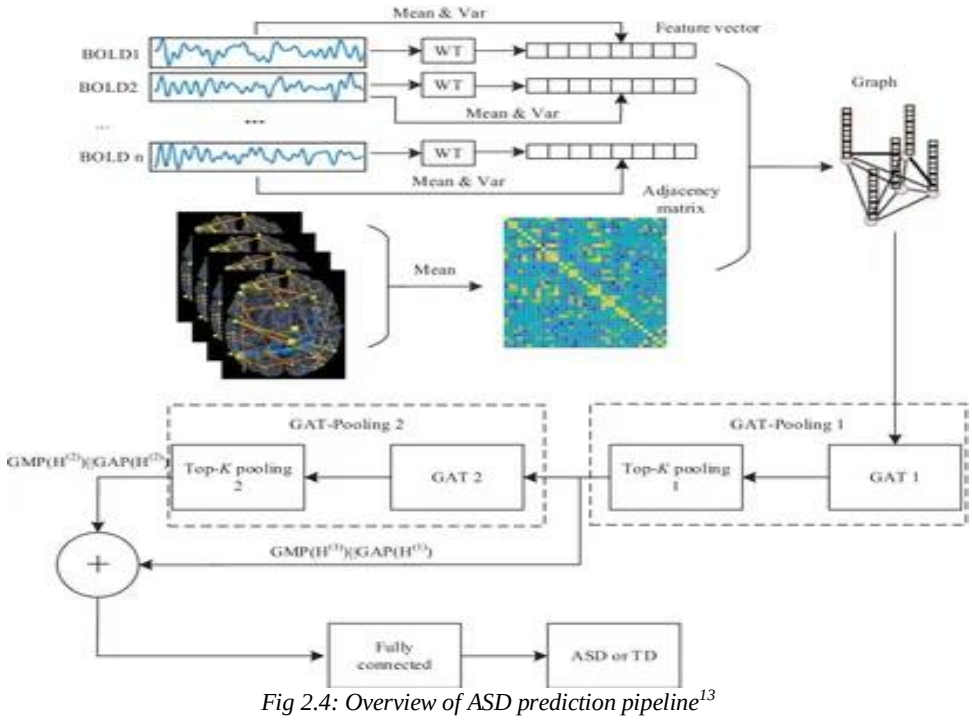

Fig 2.4: Overview of ASD prediction pipeline[13]

2.9 Transformers

Transformer models have recently been used in fMRI data for the detection of Autism Spectrum Disorder (ASD), providing benefits in identifying intricate spatial and temporal patterns. One such example is the STARFormer model, which proposes a new spatio-temporal aggregation and reorganization framework[4]. This model well identifies both spatial and temporal characteristics of BOLD signals by employing three important modules: an ROI spatial structure analysis module based on eigenvector centrality (EC) for brain region reorganization according to effective connectivity, a temporal feature reorganization module to segment the time series into equally dimensional window tokens and extract multiscale features through variable window and cross-window attention, and a spatio-temporal feature fusion module based on a parallel transformer architecture with dedicated temporal and spatial branches for integrated feature extraction. The STARFormer has been comprehensively tested on two publicly released datasets for ASD and ADHD classification, with state-of-the-art performance on a variety of evaluation metrics. This method shows the promise of transformer-based models in improving the accuracy and reliability of ASD diagnosis using fMRI data analysis

III.LIMITATIONS, CHALLENGES AND RESEARCH GAPS

3.1 Limitations

1. Data Quality and Heterogeneity

The dependability of autism spectrum disorder (ASD) classification is compromised by variations in the quality and acquisition parameters of resting-state functional magnetic resonance imaging (rs-fMRI) datasets across diverse sites and scanners.

2. Limited Generalizability:

Numerous models are developed and validated using specific datasets, which may not translate effectively to other populations or imaging facilities due to variations in demographics and scanning equipment.

3. Computational Constraints:

Methods based on deep learning frequently necessitate substantial computational resources and extensive datasets, which may not be accessible in all research environments.

4. Small Sample Sizes in Subgroups

Numerous studies are hindered by small or uneven sample sizes, particularly among younger populations or females diagnosed with Autism Spectrum Disorder (ASD), which restricts the statistical power of their conclusions.

5. Overfitting in Machine Learning Models

The high dimensionality of functional Magnetic Resonance Imaging (fMRI) data, combined with relatively small sample sizes, renders machine learning models susceptible to overfitting. This results in exaggerated performance metrics on training datasets while exhibiting inadequate generalization to new data.

6. Limited Reproducibility

Inconsistencies in study design, preprocessing techniques, and methods for feature extraction complicate the reproducibility of findings across various research endeavors.

3.2 Challenges

1. Inter-subject Variability

The significant variability in brain connectivity patterns among individuals with Autism Spectrum Disorder (ASD) complicates the establishment of reliable diagnostic biomarkers.

2. Lack of Standardized Preprocessing Pipelines

The lack of a universally recognized preprocessing protocol for resting-state functional magnetic resonance imaging (rs-fMRI) data leads to discrepancies in the features extracted and the performance of the models.

3. Multimodal Data Integration

The integration of rs-fMRI data with other neuroimaging or behavioral datasets presents a complex challenge due to issues related to alignment, scaling, and interpretability.

4. Dimensionality of fMRI Data

The high-dimensional characteristics of rs-fMRI data necessitate careful feature selection and reduction, which are both critical and challenging, often affecting the accuracy of classification.

5. Time and Cost of Data Collection

The high costs and time requirements associated with functional MRI scans restrict the scalability of research on ASD and the practicality of large-scale clinical screening.

6. Clinical Translation Gap

Despite encouraging findings in research, there exists a significant gap in the effective translation of rs-fMRI-based models for ASD into clinical practice, attributed to regulatory, interpretative, and validation challenges.

3.3 Research Gaps

1. Explainability of AI Models

The interpretability of artificial intelligence models remains a significant challenge, as most current machine learning models operate as "black boxes," which hinders their acceptance in clinical settings.

2. Longitudinal Studies are Scarce

There is a notable deficiency in longitudinal studies that can monitor brain changes associated with autism spectrum disorder (ASD) over time, which is essential for enhancing diagnostic and intervention approaches.

3. Insufficient Focus on Early Diagnosis

Despite the critical importance of early intervention in ASD, the majority of research does not concentrate on data from early childhood, thereby overlooking the potential for timely identification.

4. Lack of Cross-Cultural and Global Studies

Most research is predominantly derived from data collected in developed nations, resulting in a lack of understanding regarding the manifestations of ASD and associated brain patterns across diverse cultural and socioeconomic contexts.

5. Few Studies on Comorbid Conditions

There is a scarcity of studies examining how prevalent comorbid conditions, such as attention-deficit/hyperactivity disorder (ADHD) or anxiety, affect resting-state functional magnetic resonance imaging (rs-fMRI) patterns in individuals with ASD, which may have implications for diagnostic precision.

6. Limited Personalization in Diagnosis

Current diagnostic models prioritize population-level accuracy over individualized predictions, which restricts their utility in tailoring treatment plans to meet the specific needs of patients.

IV.CONCLUSION

A review of the current literature reveals various methodologies employed in the feature extraction and classification of Autism Spectrum Disorder (ASD), including Machine Learning models such as Support Vector Machines (SVM) and Random Forest, alongside Deep Learning techniques like Multi-Layer Perceptron (MLP), Convolutional Neural Networks (CNN), Graph Convolutional Networks (GCN), and Graph Attention Networks (GAT). A commonly utilized approach for extracting connectivity patterns among different Regions of Interest (ROIs) in the brain involves the use of Pearson Correlation, which is frequently referenced in the literature. Furthermore, certain methodologies incorporate phenotypic information of patients—including site, gender, and handedness—along with fMRI time series data to enhance accuracy. A significant concern addressed in the literature is the inadequacy of small sample sizes to effectively capture the heterogeneous data resulting from collection across multiple sites. Additionally, there exists a challenge regarding the lack of generalizability due to the limitation of data collection to the United States. The Pearson correlation, while extensively used to assess connectivity between pairs of regions, is confined to linear relationships. There is a necessity to employ more advanced algorithms capable of identifying non-linear connections. Tackling these challenges through more robust and standardized methodologies is crucial for advancing early diagnostic and intervention strategies.

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