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A comprehensive review of neuroimaging-based AI models for autism classification

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Abstract

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by challenges in social interaction, communication, and behavior. Traditional diagnostic methods rely heavily on behavioral assessments, such as the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R), which are often subjective and limited by the absence of definitive biomarkers. Recent advances in neuroimaging techniques, including structural MRI (sMRI), functional MRI (fMRI), and positron emission tomography (PET), have provided valuable insights into the structural and functional abnormalities associated with ASD. However, the analysis of neuroimaging data is complex, requiring sophisticated machine learning (ML) and artificial intelligence (AI) models.

This paper reviews state-of-the-art machine learning approaches, such as Random Forests, Support Vector Machines (SVM), and deep learning models, aimed at improving the diagnostic accuracy of ASD. We particularly focus on multimodal deep learning models that integrate neuroimaging data with behavioral assessments. In this review, we critically evaluate the strengths and limitations of these approaches, and how emerging AI tools not only enhance classification accuracy but also hold potential for identifying biomarkers and tracking the disorder's progression. Our analysis underscores the need for advanced methods that exploit both spatial and temporal features of brain data to better understand ASD, paving the way for improved diagnostics and personalized treatments.

Keywords: Autism Spectrum Disorder (ASD); Neuroimaging; Machine Learning (ML); Artifical Intelligence (AI); Biomarker; Deep Learning

1. Introduction

Autism Spectrum Disorder (ASD) is a psychiatric and developmental condition that can cause challenges with social interaction, behavior, and communication.[1] Although the cause of ASD is still being researched, it is believed to be caused by a mix of environmental, genetic, and epigenetic factors.[2] The heterogeneity of this disorder and not having a singular biomarker, makes the diagnosis of ASD highly challenging.[3,4] The current approach for diagnosis of ASD consists of behavioral assessments in which healthcare professionals will evaluate the child's behavior and compare that to the behavior of other children around the same age.[5] Professionals also use tools such as the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R) to evaluate the presence and severity of autistic traits.[6] Currently, there is no cure for ASD. Treatment is specific to each individual and aims to help patients manage their symptoms and improve their quality of life by enhancing communication, social skills, and adaptive behavior. The treatment combines Applied Behavior Analysis (ABA), speech and language therapy, and occupational therapy.[7] The prognosis of patients with ASD varies depending on each individual; while some may need lifelong support, others might be able to live a relatively independent lifestyle. ASD does not typically worsen with age; however, the symptoms one has may change over time. The life span of ASD is like that of the general population; however, co-occurring conditions

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may impact an individual's lifespan.[8] The modern noninvasive imaging techniques have improved and are being used to understand the differences in structure and function of the brain mechanisms in autistic and normal populations.

The advances in neuroimaging have enabled us to deepen our understanding of ASD. These non-invasive techniques including structural magnetic resonance imaging (sMRI), functional MRI (fMRI), and positron emission tomography (PET) are being used to investigate the structure, and function of autistic brains. These neuroimaging methods can identify the atypical brain development, and patterns tied to symptoms of ASD. sMRI for instance shows structural abnormalities in regions while fMRI detects functional differences in brain circuits during task and rest conditions. The PET scans provide data on metabolic activity, and neurotransmitter levels. These imaging methods are important for understanding the neural mechanisms behind ASD, improving diagnostic tools, and crafting targeted interventions. Although neuroimaging has the potential to identify biomarkers, the analytical methods for modeling these imaging datasets are still in development. Analyzing these datasets requires advanced methods because of the complexity of these datasets. The development of these advanced methods should exploit the spatial information of sMRI, and the dynamic interactions between brain regions captured by fMRI to understand nuanced brain-behavior links in ASD. These methods, therefore, have potential in a detailed understanding of the disorder leading to better clinical practices, and therapies. Therefore, there is an urgent need for development of such advanced analytical methods for identifying definitive autistic biomarkers.

The recent advances in machine learning and artificial intelligence (AI) can help provide these tools. The availability of large open-source datasets for disorders such as ASD has significantly enabled researchers to develop these methods. Several approaches have been developed for classifying ASDs from typical populations. Machine learning methods such as Random Forests, Support Vector Machines (SVM), and deep learning are being utilized to enhance diagnostic accuracy and efficiency. However, most of these methods aim solely at classification rather than identifying the biomarkers associated with ASD. The merits and demerits of these methods are not adequately analyzed. These advanced models ideally not only assist in classification but also in tracking the progression of the disorder over time. The application of machine learning and AI in ASD research holds the promise of earlier and more accurate diagnoses while providing a deeper understanding of ASD. We aim to provide a detailed review of machine learning tools and their applications in ASD research.

This review article aims to present the merits and demerits of various machine learning and AI models in the context of Autism Spectrum Disorder (ASD) research, striving to identify the most efficient approach for enhancing diagnostic accuracy. By critically evaluating different models, we seek to understand their strengths and limitations. This paper highlights which models offer the most significant potential for improving outcomes for individuals with ASD.

2. Methods

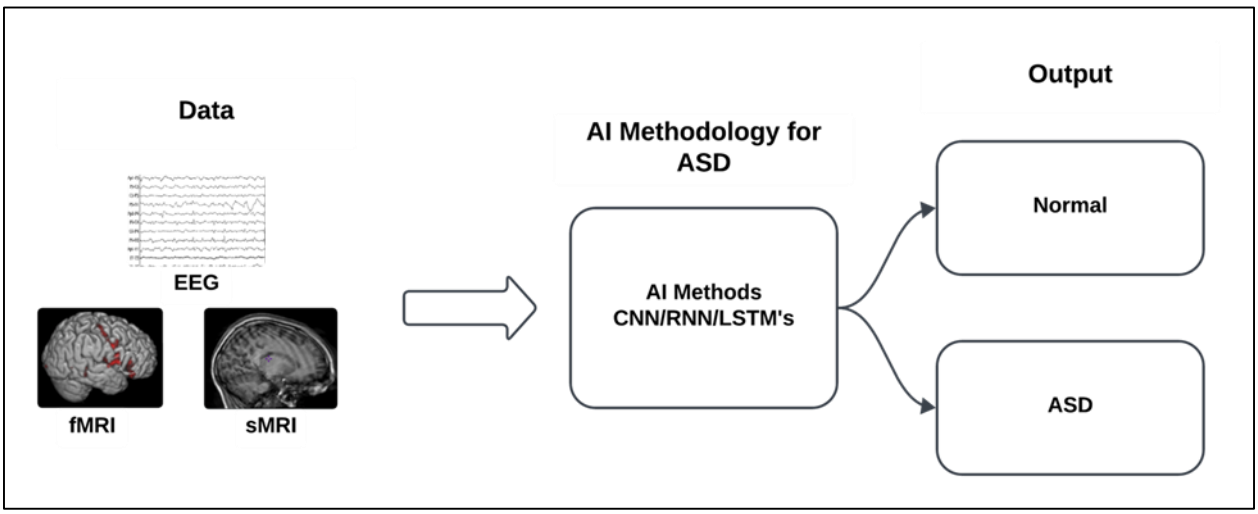

Figure 1 The figure shows the framework for the multimodal neuroimaging based AI based approaches for diagnosing autistic from the normal participants

We review below several multimodal neuroimaging approaches for diagnosing autistic from a normal population using several AI approaches. A typical framework for such AI approaches is shown in Figure 1.

Koc et al. have developed a multimodal deep learning approach to diagnose autism spectrum disorder (ASD) in subjects, distinguishing them from neurotypical controls. This study utilized both structural MRI (sMRI) and functional MRI (fMRI) modalities, incorporating data from resting-state and task-based fMRI. The researchers employed the ABIDE (Autism Brain Imaging Data Exchange) dataset, which comprises a substantial number of ASD and typically developing individuals. Their approach involved a hybrid deep learning model that combines convolutional neural networks (CNN) and recurrent neural networks (RNN), enhanced by the inclusion of Autism Diagnostic Observation Schedule (ADOS) scores to boost classification accuracy. The analysis focused on features such as region of interest (ROI) correlations and raw time series data extracted from the neuroimaging scans. The hybrid model achieved remarkable performance metrics, with an accuracy of 96.02%, sensitivity of 92.83%, and specificity of 85.70%, significantly outperforming single CNN and RNN models. Various fusion strategies (early, late, and cross fusion) were explored, with cross fusion incorporating ADOS scores yielding the highest accuracy. While the study did not explicitly test the model's generalization on an independent dataset, the high accuracy, sensitivity, and specificity suggest strong generalizability. The research identified several brain regions with a high risk for ASD, pointing to potential biomarkers, although it did not delve into cognitive measures.

Lakhan et al. developed a multimodal deep learning approach for diagnosing Autism Spectrum Disorder (ASD) by integrating data from neuroimaging (EEG, MRI), behavioral assessments, and clinical tools such as the Ages and Stages Questionnaires (ASQ), Facial Communication and Symbolic Behavior Scales (CSBS), Parents' Evaluation of Developmental Status (PEDS), and the Modified Checklist for Autism in Toddlers (M-CHAT). Their approach utilized a Federated Learning-enabled CNN-LSTM model within a distributed computing environment, where multiple ASD laboratories connected to a central hospital processed features like Region of Interest (ROI) correlations and raw time-series data. This model achieved a state-of-the-art detection accuracy of approximately 99%, significantly outperforming previous methods that typically achieved around 94%. The model's generalizability was confirmed by its high accuracy on independent datasets not used during training. Moreover, the study identified key brain biomarkers through ROI analysis and investigated how variations in brain connectivity correlated with cognitive measures, offering deeper insights into the neurological and behavioral aspects of ASD.

Dvornek et al. developed a multimodal deep learning approach to distinguish individuals with autism spectrum disorder (ASD) from neurotypical controls using both structural MRI (sMRI) and resting-state functional MRI (rsfMRI) data. They utilized the ABIDE I dataset, which contains data from 1,112 subjects (539 ASD, 573 controls) across 17 international sites. The proposed model integrates a Convolutional Neural Network (CNN) for processing sMRI and a Long Short-Term Memory (LSTM) network for analyzing the raw rsfMRI time series. This combination leverages both structural and functional features, including regional connectivity patterns, to improve classification. The model achieved an accuracy of 70.5%, which is 9% higher than single-modality approaches based on either sMRI or rsfMRI alone. Key advantages of this approach include its ability to capture both spatial and temporal patterns in the brain, allowing it to better generalize to large, heterogeneous datasets like ABIDE. The integration of multiple imaging modalities offers deeper insights into ASD-related abnormalities, enhancing diagnosis and potential treatment strategies.

Khosla et al. developed a multimodal deep learning approach to diagnose autism spectrum disorder (ASD) using resting state functional MRI (rs-fMRI) data. They employed the Autism Brain Imaging Data Exchange (ABIDE) dataset, which comprises 1,112 individuals with 539 diagnosed with ASD and 573 healthy controls from 17 sites in the first phase (ABIDE-I) and an additional 1,114 datasets in the second phase (ABIDE-II). Their model utilizes stochastic brain parcellations combined with a novel 3D Convolutional Neural Network (CNN) that leverages the full-resolution 3D spatial structure of rs-fMRI data. This approach demonstrates that models using stochastic parcellations can achieve performance comparable to those using widely accepted atlases, with classification accuracies reaching up to 75% on small sample datasets and 60-67% on large heterogeneous datasets like ABIDE. An ensemble learning strategy integrating different parcellations improves predictive accuracy further. The CNN framework outperforms traditional models in classification tasks, with an accuracy of 75% in distinguishing ASD patients from healthy controls and showing promising results in age prediction. The study does not focus on specific brain biomarkers or cognitive measures but highlights significant improvements in machine learning methods.

In 2021, Eslami and team used a 1D CNN for classifying Autism Spectrum Disorder with behavioral data. Ten behavioral questions gender age, jaundice status ethnicity, and family history of autism made up the datasets, used. Large biomarkers identified by the 1D CNN included atypical neural oscillations and connectivity patterns characteristic of ASD. These findings clarify ASD's neural mechanisms aiding early diagnosis. High classification accuracy was achieved by the model: 99.45 percent for adults 98.66 percent for children, and 90 percent for adolescents. This shows its efficacy in analyzing time-series data, and detecting temporal dependencies. The approach important for its high accuracy and

precision in adults, as well as its straightforward implementation makes it accessible for both researchers, and practitioners. The 1D CNN effectively catches temporal trends in behavioral data which is an important advantage. The study however did not assess independent datasets, thus limiting the validation of the model's robustness, and generalizability. Real-world scenarios pose challenges, due to the model's dependence on data quality, and preprocessing especially with noisy, or incomplete data.

Fan et al. developed a multimodal deep learning framework to model spatial, and temporal features. This framework consists of an encoder-decoder framework that uses a Conv-LSTM model to handle spatiotemporal data. This model was used for the analysis of Autism Spectrum Disorder (ASD) using the ABIDE I dataset which incorporates functional MRI (fMRI) data from 17 international sites. Initially, the dataset included 1112 subjects — comprising 529 people with ASD, and 573 normal controls. Following the exclusion of subjects with incomplete data the study concentrated on using ROI mean time series, and brain functional connectivity data, to classify ASD. The Conv-LSTM model was adept at identifying large biomarkers which included atypical functional connectivity patterns in different brain regions. Such biomarkers play an important role in understanding the neural mechanisms underlying ASD, and in aiding early diagnosis. With a classification accuracy of 72% on multi-site data the model showed its effectiveness in distinguishing ASD from normal controls in spite of the heterogeneity of the data. One important strength of the Conv-LSTM model is its capacity to model both spatial, and temporal aspects making it particularly suitable for complicated time-series data such as fMRI. This complete ability permits a thorough examination of spatiotemporal data offering deeper views into the neural patterns linked with ASD. Because of its flexible nature, the model can be applied across various types of spatiotemporal data — from medical imaging to behavioral analysis — broadening its overall utility. However, the Conv-LSTM model is computationally intensive, and demands large resources for both training, and inference especially with large datasets. This often necessitates specialized hardware such as GPUs which complicates implementation. Additionally, optimizing this complicated model requires wide-ranging fine-tuning, and experimentation to improve performance. The model's reliance on large amounts of labeled data also restricts its application in scenarios where such data is scarce.

For classifying ASD, Jiang et. al. developed 3D CNN models to improve effectiveness and stability. Multiple models, processed 3D fMRI data individually modeling important spatial features, from the ABIDE dataset. The dataset consisted of 871 subjects: 403 ASD patients and 468 controls, after rigorous filtering. Techniques such as averaging or voting were used to combine model outputs, which helped reduce variance and improve generalization. This method allowed the identification of subtle differences in brain structure, and connectivity acting as important ASD biomarkers. Achieving a classification accuracy of 72.46% the model, also enhanced sensitivity and specificity compared to conventional single-model methods. The 3D CNN ensemble's strength lies in its ability to extract complicated spatial, and temporal features providing augmented prediction, reliability and relieving the risk of overfitting. By integrating multiple models the approach makes sure more, strong output — particularly with data like brain scans that are highly variable. Nonetheless, this method requires large resources both for training, and inference often requiring high-performance, computing systems like GPUs. Managing, and optimizing a model ensemble also introduces complications needing expertise in model integration. The dependency on large, high-quality labeled, datasets can be another limitation — especially in environments where acquiring sufficient data proves challenging.

A neural network focused on enhancing ASD diagnosis was developed by Haweel et al. (2021) using several 2D CNNs on the same input data at the same time. Task-based fMRI data from the "Biomarkers of Autism at 12 Months" dataset which involved 100 toddlers (50 ASD and 50 typically developed) aged 12 to 40 months, was used by this architecture which allowed more detailed feature extraction. Various configurations in the parallel 2D CNN blocks such as, distinct filter sizes were used to model different spatial from brain regions tied to language and auditory processing including, the cingulate gyri and superior temporal gyrus, as well as the primary auditory cortex. The model detected key biomarkers like unusual brain activation patterns aiding the understanding of ASD-related neural processes. The benefits of this method is in modeling a broad spectrum of features with parallel blocks allowing a deeper input data analysis, and better accuracy in spotting ASD-related patterns. The architecture’s scalability permits adding more parallel blocks to increase the model’s ability to learn complicated patterns, parallel processing needed by this design, however, demands large computational power thus, raising both training time, and model complication. Challenges, such as integrating and managing the outputs from multiple blocks, arise due to an increased number of parameters and making sure the model’s stability and convergence during training requiring, advanced optimization skills, and careful model architecture design to achieve strong performance.

3. Discussion

Koc et al.'s research employed a hybrid deep learning model that combined CNNs and RNNs with structural MRI (s-MRI) and functional MRI (f-MRI) data, supplemented by Autism Diagnostic Observation Schedule (ADOS) scores. While this

approach achieved high diagnostic performance with 96.02% accuracy, it was limited by the lack of validation on independent datasets, restricting its generalizability to different populations. Moreover, the use of static correlations in fMRI data, a common approach in such studies, overlooks the non-stationary nature of biological signals. Correlations assume stationarity, which can result in the loss of critical clinical information, particularly in a disorder like Autism Spectrum Disorder (ASD), where dynamic changes in brain function are important. Future work should explore time-varying correlation techniques or other methods to capture these dynamic patterns. Additionally, although the use of RNNs is theoretically suitable for time-series data, they can suffer from vanishing gradient problems, limiting their ability to capture long-term dependencies effectively. Alternatives like attention mechanisms or gated RNNs may be more effective for improving temporal feature extraction.

Lakhan et al.'s research proposed a multimodal approach by integrating neuroimaging data (EEG, MRI) with behavioral assessments and clinical tools like the Ages and Stages Questionnaires (ASQ) and the Modified Checklist for Autism in Toddlers (M-CHAT). A Federated Learning-enabled CNN-LSTM model allowed distributed processing across multiple ASD labs, achieving high detection accuracy of 99%. However, the model's reliance on static correlations in EEG data, which assumes wide-sense stationarity, disregards the non-stationary characteristics typical of EEG signals. This could result in a loss of crucial temporal information necessary for an accurate ASD diagnosis. Additionally, the complexity of the distributed computing setup may hinder its application in resource-limited environments. Future efforts should aim to explore nonstationary methods and simplify the model's architecture while maintaining accuracy, making it more accessible for broader use in various clinical settings.

Dvornek et al.'s research utilized a cross-fusion deep learning model combining CNNs and RNNs with structural and functional MRI data, achieving an accuracy of 96.02%. However, as in the previous study, static correlations were employed, ignoring the dynamic, non-stationary nature of fMRI signals, which could limit the model's diagnostic power. Furthermore, the use of a 2D CNN on correlation maps presents a significant limitation, as the spatial arrangement of regions of interest (ROIs) in these maps is arbitrary, and treating them as coherent images leads to misleading results. Instead, graph-based models or permutation-invariant techniques could offer more robust ways to capture the relationships between brain regions. Like the earlier studies, this model failed to test its generalization on independent datasets, which limits its broader applicability. Future research should prioritize independent dataset validation and investigate biomarkers or cognitive metrics to improve diagnostic accuracy and neurobiological understanding.

Khosla et al.'s research adopted an innovative approach using resting-state fMRI data with stochastic brain parcellations and a 3D CNN, achieving reasonable accuracy (75% on smaller datasets and 60-67% on larger ones). However, the use of a 3D CNN focused primarily on spatial features, missing the temporal information that is vital for understanding brain connectivity in ASD. Temporal information is critical in time-series data like fMRI, and relying solely on a spatial model can lead to incomplete insights. Additionally, the model did not explore dynamic non-stationary features or identify biomarkers, both of which could enhance diagnostic utility. Future work should consider integrating methods that can capture both spatial and temporal features, such as Conv-LSTMs or time-varying correlations, while also exploring brain biomarkers for a more robust diagnosis.

Eslami et al.'s research employed a 1D CNN to classify Autism Spectrum Disorder (ASD) based on behavioral data, including gender, age, jaundice status, ethnicity, and family history of autism. The model achieved high classification accuracy (99.45% for adults, 98.66% for children, and 90% for adolescents). However, the study did not validate the model using independent datasets, which limits its generalizability to other populations. Moreover, the reliance on one-dimensional data restricts the model's ability to capture more complex spatial patterns that are relevant to ASD, such as atypical brain connectivity. Future research should incorporate more diverse datasets, including neuroimaging and cognitive data, and validate the model on independent datasets. While the model's simplicity and high accuracy make it accessible for researchers and clinicians, real-world applications would benefit from strategies to handle noisy or incomplete data and optimize the model for lower computational resources.

Fan et al. 's research designed A Conv-LSTM model to capture both spatial and temporal features was used to analyze Autism Spectrum Disorder (ASD) using the ABIDE I dataset, which includes functional MRI (fMRI) data from 17 international sites. The dataset contained 1,112 subjects, with 529 diagnosed with ASD. The Conv-LSTM model identified key biomarkers such as atypical functional connectivity patterns across brain regions, achieving a classification accuracy of 72%. Despite its effectiveness in capturing spatiotemporal information, the model's reliance on static correlations within certain brain regions fails to fully exploit the non-stationary nature of fMRI data, limiting its ability to capture all relevant features. Additionally, the model's heavy computational requirements pose practical challenges for resource-limited environments. Future work should focus on optimizing the model for more resource-efficient training and validating its performance on independent datasets. Exploring unsupervised learning methods or domain adaptation techniques could address issues of data scarcity and generalization.

Jiang et al.'s research introduced a CNN-GRU ensemble model for classifying Autism Spectrum Disorder (ASD) using 3D fMRI data from the ABIDE dataset, which included 871 subjects after filtering. The ensemble approach combined outputs from multiple models using techniques like averaging and voting, achieving a classification accuracy of 72.46%. While this approach captures some temporal features through the GRU units, it is limited by its use of static correlations in fMRI data, which fail to account for dynamic brain changes critical for ASD diagnosis. Additionally, the computational cost and complexity of managing multiple models reduce its practicality, particularly in resource-constrained environments. Future research should explore more scalable models that can dynamically capture both spatial and temporal features, validate on independent datasets, and reduce the reliance on large computational resources.

Haweel et al. 's research developed a parallel 2D CNN architecture to classify Autism Spectrum Disorder (ASD) using task-based fMRI data from the "Biomarkers of Autism at 12 Months" dataset, involving 100 toddlers. By using multiple 2D CNN blocks in parallel, the model was able to capture different spatial and temporal features related to language and auditory processing regions of the brain. However, the use of 2D CNNs on correlation maps assumes that the spatial arrangement of ROIs is coherent, which is not the case. This leads to limitations in capturing meaningful relationships between ROIs. Additionally, the study did not validate its findings on independent datasets, which limits the generalizability of its results. Future research should explore graph-based approaches or permutation-invariant techniques to better capture the relationships between brain regions. Simplifying the parallel architecture and reducing computational requirements could also improve scalability and broader clinical applicability.

4. Conclusions

In this review article, we reviewed several multimodal neuroimaging-based AI approaches for diagnosing autistic from the normal participants. We discussed the merits and demerits of each approach and discussed the future research directions for further improving the methods.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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