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The Role of Artificial Intelligence for Early Diagnostic Tools of Autism Spectrum Disorder: A Systematic Review

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ABSTRACT

Objective: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by challenges in social communication and repetitive behaviors. This systematic review examines the application of artificial intelligence (AI) in diagnosing ASD, focusing on pediatric populations aged 0-18 years.

Materials and methods: A systematic review was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines. Inclusion criteria encompassed studies applying AI techniques for ASD diagnosis, primarily evaluated using metric-like accuracy. Non-English articles and studies not focusing on diagnostic applications were excluded. The literature search covered PubMed, ScienceDirect, CENTRAL, ProQuest, Web of Science, and Google Scholar up to November 9, 2024. Bias assessment was performed using the Joanna Briggs Institute checklist for critical appraisal.

Results: The review included 25 studies. These studies explored AI-driven approaches that demonstrated high accuracy in classifying ASD using various data modalities, including visual (facial, home videos, eye-tracking), motor function, behavioral, microbiome, genetic, and neuroimaging data. Key findings highlight the efficacy of AI in analyzing complex datasets, identifying subtle ASD markers, and potentially enabling earlier intervention. The studies showed improved diagnostic accuracy, reduced assessment time, and enhanced predictive capabilities.

Conclusion: The integration of AI technologies in ASD diagnosis presents a promising frontier for enhancing diagnostic accuracy, efficiency, and early detection. While these tools can increase accessibility to ASD screening in underserved areas, challenges related to data quality, privacy, ethics, and clinical integration remain. Future research should focus on applying diverse AI techniques to large populations for comparative analysis to develop more robust diagnostic models.

Keywords: Autism Spectrum Disorder, artificial intelligence, deep learning, diagnosis, machine learning, screening

INTRODUCTION

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder (NDD) characterized by persistent challenges in social communication and interaction, along with restricted or repetitive patterns of behavior, interests, or activities.[1] The disorder manifests on a spectrum, with varying degrees of severity and a wide range of symptoms that can differ significantly from one individual to another.[2] The global prevalence of ASD has increased over time, with current estimates suggesting it affects approximately 1 in 36 children in the

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United States.[3] In Asian countries, particularly Southeast Asia, the prevalence is around 6 cases per 1000 persons, with a notable male predominance, although these rates tend to be lower compared to Western countries.[4]

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), updated in 2013, provides the current criteria for ASD diagnosis, consolidating previously separate diagnoses under a single umbrella.[1] However, diagnosing ASD remains challenging due to several factors.[5,6] Unlike many other neurological disorders, ASD cannot be diagnosed through specific laboratory tests or imaging studies, complicating the diagnostic process. The wide range of symptoms and their varying severity levels make each case unique, further challenging accurate diagnosis. Additionally, ASD symptoms can overlap with, be masked by, or mimic other developmental or psychiatric disorders, increasing the risk of misdiagnosis or delayed identification.[7] The fact that symptoms can change as a child develops adds another layer of complexity,[8] requiring ongoing assessment and potentially complicating early diagnosis.

Accurate diagnosis relies on careful, comprehensive behavioral observations and assessments by trained healthcare professionals. This process often involves a detailed developmental history, observation of the child's behavior and interactions, standardized assessment tools and questionnaires, and multidisciplinary evaluations (including psychologists, speech-language pathologists, occupational therapists, and other specialists).[5,6] However, these methods are often subjective, time-consuming, and may not be readily accessible to all populations. Early diagnosis and intervention are crucial for improving outcomes in individuals with ASD. However, the subtle nature of early signs and the variability in developmental trajectories complicate early detection.[9,10]

There has been a growing emphasis on improving diagnostic tools and methods for early identification and intervention as awareness of ASD continues to increase.[11] In this regard, artificial intelligence (AI) and its subfield, machine learning (ML), have emerged as transformative technologies with the potential to significantly enhance the diagnostic process of ASD.[12] Artificial intelligence refers to computational systems designed to perform tasks that typically require human intelligence (such as pattern recognition and decision-making). Within the field of AI, ML focuses on developing algorithms that enable systems to make predictions and decisions based on data, with the ability to improve performance through experience. A more advanced subset of ML, deep learning (DL), uses complex neural networks to stimulate the brain's processing mechanism, enabling more sophisticated analysis and interpretation of data.[13] AI currently encompasses a variety of interconnected models and approaches, which can be complex to understand. Key terminology is provided in the Glossary (Supplementary Table 1), while Figure 1 offers an overview of the AI models.

Recent advancements in AI have led to its increasing adoption across various fields, including healthcare, with AI mimicking the biological networks of the human brain and encompassing a wide range of technologies capable of performing cognitive functions.[14,15] Artificial intelligence models have shown promising results in reducing human error and improving diagnostic accuracy, particularly in the field of ASD research. Techniques such as support vector machines (SVMs), k-nearest neighbors (KNN), and DL have demonstrated good accuracy in diagnosing ASD,[16-18] while ML models can analyze complex datasets to identify key features associated with ASD, improving our understanding of the disorder.[19,20] This technology has been applied to genetic research,[21] neuroimaging,[22] and behavioral data analysis,[23] offering potential breakthroughs in ASD diagnosis. However, challenges remain, particularly with the

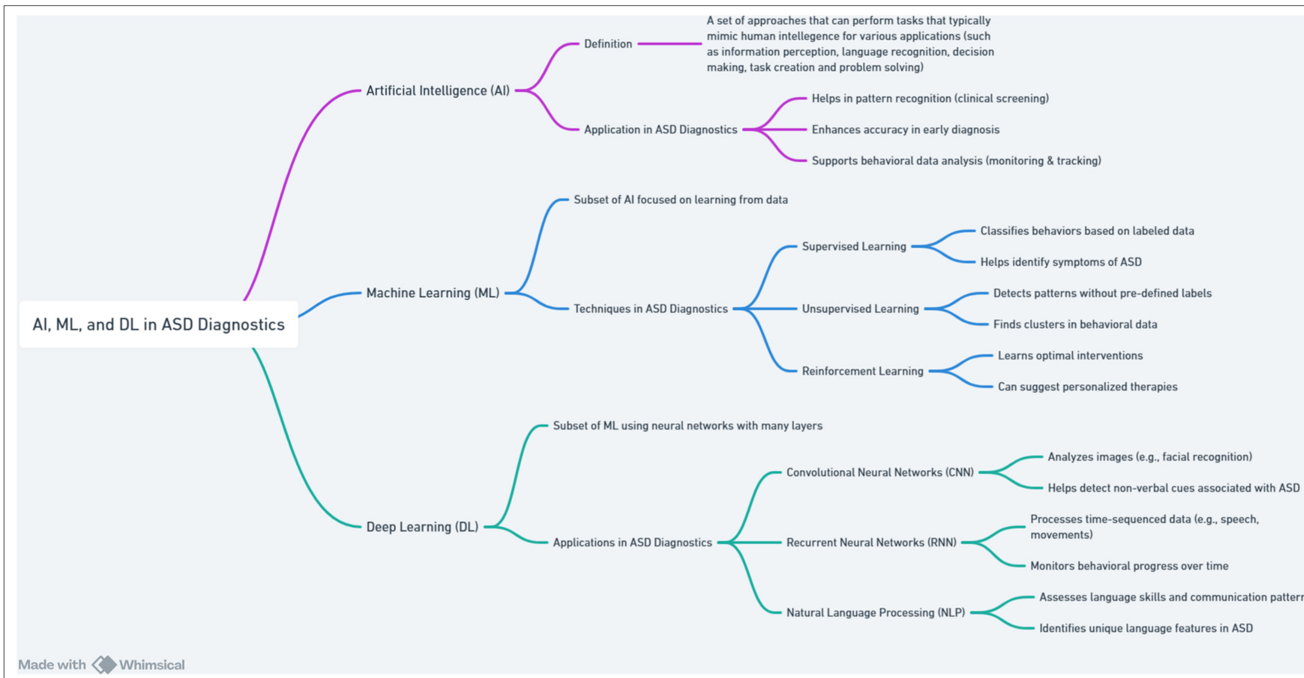

Figure 1. Relations among artificial intelligence, machine learning, and deep learning.

reliance on behavioral observation data, which can be subjective and prone to inconsistencies.[23] To address these limitations, integrating AI with advanced diagnostic tools, such as ML algorithms and DL models, could lead to more objective, efficient, and timely detection of ASD.

Despite these advancements, further research is needed to refine AI models and ensure their validity and reliability in clinical settings, especially for behavioral assessments.[15] Ongoing research is essential to refine these AI models, address the aforementioned challenges, and develop tools that are both clinically relevant and reliable. This study aims to critically evaluate the accuracy of ML algorithms in differentiating individuals with ASD from control groups and to explore how AI technologies can be incorporated into current diagnostic frameworks to enhance the precision and efficiency of ASD detection.

MATERIALS AND METHODS

Protocol and Eligibility Criteria

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[24] to summarize research on AI's application and its accuracy in diagnosing ASD. The review considered studies from clinical settings and computational experiments using various ASD datasets without race or geographical restrictions. Studies were considered for inclusion in the systematic review if they met the following criteria: (1) pediatric population (aged 0-18 years old); (2) the use of AI for diagnosis purposes; (3) calculating the accuracy of AI-based tests compared to standard procedures; and (4) cross-sectional design or relevant original research. This approach ensured a comprehensive evaluation of AI's role in the pediatric population of ASD while maintaining the focus on original, relevant, and accessible studies.

Information Sources and Search Strategy

The search process utilized five databases: PubMed, ScienceDirect, CENTRAL, ProQuest, Web of Science, with a cutoff date of November 9, 2024. To anticipate eligible gray literatures, searches on GoogleScholar were conducted as an addition, along with hand-searching relevant articles. The keywords for this study were the following: ("Autism Spectrum Disorder" OR "ASD" OR "Autism" OR "Autistic" AND "Artificial Intelligence" OR "AI" OR "Natural Language Processing" OR "Computerised" OR "Machine Learning" OR "Machine Intelligence" OR "Deep Learning").

Selecting Studies and Data Collection

Studies collected from databases and manual searches were then compiled into Rayyan.ai for deleting duplicates. After removing duplicates, the remaining articles underwent a two-stage screening process: first by titles and abstracts, then by full-text evaluation. Three independent reviewers (N.E., A.F.R., L.A.C.) screened the titles and abstracts to select appropriate studies using Rayyan.ai. The authors did not use Rayyan's automatic screening procedures but manual selections. Any discrepancies found would be discussed with the third author (P.S.). Article eligibility would be traced for full-text availability. The authors contacted the correspondence of eligible papers if full text could not be retrieved with regular steps. Articles might be excluded if the full-text articles were eventually not available. Two independent articles conducted the full-text screening and data collection process simultaneously. The decision to include studies strictly complied with predefined inclusion criteria, with a test run conducted to ensure consistency. The entire process was meticulously documented, including reasons for excluding studies that did not meet the criteria. Any disagreements between reviewers were resolved by consulting a fourth reviewer (P.S.), ensuring a thorough and unbiased selection process throughout the systematic review.

Risk of Bias of Individual Sources of Evidence

In this systematic review of diagnostic studies, the quality assessment of the studies was conducted using the Joanna Briggs Institute (JBI) checklist for critical appraisal, tailored to each study's design. The study designs evaluated included 22 cross-sectional studies, two case–control studies, one cohort study. It was found that 10% were of high quality, 55% had moderate quality, and about 35% were of low quality. All the literature included was rated as moderate quality.

RESULTS

Overview of Study Selection Process

Based on the PRISMA guidelines, the article inclusion process is illustrated in Figure 2. A total of 3572 articles were identified through database searches: 116 in PubMed, 499 in Scopus, 443 in Cochrane, 1564 in Web of Science, and 950 in Google Scholar. After removing duplicates, 2241 articles were screened. The titles and abstracts of these articles were reviewed, and 358 records were selected for full-text retrieval. In the second phase, 229 articles were excluded based on predefined exclusion criteria. In the final phase, 104 articles were excluded: 101 because AI was not the primary method used and 3 because of fewer than 10 ASD participants. In the end, 25 studies were included in this systematic review, with a total of 111760 children aged 0-18 years old (9955 ASD and 101805 typically developing [TD]).

Characteristics of Sources of Evidence

Table 1 summarizes the characteristics of the articles included in this study. This systematic review analyzed 25 studies published in the last decades, focusing on AI methods for diagnosing ASD in the pediatric population. Artificial intelligence approaches fall into two main categories: traditional ML (e.g., SVM, Random Forests) and DL (e.g., convolutional neural networks [CNNs], long short-term memory [LSTM] networks). These methods were applied to various diagnostic tools such as behavioral assessments, neuroimaging data, genetic information, visual data (facial, home videos, eye-tracking data), motor function data (gait analysis in 3D kinematic data), and microbiome data. The performance of these AI tools was primarily evaluated using metric-like accuracy, as detailed in Table 2.

SYNTHESIS OF RESULTS

Modalities Used in Autism Spectrum Disorder Detection

The identification of ASD involves a comprehensive approach utilizing diverse diagnostic tools. These methods can be broadly categorized into two main groups: neuroimaging and multimodal (non-neuroimaging) assessment. Each of these modalities plays a crucial role in assessing various facets of

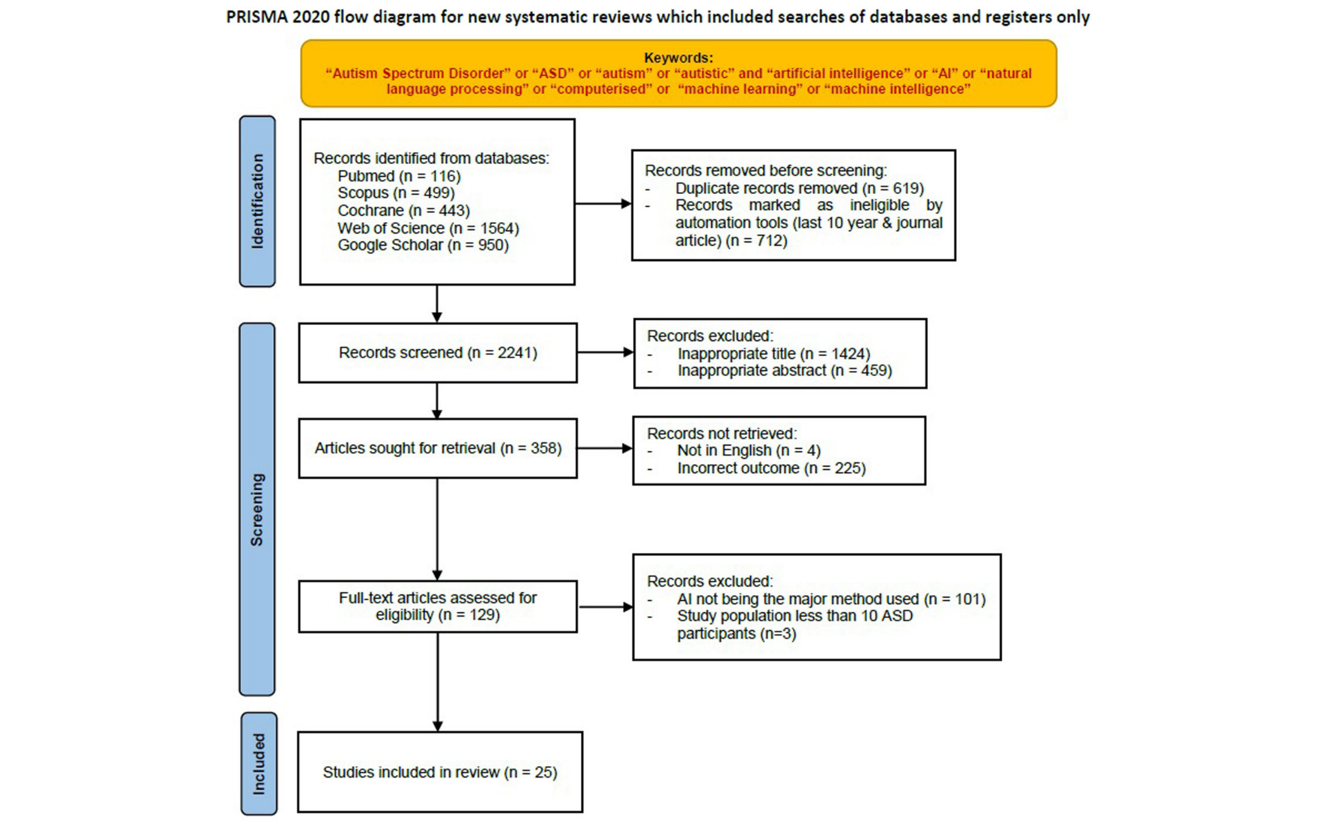

Figure 2. The PRISMA flow diagram describing selecting study process.

an individual's neurological functioning, cognitive abilities, and behavioral patterns. Table 3 summarizes these two types of modalities, highlighting their use in the early detection of ASD.

DISCUSSION

The application of AI in ASD diagnosis has shown promising results across various studies, offering potential improvements in accuracy, efficiency, and early detection. This growing body of research demonstrates the capacity of AI, to process complex, multidimensional data associated with ASD, including visual, motor function, behavioral patterns, microbiome, genetic, and neuroimaging data. The integration of AI technologies in ASD diagnostics presents opportunities for more objective assessments and the potential to identify subtle patterns that may be overlooked in traditional diagnostic approaches.

Table 3 provides an overview of key studies that apply AI (specifically ML algorithms) for classifying ASD. These studies highlight several critical challenges in using AI for ASD diagnosis, such as managing imbalanced and multidimensional data, selecting relevant features for effective classification, and ensuring the reliable performance of evaluation metrics, such as accuracy. ML is particularly effective for processing complex datasets related to ASD, including genetic information, and can handle large amounts of diverse data. By analyzing different signs and characteristics, AI can help identify patterns associated with ASD, leading to better ML models for diagnosis and prediction.

This study reviews the latest research on how AI/ML/DL methods are applied to classify ASD. Based on these studies, we identify several critical issues that need attention:

1. Improving the classification of ASD using advanced ML techniques.[30,31,44,46]
2. Reducing the time required for diagnosing ASD while minimizing human involvement.[12,37,40,42,45,48]
3. Identifying the specific features that differentiate ASD from other NDDs.[25,47]
4. Determining the critical factors that influence the development of ASD.[27,28,35,41,43]
5. Reducing the number of features used in current ASD diagnostic methods without compromising evaluation metrics such as accuracy.[25,29,32,39]

ENHANCING PREDICTIVE OUTCOMES IN AUTISM SPECTRUM DISORDER DIAGNOSIS

One of the key advancements is improving "predictive outcomes," which means using AI to predict the likelihood of ASD even before typical symptoms appear. Researchers are developing faster and more accurate diagnostic methods by combining AI with tools like neuroimaging, facial recognition, and eye-tracking. These tools aim to classify ASD and predict its severity and development over time, providing a clearer picture of each child's needs. Several studies have explored ways to enhance both the classification and early detection of ASD using technologies like ML, DL, eye-tracking, and facial recognition. Below is a summary of key studies focusing on

Table 1. Critical Appraisal Summary Based on Joanna Briggs Institute Checklist

Author	Study Design	Number of the Answer			Percentage (%)	Quality
		Yes	No	Unclear		
Choi et al (2020)	Cross-sectional	6		4	60	Moderate
Khullar et al (2021)	Cross-sectional	5		5	50	Low
Megerian et al (2022)	Cohort	8	1	1	80	High
Rahman et al (2020)	Case–control	6	2	2	60	Moderate
Ucuz and Cicek (2020)	Retrospective case–control	5	2	3	50	Low
Selvi et al (2023)	Cross-sectional	6		4	60	Moderate
Alam et al (2024)	Cross-sectional	6		4	60	Moderate
Alhakbani (2024)	Cross-sectional	4	1	5	40	Low
Awaji et al (2023)	Cross-sectional	5		5	50	Low
Meng et al (2023)	Cross-sectional	6		4	60	Moderate
Rabbi et al (2021)	Cross-sectional	6		4	60	Moderate
Hasan et al (2017)	Cross-sectional	7	1	2	70	Moderate
Lu and Perkowski (2021)	Cross-sectional	6		4	60	Moderate
Pal and Rubini (2024)	Cross-sectional	3		7	30	Low
Luongo et al (2024)	Cross-sectional	7	1	2	70	Moderate
Wang and Fu (2023)	Cross-sectional	4	1	5	40	Low
Rabie and Saleh (2023)	Cross-sectional	2		8	20	Low
Olaguez-Gonzalez et al (2023)	Cross-sectional	6	1	3	60	Moderate
Tang et al (2023)	Cross-sectional	5	1	4	50	Low
Bi et al (2018)	Cross-sectional	7	1	2	70	Moderate
Gao et al (2024)	Cross-sectional	8		2	80	High
Xu et al (2019)	Cross-sectional	6		4	60	Moderate
Manjur et al (2022)	Cross-sectional	6	1	3	60	Moderate
Abdulhay et al (2020)	Cross-sectional	8		2	80	High
Pham et al (2020)	Cross-sectional	4	1	5	40	Low

enhancing the diagnostic process and improving predictive outcomes.

Khullar et al introduced a handheld device powered by AI that uses ML algorithms, including LSTM, to diagnose ASD. The study found that the LSTM model achieved 100% accuracy in diagnosing ASD, using just 50 examples. The system performed exceptionally well in two different testing scenarios: first, in training on a set of data, and second, when assessing 20 ASD and 20 non-ASD children. The device's ability to quickly and accurately diagnose ASD demonstrates its potential for improving early detection, particularly in areas with limited access to autism specialists. This AI-powered diagnostic tool offers significant benefits, such as determining the severity of ASD, being portable for use in various settings, and providing timely diagnosis, ultimately contributing to earlier intervention and better long-term outcomes for children.

Similarly, Alam et al[30] focused on using facial image analysis to improve the accuracy of ASD diagnosis. The study aimed to determine whether aligning facial images could enhance the precision of ASD detection by reducing variations in head position and facial expressions. The researchers employed DL algorithms like ResNet50V2, achieving a prediction accuracy of 93.93% and an area under the curve(AUC) of 96.33% after aligning facial images. While face alignment significantly improved accuracy, the researchers noted that it was insufficient to dramatically boost performance. They emphasized the need for a more comprehensive, data-centric approach to improve results further. Despite challenges such as poor image quality and inadequate validation of medical data, the study opened new avenues for using facial alignment to develop diagnostic tools for ASD. This approach may offer an additional layer of early predictive capability, allowing for better identification and early intervention in children showing subtle signs of ASD.

In another study, Alhakbani[31] employed CNNs to analyze facial expressions and emotional engagement to improve understanding and support for children with ASD. The study found that CNN-based facial emotion recognition was more accurate than other traditional ML models, such as random forest (RF) and SVM, in assessing engagement in both TD children and children with ASD. Using a 2-dimensional valence-arousal emotion model to classify engagement states allowed the system to accurately predict emotional responses, which is a critical aspect of social interaction in ASD. The study's findings suggest that AI models can improve engagement detection in children with ASD, potentially leading to enhanced learning and social support systems and providing children with better development opportunities.

Meng et al[33] utilized eye-tracking technology combined with ML algorithms to identify early signs of ASD in young children. By analyzing how children with ASD and TD children responded to videos of cartoon characters and real people, the study found that eye movement patterns could differentiate between the two groups. Specifically, children with ASD were more likely to focus on cartoon characters rather than human faces, indicating a preference for non-social stimuli. The ML model used in the study achieved a diagnostic accuracy of 73%,

Table 2. Summary of Studies Using AI Technology in Autism Spectrum Disorder Assessments

Author	Sample Size and Age	Data Type	Algorithms and Accuracy	Clinical Aim
Nominal Data				
Choi et al, 2020[25]	1269 children (708 ASD, 177 PDD, 384 no diagnosis) aged 95.61 ± 62.80 months	ADI-R and ADOS	Multiclass decision forest 94.48%	Predict subgroups of ASD based on the DSM-IV-TR criteria using ML (between ASD, PDD-NOS, and no diagnosis categories) and determine a minimum set of items that could reliably predict ASD diagnosis
Khullar et al, 2021[26]	20 ASD (mean age 8.98 years), 20 TD (mean age 9.70 years)	Binary dataset (based on DSM-V)	MLP 96.4%, CNN 100%, LSTM 100%	Develop an advanced computer-based system for assisting clinicians as an alternative to traditional manual diagnosis methods
Megerian et al, 2022[12]	425 children (125 ASD, 300 TD) aged 18-72 months	Three inputs (caregiver questionnaire, two short home videos, healthcare provider questionnaire)	DT (Sen 98.4%, Spe 78.9%, PPV 80.8%, NPV 98.3%)	Designed to assist primary care healthcare providers in diagnosing ASD
Rahman et al, 2020[27]	96138 children (1397 ASD, 94741 TD) aged 8-18 years	EMR (parental sociodemographic, medical histories, prescribed medication data)	Logistic regression, ANN, RF (average accuracy 95.62%)	Predict ASD early in life in a general population sample to enhance early detection of ASD risk in large populations of children to potentially allow for earlier interventions
Ucuz and Cicek, 2020[28]	136 ASD (mean age 45.9 ± 11.1 months), 143 TD (46.5 ± 11.3 months)	Prenatal, perinatal and developmental data	ANN (specifically MLP model) 88.0%	Develop an AI to differentiate between ASD and healthy individuals by identifying key risk factors associated with ASD
Selvi et al, 2023[29]	182 children (113 ASD, 60 TD) aged 6 months to 11 years	Indian Autism Parental Questionnaire	MLR 97.85%, SVM 97.14%, DT 95.53%, KNN 97.02%, GNB 96.34%	Designed a mobile application-based tool for early ASD screening, and be accessible to parents, caregivers, and teachers in lower middle-income settings
Observational Data				
Alam et al, 2024[30]	3014 children aged 2-14 years (ASD and non-ASD)	Facial Images	CNN (ResNet50V2 93.93%, Xception 92.14%, MobileNet 84.64%)	Explore the effect of face alignment on improving the accuracy of ASD diagnosis using facial images
Alhakbani, 2024[31]	1333 images ASD (2-14 years) and 189 video recordings (12 TD aged 6-12 years)	Images and video	CNNs 76%, SVM 75%, Decision Tree 67%, RF 64%	Develop an automatic engagement detection model for children with ASD using facial emotion recognition
Awaji et al, 2023[32]	2940 facial images (1470 both ASD and TD) of children aged 2-12 years	Autism Image Dataset (from Kaggle)	XGBoost (VGG16-ResNet101 98.35%, ResNet101 97.4%, VGG16 98.66%), RF (VGG16-ResNet101 97.8%, ResNet101 98.25%, VGG16 98.8%)	Early detection using facial features and image analysis to overcome the limitations of manual diagnosis by creating an automated, AI-driven approach that could provide more objective, consistent, and efficient assessments of ASD symptoms.

(*Continued*)

Table 2. Summary of Studies Using AI Technology in Autism Spectrum Disorder Assessments (*Continued*)

Author	Sample Size and Age	Data Type	Algorithms and Accuracy	Clinical Aim
Meng et al, 2023[33]	161 children (117 ASD, 44 TD) aged 39.70 ± 12.27 months	Eye-tracking data	RF 73%	Identifying distinct eye movement patterns in response to social stimuli (such as cartoon characters versus real people) to improve early screening processes for ASD
Rabbi et al, 2021[34]	2940 face images (ASD and non-ASD) aged 2-8 years	Facial Images	CNN 92.31%, MLP 71.66%, RF 72.78%, GBM 75.23%, AB 74.56%	Develop an accurate and efficient method for early stage detection to provide a faster and more accessible screening tool for ASD
Hasan et al, 2017[35]	60 children (30 ASD aged 8.63 ± 2.16 years, 30 TD aged 9.52 ± 1.96 years)	3D kinematic gait features	ANN (Kinematic-Raw 88.3%, Kinematic-TMWU 90.0%, Kinematic-SWDA 91.7%)	Develop an automated classification system for gait abnormalities in children with ASD for effectively diagnosing ASD gait patterns
Lu and Perkowski, 2021[36]	1122 images (ASD and TD) aged 2-12 years	2D facial images of children (East Asian Dataset)	CNN (VGG16) 95%	Develop an objective, inexpensive, and easily comprehensible screening solution for early detection of ASD in children using only facial images
Pal and Rubini, 2024[37]	297 toddlers (163 ASD, 134 non-ASD)	TASD Dataset Behavioral Traits and Features	BERT 88%	Develop a reliable and efficient method for predicting behavioral traits in individuals with ASD through text-based data analysis
Luongo et al, 2024[38]	10 ASD (mean age 4 years), 10 TD (mean age 3.75 years)	Raw motion data from a drag and drop task on a tablet (motor trajectories)	ANN (2 features 90%, 4 features 76%)	Objectively assess motor behaviors related to autism, by developing tools that can accurately classify motor skills
Laboratory Data				
Wang and Fu, 2023[39]	124 children (73 ASD, 51 TD) aged 2-7 years	Metagenomic sequencing data of gut microbiota	RF (Moscow cohort 67%, Shenzhen cohort 97%, and combined 80%)	Provide a novel method for assessing ASD risk based on gut microbiome analysis by integrating data from multiple sources, cohorts, and ethnicities
Rabie and Saleh, 2023[40]	76 ASD (mean age 5.6 years), 78 TD (mean age 5.7 years)	Blood tests	EKNN (hybrid combining KNN, NB, and COA) 93%	Enhance accuracy and speed, potentially leading to better outcomes for children with ASD through earlier detection and intervention.
Olaguez-Gonzalez et al, 2023[41]	223 children (125 ASD aged 2-7 years, 98 TD aged 48 months)	Microbiome composition	SVM 90%, ANN 80%, RF 90%	Identify specific microbial predictors that could aid in understanding the role of gut microbiota in ASD development, potentially leading to new diagnostic and therapeutic strategies

(*Continued*)

Table 2. Summary of Studies Using AI Technology in Autism Spectrum Disorder Assessments (*Continued*)

Author	Sample Size and Age	Data Type	Algorithms and Accuracy	Clinical Aim
Tang et al, 2023[42]	254 toddlers (128 ASD, 126 TD)	mRNA expression data (from Gene Expression Omnibus database)	LASSO regression 86%	Identify specific genes from peripheral-blood samples that could serve as reliable indicators of ASD and create a predictive model for early detection and intervention.
Imaging Data				
Bi et al, 2018[43]	50 ASD (mean age 13.34 ± 2.41 years), 42 TD (13.05 ± 1.82 years)	rs-fMRI	Elman NN 84.7%, DT 83.4%, SVM 77.3%	Enhancing ASD diagnosis accuracy and identifying key brain regions involved in the disorder
Gao et al, 2024[44]	First site: 74 ASD (mean age 14.76 years), 98 TD (mean age 15.75 years) Second site: 47 ASD (mean age 13.71 years), 73 TD (mean age 14.84 years)	rs-fMRI	Multi-task transformer neural network (first site 67.74%, second site 72.00%)	Improve early diagnosis and intervention strategies for ASD, to provide a more objective and efficient diagnostic tool for ASD that can potentially replace or complement current subjective and time-consuming assessments
Xu et al, 2019[45]	25 ASD (mean age 9.3 ± 1.4 years), 22 TD (mean age 9.5 ± 1.6 years)	Hemodynamic fluctuations recorded by fNIRS	CGRNN (multilayer neural network combining CNN and GRU) 92.2%	Classify between ASD and TD children accurately for more efficient brain imaging and diagnosis of ASD in young children
Manjur et al, 2022[46]	143 children (96 ASD aged 13.8 ± 4.8 years, 47 TD aged 13.0 ± 4.2 years)	ERG signals	RF 86%, GBM 82%, DT 75%	Enhance the early diagnosis of ASD by providing a more accessible and efficient screening tool compared to current diagnostic procedures that require multiple consultations with specialists.
Abdulhay et al, 2020[47]	122 children (61 ASD and 61-neurotypical) aged 4-14 years	rs-EEG	CWT, Feature Extraction, PCA, ANN (Overall accuracy 95.90%)	Develop a computer-aided approach for accurately distinguishing between children with ASD and neurotypical children using resting-state EEG data.
Pham et al, 2020[48]	77 children (40 ASD, 37 TD) aged 4-13 years	EEG signals	LDA 93.51%, QDA 85.71%, SVM 93.51-97.40%, KNN 92.21%, SVMRBF 97.40%, PNN 98.70%	Develop a non-invasive and cost-effective method to detect autism using EEG signals converted into images, which could help healthcare professionals make better decisions.

AB, AdaBoost (adaptive boosting); ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autism Diagnostic Observation Schedule; ANN, artificial neural network; ASD, Autism Spectrum Disorder; BERT, Bidirectional Encoder Representations from Transformers; CGRNN, continuous graph recurrent neural network; CNN, convolutional neural network; COA, co-occurrence analysis (or component of analysis); CWT, continuous wavelet transform; DT, decision tree; EKNN, enhanced k-nearest neighbors; EMR, electronic medical record; ERG, electroretinography; fNIRS, functional near-infrared spectroscopy; GBM, gradient boosting machine; GNB, Gaussian Naive Bayes; GRUERG, gated recurrent unit with extended graph; Kinematic-SWDA, kinematic-structured wavelet domain analysis; Kinematic-TMWU, kinematic time-windowed units; KNN, k-nearest neighbors; LASSO, Least Absolute Shrinkage and Selection Operator; LDA, linear discriminant analysis; LSTM, long short-term memory; ML, machine learning; MLP, multilayer perceptron; MLR, multinomial logistic regression; NB, Naive Bayes; NN, neural network; NPV, negative predictive value; PCA, principal component analysis;PDD, pervasive developmental disorder; PDD-NOS, pervasive developmental disorder-not otherwise specified; PNN, probabilistic neural network; PPV, positive predictive value; QDA, quadratic discriminant analysis; RF, random forest; rs-EEG, resting-state electroencephalography; rs-fMRI, resting-state functional magnetic resonance imaging; Sen, sensitivity; Spe, specificity; SVM, support vector machine; SVMRBF, support vector machine with Radial Basis Function Kernel; TASD, text-based early Autism Spectrum Disorder detection dataset for toddlers; TD, typically developing; XGBoost, extreme gradient boosting.

Table 3. Various Deep Learning Autism Spectrum Disorder Detection Modalities	
Neuroimaging Assessment	
Functional Magnetic Resonance Imaging (fMRI)	• fMRI measures brain blood flow, providing insight into neural activity and connections across different brain regions • fMRI aids in ASD detection using DL to examine brain activation patterns and neural network interactions
Functional near-infrared spectroscopy (fNIRS)	• fNIRS measures brain activity by detecting changes in blood oxygenation levels in the brain • AI models can identify atypical neural patterns associated with ASD by assessing hemodynamic responses in specific brain regions
Electroencephalography (EEG)	• EEG captures brain signals • Enabling DL models to identify ASD-related patterns in brain activity through electrodes
Electroretinography (ERG)	• ERG records electrical responses of the retina to light stimuli • Used in DL techniques to analyze retinal response patterns
Multimodal (Non-Neuroimaging) Assessment	
Visual data	• Visual data, such as facial expressions and home videos, provide valuable insights into the social and behavioral patterns of individuals • Enabling DL models to automate the analysis of facial expressions, eye movement patterns, and behavioral interactions.
Motor function data	• Evaluating physical movement patterns and detecting motor abnormalities • DL models to analyze 3D kinematic data from walking patterns
Behavioral data	• Behavioral data observes and assesses an individual's behavior • DL models identify ASD traits and patterns, improving accuracy and reliability through integration with other modalities
Microbiome data	• Microbiome data for understanding gut-brain interactions • DL algorithms to analyze gut microbial profiles
Genetic data	• Genetic data in ASD detection enhances research, improving diagnosis and treatment strategies • DL integration with neuroimaging and behavioral data

demonstrating the potential of eye-tracking as a tool for early detection of ASD. The study also emphasized the importance of developmental age and suggested that future research should consider these factors to refine predictive outcomes.

Manjur et al[46] explored electroretinography (ERG) combined with ML to detect ASD. The study analyzed ERG signals from children with ASD and control subjects and found that spectral analysis of ERG waveforms offered better classification accuracy than traditional time-domain features. Using an ML approach with automatic feature selection, the researchers achieved an accuracy of 86% and a sensitivity of 98%, demonstrating the potential of ERG as a tool for ASD diagnosis. This method could offer a faster and more accessible diagnostic process than traditional methods. The study also suggested that combining ERG with other physiological measures, such as electrodermal activity or pupil response, could improve diagnostic accuracy further.

Gao et al[44] explored a multi-task learning framework to identify ASD using resting-state functional magnetic resonance imaging (rs-fMRI) data. The study aimed to improve the accuracy of ASD detection by leveraging information from multiple datasets and tasks. Using a multi-task Transformer framework with an attention mechanism, the model was able to extract ASD-related features better, improving both feature representation and the generalization of predictions across different datasets. This approach outperformed traditional single-task methods and demonstrated the potential of ML to enhance clinical practice for ASD diagnosis, though challenges like data imbalance still need to be addressed.

All these studies illustrate the diverse approaches and significant progress made in enhancing predictive outcomes for ASD diagnosis using AI, ML, and other advanced technologies. Enhanced predictive outcomes are crucial for ensuring that children receive early interventions that can significantly improve their quality of life and developmental prospects. Continued research into these technologies will be vital in overcoming current challenges, such as data quality and algorithm bias, to ensure that AI-driven diagnostic tools are reliable and applicable in clinical settings.

SIMPLIFYING AUTISM SPECTRUM DISORDER DIAGNOSIS BY REDUCING ASSESSMENT STEPS AND TIME OF DIAGNOSIS

Traditional diagnostic methods for ASD, which rely heavily on behavioral assessments, are often time-consuming, subjective, and require expert clinicians. These innovations use data from brain activity, facial images, behavioral observations, and genetic markers to offer more accessible, efficient, and reliable diagnostic tools. Early diagnosis is crucial, and linked to better intervention outcomes, especially when conducted before age 3.

Among these advancements, Pal and Rubini[37] developed an intelligent behavioral trait prediction system using the BERT (Bidirectional Encoder Representations from Transformers) model. This AI-driven tool analyzes text-based parental observations describing toddler behaviors, incorporating key features like attention response, emotional empathy, and repetitive behaviors. The model achieved 88% accuracy using the text-based early Autism Spectrum Disorder detection dataset for toddlers (TASD), demonstrating its potential for efficient early screening.

Megerian et al[12] introduced an AI-based medical device designed to aid primary care providers in diagnosing ASD in children aged 18-72 months. The device integrates three key data inputs: caregiver questionnaires, brief home videos, and healthcare provider assessments. Unlike traditional diagnostic tools, which can be lengthy and cumbersome, this device uses a streamlined approach with shorter questionnaires and videos. This efficiency is especially beneficial in primary care settings, where time constraints often hinder comprehensive assessments. The AI system maintained consistent performance across various demographic factors, including sex, race/ethnicity, income, and parental education, suggesting that the reduced assessment items did not introduce bias. This study demonstrates that even with fewer items, AI can still yield reliable diagnostic recommendations, ultimately enhancing diagnostic capacity and early intervention.

Rabie and Saleh[40] aimed to create an AI tool for early ASD diagnosis using facial images, reducing the reliance on behavioral assessments. The researchers applied ML algorithms, particularly CNN, to analyze facial features in children aged 2-8 years, achieving an impressive 92.31% accuracy. This high accuracy suggests that AI-based facial image analysis could be a valuable addition to the diagnostic toolkit for ASD. The use of facial images offers several advantages over traditional methods, particularly in settings with limited access to experienced specialists. This approach could help prioritize cases requiring more detailed evaluation by enabling faster and more objective screenings. However, the researchers note that further studies with larger, more diverse datasets are necessary to improve the model's generalizability and robustness.

Tang et al[42] explored the use of blood-based biomarkers combined with ML for early ASD detection. The researchers used advanced statistical techniques like LASSO regression to narrow down a large set of differentially expressed genes to just 21 key biomarkers. Utilizing these biomarkers, the team developed ML models that achieved high accuracy rates, with logistic regression reaching 86% accuracy and neural networks achieving 88% accuracy. The reduced number of biomarkers makes this approach more efficient and cost-effective than traditional methods, which typically involve more extensive genetic testing. Furthermore, blood-based tests are non-invasive and could be especially appealing for young children, who may find behavioral assessments challenging. This study also demonstrated that fewer biomarkers can still lead to highly accurate predictions, opening the door to simpler and more accessible diagnostic tests. However, the researchers emphasize the need for further validation in larger, more diverse populations to confirm the tool's reliability and applicability.

Xu et al[45] introduced a multilayer neural network called continuous graph recurrent neural network (CGRNN), combining CNN and gated recurrent units (GRU) to analyze functional near-infrared spectroscopy (fNIRS) signals to diagnose ASD. One of the key challenges in ASD diagnosis is the limited availability of large, labeled datasets for training ML models. The researchers implemented a sliding window technique to address this issue, dividing long-duration time-series data (480 seconds) into overlapping 7-second segments. This approach allowed the model to effectively capture relevant features despite the small sample size (25 children with ASD and 22 TD children). The results were promising, with the CGRNN model achieving 92.2% accuracy, 85.0% sensitivity, and 99.4% specificity, suggesting that even short-duration hemodynamic fluctuations from a single optical channel can provide valuable discriminative information between ASD and TD children. Moreover, the study revealed that certain brain regions might be more indicative of ASD, which could help refine diagnostic processes. Interestingly, the study also found that total hemoglobin measurements offered better discriminative power than oxygenated or deoxygenated hemoglobin. These findings emphasize the potential for fNIRS as a non-invasive, efficient method for early ASD detection, and point toward the need for further research to optimize these approaches.

Pham et al[48] developed a non-invasive, cost-effective diagnostic system for ASD using electroencephalogram (EEG) signals. Electroencephalogram is a well-established technique for monitoring brain activity, and the researchers focused on extracting just five key features from EEG data to distinguish between children with ASD and TD children. The resulting system achieved an impressive 98.7% accuracy, demonstrating the potential for EEG to provide rapid and reliable ASD diagnoses. This method has several advantages, including its non-invasive nature and the ability to perform diagnostic testing quickly, potentially reducing wait times for ASD evaluations. While the study was limited by sample size and the manual nature of feature extraction, the authors propose that future research incorporating DL models and larger datasets could further enhance the system's performance.

These studies highlight the growing potential of advanced technologies—ranging from neural networks and AI-based devices to biomarkers and EEG signals. By simplifying the diagnostic process, reducing the need for lengthy and invasive assessments, and improving diagnostic accuracy, these approaches promise to increase the speed and accessibility of ASD detection, particularly in underserved areas. However, while the results are promising, further validation and research are necessary to refine these methods and ensure their reliability in diverse clinical settings.

CLASSIFICATION BETWEEN DIFFERENT NEURODEVELOPMENTAL DISORDERS

Autism spectrum disorder is one of the most widely studied and diagnosed among NDDs. However, it shares several overlapping features with other conditions, such as Attention-Deficit/Hyperactivity Disorder, intellectual disabilities, and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS). It is important to note that the neurological categorization mentioned aligns with the DSM-IV framework, which has been updated in the DSM-V. Precise differentiation and classification of these disorders are essential for implementing targeted interventions and therapies, as the symptoms and severity can vary significantly. With the growing recognition of the complexity of these disorders, there has been a push for more sophisticated diagnostic methods that can differentiate ASD from other NDDs. Recent advancements in ML, neuroimaging, and biosignal analysis offer promising solutions for more accurate, efficient, and objective diagnoses, which are essential for early intervention and personalized treatment.

Choi et al[25] employed a multiclass decision forest algorithm to classify children with different neurodevelopmental conditions using 1269 Korean ADI-R test data. The goal was to differentiate between ASD, PDD-NOS, and no-diagnosis groups. By applying the decision forest model, the team found high accuracy in categorizing these groups, particularly as the number of decision trees increased from 1 to 8. The results showed that using 4 or 8 trees led to an accuracy of 81% in predicting PDD-NOS, highlighting the model's effectiveness in distinguishing between NDDs. The approach used in this study demonstrates the potential of ML techniques to handle complex data from neurodevelopmental assessments. By integrating multiple decision trees, the decision forest algorithm can process and classify various patterns in diagnostic data, making it an efficient tool for recognizing subtle differences between disorders like ASD and PDD-NOS.

Meanwhile, Abdulhay et al[47] focused on resting-state EEG data to differentiate ASD from neurotypical children. The study utilized continuous wavelet transform (CWT) to analyze EEG data, revealing significant differences in neural discharge frequencies and brain activity between children with ASD and neurotypical children. These differences were reflected in the CWT plots, which showed larger areas for ASD cases compared to neurotypical cases. The researchers applied an artificial neural network (ANN) classification method to the extracted features, achieving an impressive overall accuracy of 95.90%, with a sensitivity of 96.72% and specificity of 95.08%. The study included 122 participants (61 ASD and 61 neurotypical children), which strengthened the reliability of the results by addressing the limitations of previous studies with smaller samples. The main advantage of this EEG-based method is its simplicity and accessibility. Unlike fMRI or CT scans, EEG can be easily collected and analyzed, making it suitable for routine clinical use. Additionally, EEG provides a more detailed view of brain activity by looking at both the timing and patterns of the signals, offering deeper insights into the brain functions involved in ASD and other NDDs.

Both studies highlight promising advancements in the classification and diagnosis of NDDs. Choi et al's decision forest model and Abdulhay et al's EEG-based method represent two different approaches to improving diagnostic accuracy. However, they shared a common goal: to provide more objective, accessible, and accurate tools for distinguishing ASD from other conditions such as PDD-NOS and other NDDs, which was a diagnostic category in DSM-IV but has been superseded in the current DSM-V classification. While these methods have shown promising results, further validation is needed. The studies emphasize the importance of large, diverse sample sizes to ensure the generalizability of these approaches across various populations.

DETERMINING CRITICAL FACTORS OF AUTISM SPECTRUM DISORDER

Autism spectrum disorder is an NDD that impacts social interaction, communication, and behavior, with rising prevalence highlighting the need for early identification and intervention. Despite the complex and multifactorial nature of ASD, studies suggest both genetic and environmental factors contribute to its onset. Identifying critical risk factors is critical to improving screening and personalized interventions. Early diagnosis significantly improves outcomes for children with ASD, making research into potential predictors, including genetic, environmental, and novel markers like gait abnormalities and brain activity, essential.

Several studies have identified key predictors for early ASD detection. Rahman et al[27] identified critical factors for the early prediction of ASD by analyzing EMRs from a large cohort. The study found several maternal and paternal factors, such as parental age and medication use, were significant predictors. This study highlights key predictors for ASD classification, which include previously proposed risk factors such as advanced parental age, medication use, and demographic characteristics like education level and socioeconomic status. However, it also suggests that these associations are not causative but may reflect underlying genetic predispositions or environmental influences that interact with genetic risk factors.

Ucuz and Cicek[28] used an ANN to predict ASD by considering a range of prenatal, perinatal, and developmental factors. The study found that early developmental milestones—such as age of first words, head control, and sitting independently—were among the strongest predictors of ASD. Family history of autism and paternal age at the time of pregnancy also emerged as critical factors. This study underscores the importance of developmental milestones in predicting ASD risk and suggests that early developmental screenings could serve as valuable tools for early diagnosis. These milestones, such as when a child speaks their first words or achieves motor control, are often delayed in children with ASD. Early identification of these delays could help clinicians diagnose ASD at younger ages, allowing for early interventions that improve outcomes.

Hasan et al[35] took a different approach by focusing on the gait patterns of children with ASD. Using 3-dimensional kinematic data, the researchers found that children with ASD exhibited specific gait abnormalities that could help differentiate them from TD children. These gait features, such as knee flexion during foot contact, maximum ankle plantarflexion during stance, maximum ankle adduction during the gait cycle, and maximum ankle abduction during the gait cycle, were highly predictive of ASD. By applying ML to the kinematic data, the researchers achieved high classification accuracy (91.7%) in detecting gait abnormalities associated with ASD. This study demonstrates the potential of biomechanical analysis to identify motor-related symptoms of ASD, which could be integrated into existing diagnostic protocols to aid in early detection.

Olageuz-Gonzalez et al[41] explored the potential of the gut microbiome as a biomarker for ASD. By analyzing microbiome data from two different countries, the researchers identified specific bacterial genera that were significantly associated with ASD. Notably, bacteria such as "*Bacteroides*," "*Lachnospira,*" and "*Ruminococcus*" were found to play an important role in ASD classification. This research suggests that the gut-brain axis may be an important factor in ASD development. The findings challenge conventional microbiome research, which typically focuses on the most abundant bacteria, showing that less abundant bacteria may also play a critical role in ASD. This study highlights the potential of microbiome analysis as a new diagnostic tool for ASD, but further research is needed to confirm these findings and explore their clinical applications.

Bi et al[43] used fMRI data to develop an improved diagnostic method for ASD. By applying a novel ML technique called the "random neural network cluster," the researchers achieved high classification accuracy (95%-100%) in differentiating individuals with ASD from TD children. This method identified specific brain regions, such as the supplementary motor area and fusiform gyrus, that showed abnormal activity in individuals with ASD. These brain regions have been previously implicated in ASD, reinforcing the neurological basis of the disorder. The high classification accuracy of this method suggests that fMRI could become an important tool in the early and accurate diagnosis of ASD, aiding in the development of targeted interventions.

These studies illustrate the growing potential of using advanced technologies like AI, ML, and brain imaging to uncover critical risk factors and improve early diagnosis of ASD. By analyzing diverse data sources, such as electronic health records (EHR), developmental milestones, gait patterns, microbiome composition, and brain activity, researchers are beginning to identify key factors that contribute to the development of ASD. While many of these studies have demonstrated promising results, the field is still in the early stages of validating these predictive models and identifying causative risk factors. Continued research, including larger sample sizes and longitudinal studies, will be crucial for refining these tools and ensuring they can be effectively integrated into clinical practice.

REDUCING THE NUMBER OF FEATURES WITHOUT COMPROMISING ACCURACY

In many AI/ML/DL applications, especially in medical diagnosis, the crucial goal is the ability to reduce the number of features in a model without sacrificing predictive accuracy. This process, often called "feature selection," involves identifying and retaining only the most important variables that contribute meaningfully to the model's predictions, while eliminating less informative or redundant features. Feature selection methods, such as mutual information, RF, and dimensionality reduction techniques like t-distributed Stochastic Neighbor Embedding (t-SNE), have been employed in various ASD studies to optimize the diagnostic process. Below, we explore several studies that have applied feature reduction techniques to improve the efficiency and accuracy of ASD diagnosis.

Choi et al[25] focused on optimizing ASD diagnosis by applying ML techniques to the ADI-R algorithm. Their study used mutual information methods to rank the importance of 78 diagnostic items based on data collected from 539 verbal individuals over 48 months old. The analysis showed that the most important features for ASD diagnosis were predominantly related to communication and social interaction, with seven of the top 10 items coming from the communication domain, and three from reciprocal social interaction. To further streamline the diagnosis, the researchers selected only the top 5 ranked items from the list, which achieved exceptional results by reaching 100% specificity and 97.6% sensitivity for classifying ASD. These findings highlight the potential for improving ASD diagnostic tools by focusing on a smaller set of highly predictive features. While the study demonstrated the promise of ML, the authors noted that their results were based on older DSM-IV criteria, and integrating clinical and biological data in future iterations could lead to even more accurate and efficient screening methods.

Selvi et al[29] sought to develop a practical tool for early ASD screening, particularly in areas with limited access to clinical specialists. They introduced the Indian Autism Grading Tool (IAGT), a mobile app designed to simplify the screening process by using a 37-item questionnaire called the Indian Autism Parental Questionnaire (IAPQ), which assesses various developmental aspects, including social, language, and cognitive skills. The researchers applied ML algorithms to the IAPQ data to create an efficient classification model for ASD. They tested five algorithms, including DT, Gaussian Naive Bayes, and multinomial logistic regression (MLR), with the MLR model achieving the highest accuracy at 97.85%. The IAGT app was developed to allow parents and caregivers to easily complete the questionnaire and receive immediate predictions of autism severity, which could be used to determine whether further clinical evaluation is necessary. One key advantage of this tool is its ability to maintain high predictive accuracy with a reduced set of 37 items. By focusing on the most relevant questions, the researchers demonstrated how ML could enhance diagnostic efficiency without compromising the quality of the results.

Awaji et al[32] explored the potential of using facial feature analysis combined with ML algorithms to improve the accuracy and efficiency of ASD diagnosis. The researchers aimed to develop a hybrid system integrating CNN with traditional ML models to identify subtle facial features that might indicate ASD. This approach focuses on reducing the number of features derived from facial images without sacrificing the model's ability to differentiate between ASD and TD individuals. They used pretrained CNN models, such as VGG16, ResNet101, and MobileNet, to extract complex features from facial images. These models effectively capture intricate, hierarchical patterns within raw image data. To optimize the analysis, they applied the t-SNE algorithm to reduce the dimensionality of the feature space, ensuring that only the most significant features were retained while eliminating less informative ones. By combining the power of DL for feature extraction with traditional ML algorithms like XGBoost and RF for classification, the researchers developed a robust system for ASD diagnosis that maintained high accuracy while reducing the computational complexity of the model. This hybrid approach highlights the potential for feature reduction techniques to improve diagnostic tools by focusing on the most relevant data points, such as facial features, which may provide valuable insights for clinicians in identifying ASD.

Wang and Fu[39] investigated the role of gut microbiota as a potential biomarker for ASD, utilizing ML to identify which microbial species could be used to predict the disorder. The researchers collected data from multiple cohorts across different regions and ethnicities, integrating microbiome data into the analysis to identify any correlations between gut microbiota composition and ASD. To refine the dataset and improve predictive accuracy, the team applied an RF algorithm and an iterative feature selection process, specifically using the mean decrease accuracy method to assess the importance of each microbial species. This iterative approach enabled the researchers to reduce the number of features (microbial species) in the dataset while ensuring that only the most informative species remained. The researchers repeated this process until further feature reductions did not improve the area under the receiver operating characteristic curve, indicating an optimal set of features for predicting ASD. The study shows how ML can be applied to complex microbiome datasets to identify specific biomarkers for ASD, thus simplifying the diagnostic process without compromising accuracy.

The studies reviewed above demonstrate the powerful impact of feature reduction techniques in enhancing the efficiency and accuracy of ASD diagnosis. By reducing the number of features without compromising accuracy, clinicians can benefit from faster, more efficient diagnostic tools, which could ultimately lead to earlier identification and better-targeted interventions for children with ASD.

CHALLENGES AND LIMITATIONS

Limitations of AI in diagnosing ASD include data limitations, as models often rely on datasets that may not represent the diverse ASD population, leading to biased results. The complexity of ASD, characterized by a wide spectrum of symptoms, poses challenges for AI in capturing all variations. Moreover, AI may lack the contextual understanding to interpret subtle social and behavioral cues crucial for diagnosis. There are also ethical concerns related to privacy, consent, and the "black box" nature of AI decisions. Implementing ASD diagnostic tools requires careful consideration of ethical implications and proper consent from patients' guardians. A collaborative effort is essential to effectively integrate large-scale ASD patient data into bioinformatics systems for treatment and cure development. This collaboration should involve various experts, including medical professionals, bioinformaticians, computer scientists, bioethicists, and specialists from other relevant fields.[49]

Limited integration with clinical expertise can result from AI tools being developed without sufficient clinician input, leading to over-reliance on technology.[50] Additionally, many AI models lack extensive validation across diverse populations and settings, raising questions about their generalizability. Developmental considerations are important; changes in ASD symptoms over time may not be adequately accounted for in AI models. Furthermore, integrating diverse data types (behavioral, genetic, neuroimaging) presents challenges for AI systems. A lack of longitudinal data also exists, as many models are based on cross-sectional data, missing critical developmental changes. Finally, regulatory and implementation challenges pose significant hurdles in integrating AI tools into clinical practice.

CONCLUSION

The integration of AI technologies in ASD diagnosis offers significant potential for improving diagnostic accuracy, efficiency, and early detection. Artificial intelligence-driven methods, particularly ML and DL algorithms, have demonstrated high accuracy across various data modalities such as nominal, observational, laboratory, and neuroimaging data. These approaches provide several advantages, including improved diagnostic precision, reduced assessment time, more objective analysis, and enhanced predictive capabilities.

Furthermore, AI tools have the potential to significantly increase the accessibility of ASD screening, particularly in underserved areas where specialized resources may be limited. Looking ahead, a valuable research direction would involve applying various AI techniques, despite their heterogeneity, to a single, preferably large population. This approach would enable the verification and comparison of respective results, potentially leading to more potent and generalizable diagnostic models for ASD.

However, challenges such as data quality, privacy concerns, ethical issues, and the need for clinical integration remain. Further research is needed to improve the robustness of AI models, ensure data privacy, and develop guidelines for their use in clinical settings. A multidisciplinary approach combining AI with traditional diagnostic methods and clinical judgment will be essential for effective ASD assessment. Continued advancements in AI technology, along with careful attention to ethical and practical considerations, will ultimately lead to more accurate, timely, and personalized interventions for individuals with ASD.

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REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-V*. 5th ed. Washington DC: American Psychiatric Publishing: 2013.
2. Hodges H, Fealko C, Soares N. Autism spectrum disorder: definition, epidemiology, causes, and clinical evaluation. *Transl Pediatr*. 2020;9(suppl 1):S55-S65. [CrossRef]
3. Maenner MJ, Warren Z, Williams AR, et al. Prevalence and characteristics of autism spectrum disorder among children aged 8

years - autism and developmental disabilities monitoring network, 11 sites, United States, 2020. *MMWR Surveill Summ.* 2023;72(2):1-14. [CrossRef]

4. Shrestha M, Basukala S, Thapa N, et al. Prevalence of autism spectrum disorder among children in Southeast Asia from 2002 to 2022: an updated systematic review and meta-analysis. *Health Sci Rep.* 2024;7(4):e2005. [CrossRef]
5. Huerta M, Lord C. Diagnostic evaluation of autism spectrum disorders. *Pediatr Clin North Am.* 2012;59(1):103-111. [CrossRef]
6. Hus Y, Segal O. Challenges surrounding the diagnosis of autism in children. *Neuropsychiatr Dis Treat.* 2021;17:3509-3529. [CrossRef]
7. Gesi C, Migliarese G, Torriero S, et al. Gender differences in misdiagnosis and delayed diagnosis among adults with autism spectrum disorder with no language or intellectual disability. *Brain Sci.* 2021;11(7):912. [CrossRef]
8. Wiggins LD, Durkin M, Esler A, et al. Disparities in documented diagnoses of autism spectrum disorder based on demographic, individual, and service factors. *Autism Res.* 2020;13(3):464-473. [CrossRef]
9. Webb SJ, Jones EJH, Kelly J, Dawson G. The motivation for very early intervention for infants at high risk for autism spectrum disorders. *Int J Speech Lang Pathol.* 2014;16(1):36-42. [CrossRef]
10. Falkmer T, Anderson K, Falkmer M, Horlin C. Diagnostic procedures in autism spectrum disorders: a systematic literature review. *Eur Child Adolesc Psychiatry.* 2013;22(6):329-340. [CrossRef]
11. Can Demirbaş K, Yıldız M, Saygılı S, Canpolat N, Kasapçopur Ö. Artificial intelligence in pediatrics: learning to walk together. *Turk Arch Pediatr.* 2024;59(2):121-130. [CrossRef]
12. Megerian JT, Dey S, Melmed RD, et al. Evaluation of an artificial intelligence-based medical device for diagnosis of autism spectrum disorder. *npj Digit Med.* 2022;5(1):57. [CrossRef]
13. Segato A, Marzullo A, Calimeri F, De Momi E. Artificial intelligence for brain diseases: a systematic review. *APL Bioeng.* 2020;4(4):041503. [CrossRef]
14. Noorbakhsh-Sabet N, Zand R, Zhang Y, Abedi V. Artificial intelligence transforms the future of health care. *Am J Med.* 2019;132(7):795-801. [CrossRef]
15. Jiang F, Jiang Y, Zhi H, et al. Artificial intelligence in healthcare: past, present and future. *Stroke Vasc Neurol.* 2017;2(4):230-243. [CrossRef]
16. Shahamiri SR, Thabtah F. Autism AI: a new autism screening system based on artificial intelligence. *Cognit Comput.* 2020;12(4):766-777. [CrossRef]
17. Moon SJ, Hwang J, Kana R, Torous J, Kim JW. Accuracy of machine learning algorithms for the diagnosis of autism spectrum disorder: systematic review and meta-analysis of brain magnetic resonance imaging studies. *JMIR Ment Health.* 2019;6(12):e14108. [CrossRef]
18. Helmy E, Elnakib A, ElNakieb Y, et al. Role of artificial intelligence for autism diagnosis using DTI and fMRI: a survey. *Biomedicines.* 2023;11(7):1858. [CrossRef]
19. Deo RC. Machine learning in medicine. *Circulation.* 2015;132(20):1920-1930. [CrossRef]
20. Strauß S. From big data to deep learning: a leap towards strong AI or 'intelligentia obscura'? *BDCC.* 2018;2(3):16. [CrossRef]
21. Xiao X, Fang H, Wu J, et al. Diagnostic model generated by MRI-derived brain features in toddlers with autism spectrum disorder. *Autism Res.* 2017;10(4):620-630. [CrossRef]
22. Mahajan R, Mostofsky SH. Neuroimaging endophenotypes in autism spectrum disorder. *CNS Spectr.* 2015;20(4):412-426. [CrossRef]
23. Thabtah F. Machine learning in autistic spectrum disorder behavioral research: a review and ways forward. *Inform Health Soc Care.* 2019;44(3):278-297. [CrossRef]
24. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71. Published online March 29, 2021. [CrossRef]
25. Choi ES, Yoo HJ, Kang MS, Kim SA. Applying artificial intelligence for diagnostic classification of Korean autism spectrum disorder. *Psychiatry Investig.* 2020;17(11):1090-1095. [CrossRef]
26. Khullar V, Singh HP, Bala M. Deep neural network-based handheld diagnosis system for autism spectrum disorder. *Neurol India.* 2021;69(1):66-74. [CrossRef]
27. Rahman R, Kodesh A, Levine SZ, Sandin S, Reichenberg A, Schlessinger A. Identification of newborns at risk for autism using electronic medical records and machine learning. *Eur Psychiatry.* 2020;63(1):e22. [CrossRef]
28. Ucuz I, Cicek AU. Artificial neural networks based-prediction of autism spectrum disorder. *J Cogn Syst.* 2020;5(2):47-51.
29. Selvi CSK, Jayaprakash D, Poonguzhali S. Early diagnosis of autism using Indian autism grading tool. *IFS.* 2023;44(3):3851-3865. [CrossRef]
30. Alam MS, Rashid MM, Faizabadi AR, Zaki HFM. Power of alignment: exploring the effect of face alignment on ASD diagnosis using facial images. *IIUM Eng J.* 2024;25(1):317-327. [CrossRef]
31. Alhakbani N. Facial emotion recognition-based engagement detection in autism spectrum disorder. *IJACSA.* 2024;15(3). [CrossRef]
32. Awaji B, Senan EM, Olayah F, et al. Hybrid techniques of facial feature image analysis for early detection of autism spectrum disorder based on combined CNN features. *Diagnostics (Basel).* 2023;13(18):2948. [CrossRef]
33. Meng F, Li F, Wu S, et al. Machine learning-based early diagnosis of autism according to eye movements of real and artificial faces scanning. *Front Neurosci.* 2023;17:1170951. [CrossRef]
34. Rabbi MF, Hasan SMM, Champa AI, Zaman MA. A convolutional neural network model for early-stage detection of autism spectrum disorder. In: International Conference on Information and Communication Technology for Sustainable Development (ICICT4SD). 2021:110-114. [CrossRef]
35. Hasan CZ, Jailani R, Tahir NM. Automated classification of gait abnormalities in children with autism spectrum disorders based on kinematic data. *Int J Pharmacol Physiol.* 2017;4:1-8.
36. Lu A, Perkowski M. Deep learning approach for screening autism spectrum disorder in children with facial images and analysis of ethnoracial factors in model development and application. *Brain Sci.* 2021;11(11):1446. [CrossRef]
37. Pal M, Rubini P. Fusion of Brain Imaging Data with Artificial Intelligence to detect autism Spectrum Disorder. *Front Psychiatry Artif Intell.* 2024;14:1-8. [CrossRef]
38. Luongo M, Simeoli R, Marocco D, Milano N, Ponticorvo M. Enhancing early autism diagnosis through machine learning: exploring raw motion data for classification. *PLoS One.* 2024;19(4):e0302238. [CrossRef]
39. Wang W, Fu P. Gut microbiota analysis and in silico biomarker detection of children with autism spectrum disorder across cohorts. *Microorganisms.* 2023;11(2):291. [CrossRef]
40. Rabie AH, Saleh AI. A new diagnostic autism spectrum disorder (DASD) strategy using ensemble diagnosis methodology based on blood tests. *Health Inf Sci Syst.* 2023;11(1):36. [CrossRef]
41. Olaguez-Gonzalez JM, Chairez I, Breton-Deval L, Alfaro-Ponce M. Machine learning algorithms applied to predict autism spectrum disorder based on gut microbiome composition. *Biomedicines.* 2023;11(10):2633. [CrossRef]
42. Tang H, Liang J, Chai K, et al. Artificial intelligence and bioinformatics analyze markers of children's transcriptional genome to predict autism spectrum disorder. *Front Neurol.* 2023;14:1203375. [CrossRef]
43. Bi XA, Liu Y, Jiang Q, Shu Q, Sun Q, Dai J. The diagnosis of autism spectrum disorder based on the random neural network cluster. *Front Hum Neurosci.* 2018;12:257. [CrossRef]
44. Gao L, Wang Z, Long Y, et al. Autism spectrum disorders detection based on multi-task transformer neural network. *BMC Neurosci.* 2024;25(1):27. [CrossRef]

45. Xu L, Geng X, He X, Li J, Yu J. Prediction in autism by deep learning short-time spontaneous hemodynamic fluctuations. *Front Neurosci.* 2019;13:1120. [CrossRef]
46. Manjur SM, Hossain MB, Constable PA, et al. Detecting autism Spectrum Disorder Using Spectral Analysis of Electroretinogram and Machine Learning: preliminary results. In: 2022 44th Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC). Glasgow, Scotland, United Kingdom: IEEE; 2022;2022:3435-3438. [CrossRef]
47. Abdulhay E, Alafeef M, Hadoush H, Arunkumar N. Resting state EEG-based diagnosis of autism via elliptic area of continuous wavelet transform complex plot. *J Intell Fuzzy Syst.* 2020;39(6):8599-8607. [CrossRef]
48. Pham TH, Vicnesh J, Wei JKE, et al. Autism spectrum disorder diagnostic system using HOS bispectrum with EEG signals. *Int J Environ Res Public Health.* 2020;17(3):971. [CrossRef]
49. World Health Organization. *Ethics and Governance of Artificial Intelligence for Health: WHO Guidance*. 1st ed. Geneva: World Health Organization; 2021.
50. El-Ashram REM, Aldaghmi OA, Mohammed SMM. Requirements for the application of artificial intelligence in diagnosing autism spectrum disorder: specialists' perception. *J Disabil Res.* 2024;3(7). [CrossRef]

Supplementary Table 1. Glossary Box[13]	
Artificial intelligence (AI)	Refers to the development of algorithms and computer systems capable of mimicking cognitive functions typically associated with human intelligence (including data analysis, pattern recognition, diagnostic reasoning, image interpretation, and natural language processing). It covers machine learning, deep learning and natural language processing under its umbrella.
Machine learning (ML)	It is a subset of artificial intelligence that allows computers to learn from data. ML algorithms use statistical methods to improve at a specific task as they process more data.
Artificial neural network (ANN)	A computational model inspired by the human brain's structure. It consists of connected nodes, or "neurons," arranged in layers that process information by responding dynamically to inputs. This setup enables the network to learn complex patterns and relationships in data. ANNs are widely used for tasks like classification and regression and form the basis for advanced methods like deep learning, which uses many layers to capture detailed patterns automatically.
Convolutional neural network (CNN)	The type of ANN where the typical fully connected layers are replaced by convolutional operations using a set of trainable filters.
Multilayer perceptron (MLP)	The type of ANN used in ML, consists of multiple layers of neurons (input, hidden, and output layers). MLPs are used to model complex relationships between inputs and outputs using non-linear activation functions.
Recurrent neural network (RNN)	Enables the modeling of temporal dynamics based on information received at previous time points by connecting higher and lower levels.
Gated recurrent unit (GRU)	A type of RNN that is designed to handle sequential data. It uses gating units to control the flow of information, allowing it to capture long-term dependencies in data more efficiently than traditional RNNs.
Deep learning (DL)	An advanced subfield of Machine Learning that uses neural networks with multiple layers, called deep neural networks. It's especially effective for complex tasks like recognizing images and speech, allowing systems to understand detailed patterns in data automatically. This approach uses powerful computing and works well with large datasets to build more advanced and capable models.
Natural language processing (NLP)	A branch of AI that helps computers understand and work with human language. It enables machines to interpret, process, and generate language, making communicating easier for computers and people.
Bidirectional Encoder Representations from Transformers (BERT)	A transformer-based model designed to pre-train deep bidirectional representations by join conditioning on both left and right context in all layers. It's a powerful model for natural language processing (NLP) tasks. ERT is used for tasks like question answering, language understanding, and text classification.
Regression algorithms	Regression is used to model the relationship between variables, adjusting the model based on errors in its predictions to improve accuracy over time.
Linear discriminant analysis (LDA)	Projects a dataset of n-dimensional samples onto a latent subspace k (k n 1) while preserving class-discriminatory information
Quadratic discriminant analysis (QDA)	A variant of LDA that assumes each class has its own covariance matrix. It models the decision boundary between classes as a quadratic function instead of a linear one, making it more flexible in capturing the differences between classes.
Linear regression	Relationships between variables are modeled by fitting a linear equation to observed data.
Least Absolute Shrinkage and Selection Operator (LASSO)	A linear regression technique that performs both variable selection and regularization. It involves adding a penalty term to the regression loss function, which helps to shrink some coefficients to zero, effectively selecting a simpler model.
Logistic regression	Explains the relationship between one dependent binary variables and one or more independent variable regressing for the probability of a categorical outcome using a logistic function.
Clustering algorithms	Clustering, like regression, describes the class of problems and methods.
AdaBoost	The algorithm generates H hypotheses through an ensemble of learning algorithms. The output of the learning algorithms is combined into a weighted sum that represents the final output of the boosted classifier
Decision or Random Forest (RF)	An ensemble learning technique that aggregates predictions from multiple decision trees, with the final output determined by the majority vote, enhancing model accuracy and robustness.
k-nearest neighbor (KNN)	A classification algorithm that labels new data points based on the majority class of their k closest neighbors in the feature space, typically uses Euclidean distance as a similarity measure.
Support vector machines (SVM)	A type of supervised machine learning algorithm used for classification tasks. They work by identifying the optimal hyperplane that separates different classes in a dataset while maximizing the margin, which is the distance between the hyperplane and the nearest data points from each class

Gradient boosting machine (GBM)	An ensemble ML technique that builds a model in a stage-wise manner. It builds trees sequentially, where each tree tries to correct the errors made by the previous one. Each subsequent tree is trained to predict the residuals (errors) of the prior trees.
Extreme gradient boosting (XGBoost)	An optimized version of gradient boosting that improves the efficiency, flexibility, and scalability of traditional gradient boosting machines (GBM). It uses a gradient descent algorithm to optimize a loss function and create accurate predictions.
Bayesian algorithms	Statistical methods that apply Bayes' Theorem to solve classification and regression problems by updating probabilities based on new evidence.
Genetic algorithm	Optimization techniques inspired by natural selection, where a population of potential solutions evolves over generations through selection, crossover, and mutation processes to find the best solution to a given problem.