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REVIEW ARTICLE

Generative Models in Early Detection of Neurodevelopmental Disabilities: A Comprehensive Review of Applications, Innovations, and Challenges

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ABSTRACT

Neurodevelopmental disorders are a broad category that estimates fifteen million people and include autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), and intellectual disabilities that, if not found at an early age, present substantial lifelong challenges. Modern technologies in artificial intelligence with generative models mean new possibilities in early diagnostics and prevention. This review aims to review the biomarker potentials of generative models, including GANs, VAEs, and diffusion models, in the early diagnosis of neurodevelopmental disabilities. Having synthesized what is currently known about these models, we explore how the models improve diagnostic precision, minimize the use of invasive procedures, and manage data deficiency. The significant applications discussed involve generative models in analyzing neuroimaging data, modeling speech and behavior, and synthesizing new datasets that are valuable in handling privacy issues and biased datasets. In addition, this paper discusses some of the limitations associated with generative model deployment in clinical practice; these include interpretability, model stability, and the fact that the models rely on extensive and diverse datasets. Finally, we bridge the gap by looking into the future and discussing what future research could bring and ethical concerns regarding generative models and their potential to revolutionize handling cases of early neurodevelopmental disorders and enable early, more effective interventional approaches.

Keywords: Neurodevelopmental disorders ▪ Generative models ▪ Early diagnosis ▪ Artificial intelligence ▪ Personalized medicine

1. INTRODUCTION

Neurodevelopmental disorders (NDDs) are a broad group of developmental conditions that influence the thinking and learning abilities, behavior, and emotions of an individual. These disorders include autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), and intellectual disability (ID). They are estimated to affect a substantial number of individuals worldwide and can present long-term challenges, particularly when early diagnosis and treatment are unavailable. Therefore, early diagnosis and timely intervention are essential because they can improve treatment outcomes and support better developmental trajectories. In this context, the development of new diagnostic approaches has become an important research direction.

The development of artificial intelligence (AI) technologies has advanced rapidly and has enabled major progress in healthcare. Among these technologies, generative models, including generative adversarial networks (GANs), variational autoencoders (VAEs), and diffusion models, are especially

useful for supporting the early diagnosis of NDDs. These models can improve diagnostic accuracy, reduce reliance on invasive tests, and address data-related challenges that have previously limited research in this field [1].

This review paper is written from the perspective of using generative models to develop new approaches for the early diagnosis of NDDs. In relation to biomarker identification and predictive analysis, this paper critically analyzes how these models can transform clinical practice. The ability of generative models to process neuroimaging, neurological, speech, and behavioral data makes them flexible diagnostic tools for complex neurodevelopmental conditions.

Generative models are particularly valuable because they can address data deficiency and privacy concerns, which are common challenges in clinical research. Synthetic data generated by these models can enhance existing datasets and improve the stability of diagnostic algorithms without compromising patient identities. This supports safer and more ethical machine-learning training procedures [2].

This paper also discusses the potential of generative models in modeling neuroimaging data, speech, and behavior, as well as in synthesizing datasets for diagnostic purposes. These applications can improve diagnostic efficiency and deepen understanding of the mechanisms underlying NDDs. Consequently, they may contribute to more accurate and individualized interventions.

However, several challenges must be addressed before generative models can be fully incorporated into clinical practice. These include model interpretability, model stability, and the need for large and diverse datasets. Recognizing these limitations is essential for developing reliable AI-based solutions that can be applied within healthcare systems [3].

Ethical concerns are also central to the deployment of generative models for diagnosing NDDs. Maintaining transparency, avoiding algorithmic bias, and protecting patient rights are essential requirements in AI-based healthcare. These ethical dimensions require interdisciplinary collaboration among AI researchers, clinicians, and ethicists [4].

Finally, this review emphasizes the need for future research to address current gaps in knowledge. Promising future directions include multimodal integration of data types and the development of real-time diagnostic tools. Collaboration between AI developers, clinicians, and ethical experts will be necessary to ensure that these technologies are used responsibly and effectively.

2. RELATED WORK

The burden of brain-related conditions is increasing, which creates a strong need for new methods to diagnose, manage, and understand neurodevelopmental disorders and other complex neurological conditions. Technological developments, particularly generative models and graph-based learning, have expanded the possibilities of healthcare and neurodevelopmental research. These tools help researchers identify hidden patterns in high-dimensional data, including neuroimaging, multi-omics, and behavioral datasets. They also help address limitations such as data scarcity, privacy concerns, and model reliability.

Recently, functional magnetic resonance imaging (fMRI) has become an important tool for identifying biomarkers of brain disorders such as Alzheimer's disease and ASD. Deep learning models have achieved major progress in interpreting complex neural data. Yan et al. proposed the spatio-temporal collaborative Transformer block structure (STCTB), which addresses the challenge of processing spatial and temporal features in fMRI time series. By incorporating multi-scale spatiotemporal data and using a two-branch architecture inspired by the Swin Transformer, STCTB improves sensitivity and specificity in detecting brain activity signals [5].

Autism spectrum disorder is associated with atypical dynamic functional connectivity patterns. However, the temporal changes in intrinsic brain activity and the molecular mechanisms behind these atypical patterns remain unclear. Shan et al. used a Hidden Markov Model (HMM) to analyze resting-state fMRI data from the Autism Brain Imaging Data Exchange. Their study identified eight distinct HMM states with atypical temporal features in individuals with ASD. These features included state occurrences, mean lifetimes, and transition probabilities, which were predictive of communication difficulties in ASD [6].

With the rapid development of large language models (LLMs), there is increasing demand for domain-specific AI agents. Sung et al. proposed a pipeline that uses LLMs and retrieval-augmented generation (RAG) to construct high-quality instruction datasets for domain-specific fine-tuning. This approach is useful in data-scarce domains because it can generate relevant and context-aware instruction datasets from custom document collections [7].

Ibanez et al. evaluated the interconnected roles of the exposome, One Health, and brain capital in shaping health and disease outcomes. Their work highlights how physical and social exposomes influence brain health and emphasizes the importance of "green brain skills" for environmental health strategies [8].

Graph neural networks (GNNs) are important for learning brain network representations, particularly in brain age estimation. However, over-squashing can limit interactions between distant nodes and reduce the ability of GNNs to capture brain network topology. Li et al. introduced a Signed Curvature GNN (SCGNN), which incorporates node features and signed curvature into graph rewiring. This model improves information flow and enhances brain age estimation performance [9].

Recent studies have shown that contrastive learning can improve medical image segmentation when only limited labeled data are available. You et al. introduced Mine yOur owN Anatomy (MONA), a framework designed to address challenges such as long-tail class distributions, intra-class variations, and neglected intra-slice correlations. MONA decomposes medical images into meaningful anatomical features in an unsupervised manner and achieves strong performance in semi-supervised segmentation settings [10].

The brain is the central hub of the nervous system, and its development is essential for understanding human cognition and neurological disorders. Zhuo et al. developed MAPbrain, a multi-omics atlas of the primate brain. This platform integrates data from millions of brain cells across multiple brain regions and developmental time points. It supports compara-

tive and developmental brain research through transcriptomic, epigenomic, and spatial transcriptomic data [11].

Deep generative models have also been increasingly used in biological research. Bourou et al. introduced PhenDiff, a multiclass conditional diffusion model for detecting cellular phenotype changes. Unlike GAN-based methods, which may suffer from training instability and mode collapse, diffusion models provide a more stable approach for synthesizing and manipulating biological images [12].

Deep learning is also being used for automated detection of neurodevelopmental disorders, particularly ASD. Rakhimberdina proposed methods based on resting-state and task-based fMRI data to improve ASD detection. The study introduced a GNN-based prediction framework and a multimodal framework integrating visual stimuli data, supporting more accurate automated diagnosis [13].

PhenoScore is another important AI-based phenomics framework. Dingemans et al. developed this framework to integrate facial recognition and Human Phenotype Ontology data for quantifying phenotypic similarity. PhenoScore improves the diagnosis of rare neurodevelopmental disorders and supports genotype–phenotype studies [14].

Bioelectric regulation is also relevant to neurodevelopment. Manicka et al. developed a minimal dynamical model to analyze how multicellular voltage patterns influence collective gene expression. Their findings show that bioelectric patterns are involved in morphogenesis and gene regulation during development [15].

Razban et al. studied brain network communication using a targeted attack method. Their work demonstrated that early developing white matter tracts tend to become the longest and densest, suggesting that early connectivity plays a foundational role in neurodevelopment [16].

Zaripova et al. introduced Graph-in-Graph (GiG), a neural network architecture for biological and healthcare applications. GiG learns interpretable latent graph structures and improves downstream performance in tasks such as protein classification and brain imaging analysis [17].

Table 1 presents a comparative overview of recent AI-based and generative modeling approaches applied to neurodevelopmental disorder diagnosis and brain-health research. The summarized studies demonstrate the growing diversity of computational methods used in this field, including spatio-temporal Transformer models, Hidden Markov Models, graph neural networks, diffusion models, contrastive learning, retrieval-augmented generation, and multi-omics platforms. Collectively, these approaches contribute to improved biomarker discovery, automated ASD detection, medical image segmentation, brain-network modeling, and phenotype analysis. The table also shows that AI methods are increasingly moving beyond single-modality analysis toward multimodal and integrative frameworks that combine neuroimaging, behavioral, phenotypic, genetic, and biological data. However, despite their promising diagnostic and research value, several limitations remain, including the need for large and diverse datasets, model interpretability, computational complexity, bias reduction, and clinical validation. Therefore, the reviewed studies indicate that while AI and generative models offer strong potential for advancing early diagnosis and personalized intervention in neurodevelopmental disorders, their reliable clinical adoption requires further methodological refinement, ethical governance, and validation across heterogeneous populations.

To further support the interpretation of Table 1, five visual summaries were generated to highlight the main methodological, application-level, and research-gap patterns across the reviewed studies. Each figure provides a different analytical perspective on the literature, including the distribution of AI approaches, application areas, methodological emphasis, recurring limitations, and temporal publication trends. Figure 1 illustrates the distribution of the main AI-based methodological approaches identified across the reviewed studies. The figure shows that graph-based learning represents one of the most frequently used directions, reflecting the importance of graph neural networks and latent graph structures in modeling brain connectivity, biological relationships, and healthcare data. Neuroimaging temporal modeling, generative and diffusion models, and multi-omics/phenomics approaches also appear as major research directions, indicating a clear movement toward computational methods capable of handling complex, high-dimensional, and heterogeneous biomedical data. This distribution suggests that recent research on neurodevelopmental disorders is not limited to one AI paradigm but increasingly combines multiple computational strategies to improve diagnosis, biomarker discovery, and mechanistic understanding.

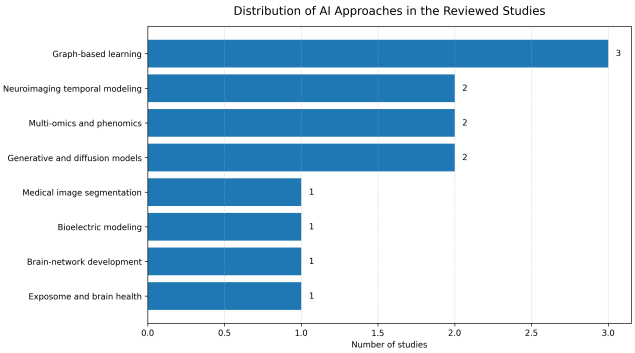

Figure 1. Distribution of AI-based methodological approaches across the reviewed studies.

Figure 2 summarizes the dominant application areas covered by the reviewed studies. Diagnosis and classification appear as the most represented application area, which reflects the strong focus of recent AI research on improving the early detection of neurodevelopmental disorders such as autism spectrum disorder. Biomarker and phenotype discovery, brain-network analysis, and medical image analysis are also strongly represented, demonstrating the growing role of AI in identifying clinically meaningful patterns from neuroimaging, phenotypic, and biological data. Overall, this figure highlights that AI-based models are increasingly being used not only for classification tasks but also for deeper interpretation of disease mechanisms and personalized healthcare applications.

Figure 3 provides a heatmap-style comparison of the relative methodological emphasis across the main research directions. The figure compares each methodological group according to several important dimensions, including diagnosis, biomarker discovery, multimodal integration, interpretability, and clinical translation. Multi-omics and phenomics approaches show

Table 1. Comparative Summary of Recent AI-Based and Generative Modeling Approaches for Neurodevelopmental Disorder Diagnosis and Brain-Health Research

Study Reference	Generative Model/Focus	Key Contributions	Applications	Limitations/Challenges
[5]	Spatio-temporal Transformer model for fMRI analysis	Introduced the STCTB architecture to jointly capture spatial and temporal features from fMRI time-series data, improving sensitivity and specificity in brain-activity classification.	Early diagnosis of neurological and neurodevelopmental disorders using functional neuroimaging biomarkers.	Requires large-scale and high-quality fMRI datasets; clinical translation may be limited by computational complexity and interpretability issues.
[6]	Hidden Markov Model for ASD neural dynamics	Identified eight atypical dynamic neural states in ASD and linked state-specific temporal features to communication difficulties and gene-expression profiles.	Understanding moment-to-moment neural dynamics in ASD and supporting biomarker discovery.	Findings depend on rs-fMRI quality and cohort characteristics; biological interpretation of HMM states remains challenging.
[7]	RAG-based instruction dataset generation	Proposed a retrieval-augmented generation pipeline for creating domain-specific instruction datasets from custom document collections.	Development of specialized AI systems for psychiatry, healthcare, and other data-scarce domains.	Generated instructions may inherit biases from source documents; output quality depends on retrieval accuracy and domain-document coverage.
[8]	Exposome, One Health, and brain-health framework	Highlighted the relationship between physical and social exposomes, One Health, and brain capital, emphasizing environmental influences on brain health.	Policy development, environmental health strategies, and prevention-oriented brain-health research.	Requires interdisciplinary integration; empirical validation across diverse populations remains limited.
[9]	Signed Curvature GNN for brain-network learning	Developed SCGNN using signed curvature, graph rewiring, and topology-aware pooling to improve brain-age estimation and disease classification.	Brain-age prediction, Alzheimer's disease classification, and structural brain-network analysis.	Graph rewiring can increase model complexity; interpretability and generalization across datasets require further validation.
[10]	Contrastive learning for medical image segmentation	Introduced MONA to decompose medical images into meaningful anatomical features under extremely limited labeled-data conditions.	Semi-supervised medical image segmentation and improved diagnostic image analysis.	Performance may vary across imaging modalities; requires careful evaluation under real clinical-data distributions.
[11]	Multi-omics atlas for primate brain research	Developed MAPbrain, integrating transcriptomic, epigenomic, and spatial transcriptomic data across brain regions and developmental stages.	Brain development studies, cross-species comparison, and neurodevelopmental mechanism discovery.	Large multi-omics integration is computationally demanding; harmonization across datasets and platforms remains difficult.
[12]	Diffusion model for subtle phenotype detection	Introduced PhenDiff, a conditional diffusion-model approach for translating biological images across conditions and detecting subtle cellular phenotype shifts.	Biomarker discovery, microscopy image analysis, disease understanding, and drug-discovery research.	Requires high-quality annotated biological images; subtle synthetic changes must be carefully validated to avoid misleading interpretations.
[13]	Deep learning and GNN frameworks for ASD detection	Developed frameworks using resting-state and task-based fMRI data, including multimodal integration of visual stimuli for ASD classification.	Automated ASD diagnosis and investigation of neural responses to social and visual stimuli.	Model robustness depends on sample size, scanner variability, and multimodal data availability.
[14]	AI-based phenomics using facial and phenotype data	Presented PhenoScore, integrating facial recognition and Human Phenotype Ontology data to quantify phenotypic similarity in rare diseases.	Rare neurodevelopmental disorder diagnosis, genotype–phenotype correlation, and variant interpretation.	Potential bias in facial-recognition systems; requires diverse datasets and careful ethical governance.
[15]	Bioelectric modeling of morphogenesis	Modeled how multicellular voltage patterns regulate collective gene expression and morphogenesis in embryonic brain development.	Developmental biology, regenerative medicine, and computational modeling of morphogenetic processes.	Findings from experimental models may not directly generalize to human neurodevelopment; biological mechanisms remain complex.
[16]	Targeted attack and percolation analysis of brain networks	Showed that early developing white-matter tracts become the longest and densest, supporting early path dominance as a neurodevelopmental principle.	Brain-network development modeling and investigation of disease-related connectivity patterns.	Network-based conclusions depend on tractography quality and assumptions used in computational attack models.
[17]	Graph-in-Graph latent graph learning	Introduced GiG to learn interpretable latent relationships among graph-structured samples for biological and healthcare applications.	Protein classification, brain imaging analysis, and interpretable patient-population modeling.	Latent graph interpretation can be complex; performance depends on graph construction quality and task-specific data representation.

strong relevance to biomarker discovery and multimodal integration because they combine different biological and phenotypic data sources. Neuroimaging modeling demonstrates high diagnostic relevance, particularly in studies focused on ASD detection and brain activity analysis. However, the heatmap also shows that interpretability remains a relatively weaker dimension for several AI methods, especially deep generative and neuroimaging-based models. This indicates that future research should place greater emphasis on explainable AI methods to support clinical trust and real-world implementation. Figure 4 presents the most recurring limitations and challenges identified across the reviewed literature. Dataset size and diversity appear as major challenges, indicating that many AI-based models still require larger, more representative, and clinically diverse datasets to achieve reliable generalization. Model interpretability is another critical issue, as clinicians often need transparent explanations before adopting AI-driven diagnostic tools in practice. Clinical validation, computational complexity, bias, ethical governance, and multimodal harmonization are also important barriers. These challenges suggest that although AI and generative models have strong potential in neurodevelopmental disorder research, their practical application requires careful validation, ethical design, and robust testing across different populations and clinical environments. Figure 5 shows the temporal distribution of the reviewed studies according to publication year. The increase in recent publications, particularly in 2023 and 2024, reflects the rapid growth of AI-based research in neurodevelopmental disorder diagnosis and brain-health analysis. This trend suggests that advanced computational models, including graph neural networks, diffusion models, contrastive learning, and multimodal AI frameworks, are becoming increasingly important in biomedical research. The concentration of studies in recent years also indicates that this

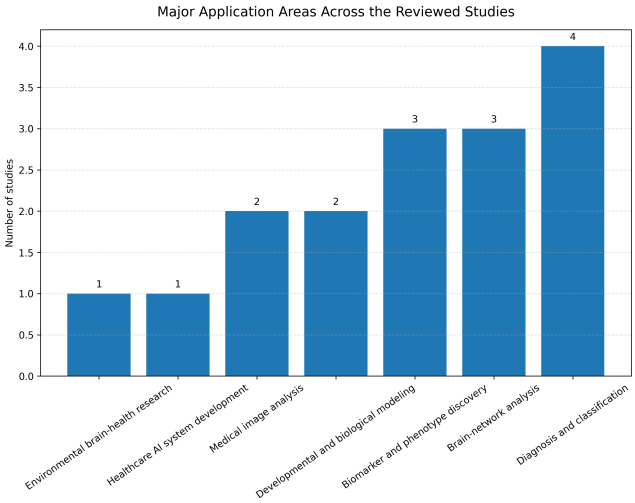

Figure 2. Major application areas represented in the reviewed AI and generative modeling studies.

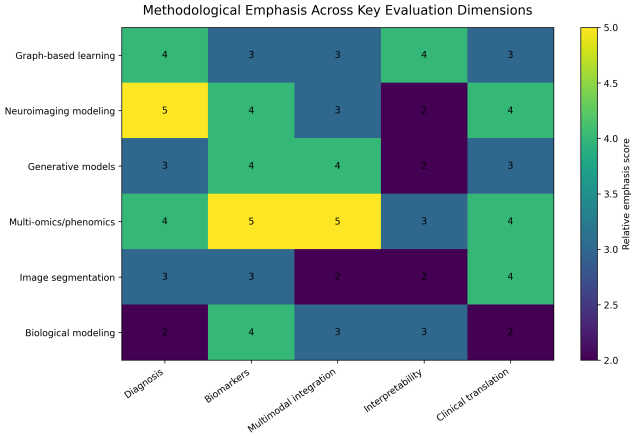

Figure 3. Heatmap-style comparison of methodological emphasis across major research directions.

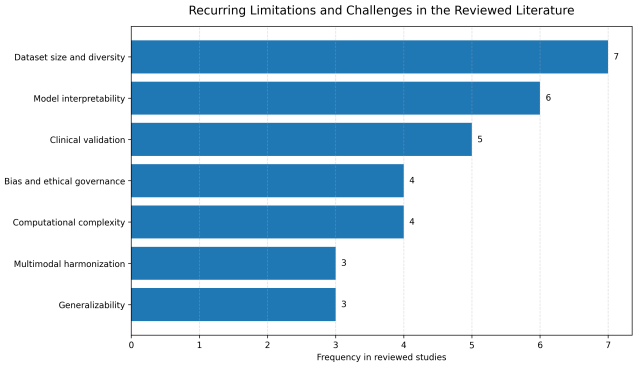

Figure 4. Recurring limitations and challenges reported across the reviewed literature.

field is still developing quickly, with many methods requiring further refinement, benchmarking, and clinical validation before they can be fully translated into routine healthcare practice.

3. CONCLUSION

The application of AI technologies, particularly generative models, has produced significant progress in neurodevelopmental research. NDDs, including ASD, ADHD, and ID, affect many individuals worldwide, and early identification is essential for improving clinical and developmental outcomes. GANs, VAEs, and diffusion models can enhance diagnosis,

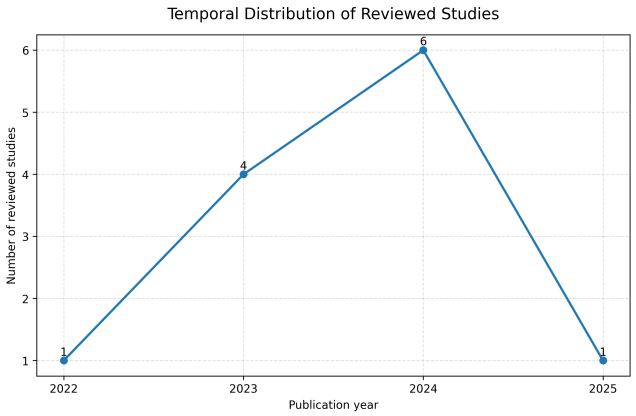

Figure 5. Temporal distribution of the reviewed studies according to publication year.

reduce the need for invasive procedures, and address limitations related to data scarcity. By integrating neuroimaging, behavioral, and multi-omics data, these models have the potential to transform the diagnosis and treatment of NDDs.

Nevertheless, several barriers must be addressed before AI can be widely implemented in clinical practice. These include interpretability, stability, dataset diversity, transparency, bias, and privacy. Addressing these challenges requires collaboration among engineers, clinicians, researchers, and ethicists. Such collaboration is necessary to establish reliable, fair, and ethically grounded AI systems in healthcare.

Future research should focus on multimodal and real-time diagnostic tools. These tools may combine neuroimaging, speech, behavioral, and biomolecular data to provide more comprehensive diagnoses of NDDs and other brain-related conditions. Collaboration among academic institutions, industry, and healthcare organizations will be necessary to support the translation of these innovations into clinical practice.

In conclusion, AI, especially generative models, has significant potential to revolutionize the early diagnosis and management of NDDs. These technologies can improve clinical outcomes, support individualized interventions, and enhance the quality of life for individuals with neurodevelopmental disorders. Continued interdisciplinary research is therefore essential for advancing this rapidly growing field.

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