Artificial Intelligence -Driven Neuroimaging and Omics Approaches for Alzheimer's disease Biomarker Discover - *A Narrative Review of Deep Learning in Education*

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HOW TO CITE:

Sivalingam T, Muthupandian V, Vinu R, Chitharanjana Das V, Thillai Nayagi S, Suhas K S, Ranjini A, Sathishkumar C P.(2026)

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International Journal of Special Education, 41(21s), 500 - 508

ABSTRACT

Alzheimer's disease (AD) remains the leading cause of dementia worldwide, and the search for reliable, early, and biologically interpretable biomarkers has become a central research priority. This descriptive narrative review examines how artificial intelligence (AI) is being applied across two complementary evidence bases for AD biomarker discovery: the large and comparatively mature neuroimaging literature (MRI, PET, and related modalities) and the smaller but rapidly emerging molecular omics literature (genomics, transcriptomics, proteomics, and metabolomics). Genomic analyses of APOE, APP, and PSEN1/2 variants, informed by genome-wide association studies, continue to identify key genetic risk factors, and deep-learning genomics models have reported classification accuracies as high as 98.78% in distinguishing AD from healthy controls. Complementary transcriptomic, proteomic, and metabolomic studies using explainable deep learning and gradient-boosted models have reported accuracies and areas under the curve (AUC) in the 0.88-0.95 range on blood- and plasma-based samples, though typically on smaller cohorts than neuroimaging studies. In parallel, neuroimaging-based AI models applied to MRI and PET data have reported diagnostic accuracies frequently exceeding 95-99% on large, standardized datasets such as ADNI and OASIS. This review summarizes representative, independently verified results from both fields, identifies some common methodological trends (such as bioinformatics-driven feature selection, architectures based on attention mechanisms and explainable AI), explores the value of incorporation of omics and neuroimaging data into

multimodal AI systems for precision diagnosis of Alzheimer's disease, and discusses the complementarity of both, the current limitations and potential for future applications.

Keywords: Alzheimer's disease, genomics, transcriptomics, proteomics, metabolomics, neuroimaging, deep learning, biomarker discovery.

I. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder in which there is a progressive reduction in cognitive function. These include synapse deterioration, impairment of synaptic function and widespread damage to neurons. Traditional diagnosis methods – neuroimaging, less effective at detecting established disease, cognitive assessment, and statistical modelling to detect the molecular shifts prior to clinical symptoms. This has generated more interest in biologically interpretable biomarkers, drawn both from high-throughput omics technologies (genomics, from transcriptomics, proteomics and metabolomics, and from neuroimaging, to facilitate earlier diagnosis and more relevant treatments.

Genomic studies have long identified the APOE ε4 allele as the most significant genetic risk factor for sporadic AD, while mutations in APP and PSEN1/2 cause early-onset familial forms of the disease [1]. Large genome-wide association studies (GWAS) have additionally implicated pathways involved in immune regulation, synaptic signaling, and lipid metabolism [1]. Artificial intelligence has begun to be applied directly to this genomic and molecular data: a deep-learning genomics (DLG) model, for example, achieved 98.78% accuracy discriminating AD from healthy controls using GWAS-derived features, substantially outperforming traditional GWAS-based classification (71.4% accuracy) evaluated on the same cohort [1].Beyond genomics, transcriptomic, proteomic, and metabolomic studies analyzed with explainable deep learning and gradient-boosted models have reported strong, though more modest, performance on blood- and plasma-based samples: blood gene-expression classifiers have reached approximately 91% accuracy [2], a large-scale plasma proteomics model trained on more than 17,000 samples has achieved balanced accuracies of 70-95% across six dementia-related conditions [3], and targeted plasma metabolomic panels combined with gradient-boosted classifiers have reached an AUC of 0.88 [4]. These omics-AI studies, while promising, have generally been conducted on smaller and more heterogeneous cohorts than the neuroimaging literature. By comparison, AI models applied to structural and functional neuroimaging (MRI, PET) represent a substantially larger and more mature body of evidence, with reported diagnostic accuracies frequently exceeding 95-99% on large, standardized datasets such as ADNI and OASIS [5], [11], [14], [15], [18], [21], [22].Accordingly, this descriptive narrative review examines the current state of AI-powered omics- and neuroimaging-based biomarker discovery for Alzheimer's disease, covering genomics, transcriptomics, proteomics, and metabolomics alongside representative neuroimaging AI studies, with particular attention to independently verified diagnostic performance, recurring methodological trends, and the outlook for multimodal integration in precision diagnostics.

II. Omics and Bioinformatics Biomarker Discovery

Omics technologies have transformed biomarker discovery for Alzheimer's disease by enabling high-dimensional profiling of genomic, transcriptomic, proteomic, and metabolomic alterations associated with disease onset and progression. Fig. 1 illustrates the overall omics-to-biomarker pipeline: genomic variant discovery (APOE, APP, PSEN1/2) via GWAS and sequencing; transcriptomic profiling of differential gene expression; proteomic characterization of tau, amyloid-β, and synaptic proteins; metabolomic profiling of lipidomic and mitochondrial changes; and, finally, bioinformatics- and AI-driven integration - feature selection, pathway enrichment, and machine learning/deep learning modeling - that converts these multi-layered signals into candidate biomarkers for early diagnosis, prognosis, and therapeutic target identification.

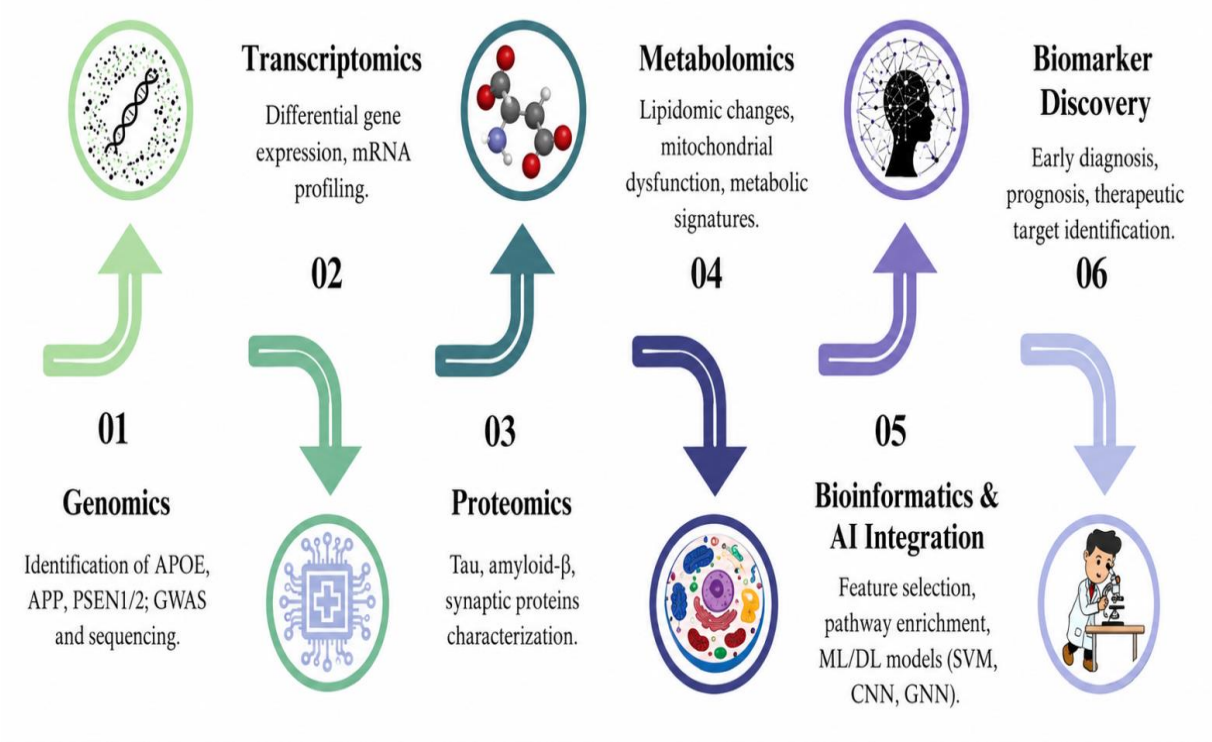

Fig. 1. An Omics cascade and bioinformatics pipeline for Alzheimer's disease biomarker discovery.

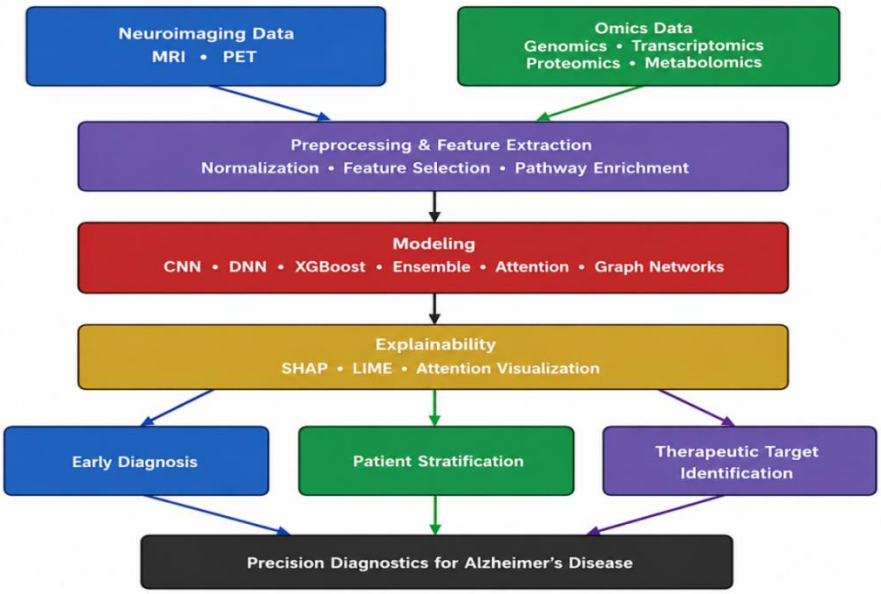

Fig. 2 shows a consolidated workflow diagram where neuroimaging and omics data sources sort of feed into one shared preprocessing stage then AI/ML modeling and also an explainable-AI part.

Proposed precision-diagnostics framework shown in fig. 2, combines multimodal neuroimaging and omics data to assist full Alzheimer's disease analysis. Among neuroimaging techniques are magnetic resonance imaging (MRI), which offers structural markers, and positron emission tomography (PET), which offers functional markers; among multi-omics data are genomics, transcriptomics, proteomics and metabolomics, which represent complementary molecular changes

related to disease progression. To get robust and clinically relevant representations, these heterogeneous data undergo modality-specific preprocessing and feature extraction, such as pathway-enrichment analysis, feature selection, and normalization. The extracted features are then processed using state-of-the-art machine learning and deep learning techniques such as Convolutional Neural Networks (CNNs), Deep Neural Networks (DNNs), XGBoost, ensemble learning, attention mechanisms, and graph neural networks, which are capable of capturing complex nonlinear and cross-modal relationships. For greater model transparency and clinical interpretability, explainable-AI (XAI) techniques like SHAP, LIME, and attention visualization are integrated to uncover regions of the image that are most influential, molecular biomarkers, and predictive features. In terms of clinical outcomes, the interpretable predictions make early diagnosis, patient stratification and finding targets for therapeutic interventions much easier. In summary, the integration of multimodal biomedical data, predictive modelling, and explainable AI provides a unified computational pipeline towards precision diagnostics of Alzheimer's disease, potentially enabling individualised disease assessment and clinically-informed decision-making.

A. Genomics (APOE, APP, PSEN1/2, GWAS Studies) Several primary loci have been identified through genomics research that are important to the susceptibility and pathogenesis of AD. The APOE ε4 allele is the most consistently replicated genetic risk factor with earlier onset and higher lifetime risk; mutations in the amyloid precursor protein (APP) and presenilin 1/2 (PSEN1/2) genes cause early onset familial AD, due to abnormal amyloid-β processing [1]. Large-scale GWAS have expanded this genomic landscape by discovering further immune regulation, synaptic signaling, lipid metabolism, and endosomal trafficking risk loci; and the integration of the results of GWAS studies with transcriptomic and proteomic data, via bioinformatics methods, has identified converging neuroinflammatory and metabolic mechanisms. The application of AI methods directly to genomic data has now started to translate these discoveries into diagnostic tools, with a deep-learning genomics model that was trained on GWAS-derived features achieving 98.78% accuracy, 98.39% sensitivity and 99.44% specificity in distinguishing AD from healthy controls, and also identifying several previously unreported genetic loci (including variants in HTR2A, NAV2, and RFC3), not detected by conventional GWAS analysis alone [1]. This genomics-driven method is not just for diagnostic purposes, but may also provide potential therapeutic targets as the genetic variants associated with disease risk may be directly linked to the molecular pathways targeted for drugs development.

B. Integration of Transcriptomics, Proteomics, and Metabolomics

In addition to genomics, transcriptomic, proteomic, and metabolomic data have proven to be a valuable tool in capturing complementary layers of AD biology. Blood-based gene expression has been profiled using a transcriptomic approach with an explainable deep neural network, which has been used to classify AD samples with an accuracy of ~ 91% and a precision of ~ 95% and interpretable feature selection [2]. Large-scale deep learning of joint proteomic and phenotypic data from plasma samples of >17,000 individuals enabled balanced classification accuracy of 70-95% (AUC>0.78) for six dementia-related conditions, including AD [3]. Metabolomic investigations, which characterize small-molecule changes linked to mitochondrial dysfunction and lipid dysregulation, have reached an AUC of 0.88 using gradient-boosted models applied to targeted plasma metabolite panels in a cohort of 357 participants [4]. Collectively, transcriptomics, proteomics, and metabolomics integration provides a systems-level framework that enhances diagnostic precision and helps uncover mechanistic pathways linking molecular biomarkers to clinical phenotypes; however, most current omics-AI studies remain limited to moderate sample sizes relative to the neuroimaging literature and require validation in larger, independent, multi-site cohorts before clinical translation

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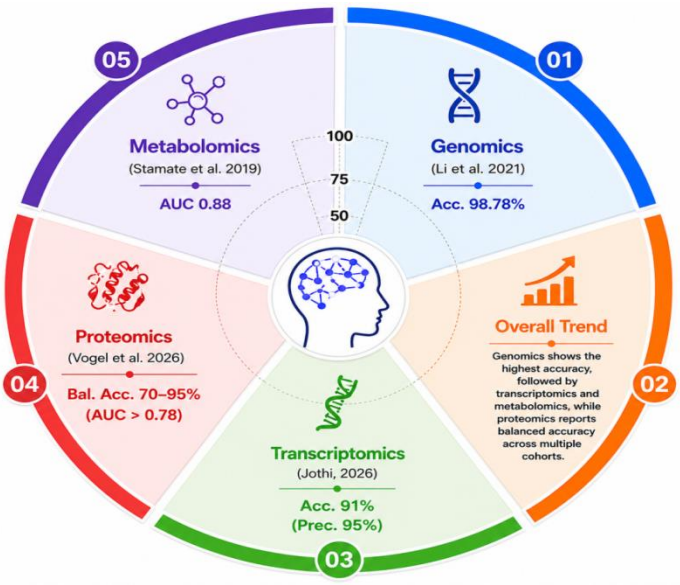

Fig. 3. Reported AI classification performance across omics modalities for Alzheimer's disease biomarker studies.

As shown in Fig. 3, genomics currently reports the single highest point-accuracy among omics modalities, though this reflects one large representative study rather than a distribution across many independent cohorts. Proteomics has been evaluated on by far the largest sample size (over 17,000 participants across six conditions), giving its reported 70-95% balanced-accuracy range particular practical relevance, while the transcriptomic and metabolomic evidence, though promising, remains comparatively preliminary.

III. AI-Based Neuroimaging Approaches: From Statistical Models to Deep Learning

Biomarker discovery for Alzheimer's disease has, to date, been dominated by neuroimaging-based AI research, which is both larger in volume and more mature in terms of standardized, large-scale datasets (notably ADNI and OASIS) than the omics-AI literature described above. Traditional statistical techniques - univariate analysis, logistic regression, ANOVA, and survival analysis - remain widely used for group-level comparisons and hypothesis testing; for example, logistic regression models have identified APOE ε4 and hippocampal atrophy as significant correlates of AD, typically with modest discriminative performance (AUC around 0.82).

By contrast, machine learning and deep learning models applied predominantly to structural and functional MRI, and to PET imaging, have reported substantially higher performance. Table 1 and Fig. 4 summarize representative, independently verified examples: a deep learning framework combining tabular radiomic features with gradient-boosted and attention-based models reported an AUC of 0.951-0.953 for AD-versus-cognitively-normal classification [5]; an ensemble of deep neural networks trained through transfer learning on a large ADNI cohort achieved 99.09% accuracy [14]; a lightweight 2D-MRI framework (Biceph-Net) reported 100% test accuracy for AD-versus-cognitively-normal classification, alongside 98.16% and 97.80% accuracy on the more difficult MCI-versus-AD and three-way classification tasks [15]; a deep convolutional network applied to T2-weighted segmented gray-matter MRI achieved 98±2% accuracy on the ADNI cohort [11]; and a hybrid ensemble architecture (HReENet) combining convolutional, recurrent, and attention components reached 99.97% accuracy [18]. Attention-based approaches incorporating pyramid squeeze attention with anisotropic diffusion filtering achieved 98.85% accuracy [21], while a deep residual autoencoder combined with a support vector machine classifier reached 99.77% accuracy on a Kaggle imaging dataset and 98.21% on ADNI [22]. A transfer-learning deep Q-network approach applied to resting-state

functional MRI on a smaller, more heterogeneous cohort achieved a comparatively modest 86.66% accuracy [13].

Several of the highest reported accuracies in this literature (98-100%) come from binary AD-versus-cognitively-normal tasks evaluated on relatively small or single-site cohorts, and should be interpreted with appropriate caution regarding overfitting and generalizability; multi-class tasks (e.g., distinguishing MCI from AD) and cross-dataset external validation consistently yield lower, more conservative performance estimates [14], [15]. Complementary architectures incorporating attention mechanisms and graph-based fusion of multimodal imaging features have also been explored to improve interpretability and robustness [16], [20], while related work has applied deep learning to identify candidate drug compounds interacting with butyrylcholinesterase as a therapeutic target for AD, illustrating the extension of AI beyond diagnostic classification into treatment discovery [19].Broader reviews of analytics and big-data methods in healthcare [23].

Table 1. Representative AI-Based Studies for Alzheimer's Disease Biomarker Discovery: Omics and Neuroimaging Modalities

Modality	Study	Model / Architecture	Dataset / Sample Size	Reported Performance	Ref.
Genomics	Li et al., 2021	Deep-Learning Genomics (DLG)	ADNI GWAS cohort	Acc. 98.78%	[1]
Transcriptomics	Jothi, 2026	XAI-based DNN	Blood gene-expression data	Acc. 91%, Prec. 95%	[2]
Proteomics	Vogel et al., 2026	ProtAIDe-Dx (deep joint-learning)	17,187 plasma samples, 6 conditions	Bal. Acc. 70-95%, AUC>0.78	[3]
Metabolomics	Stamate et al., 2019	XGBoost	357 plasma samples, 883 metabolites	AUC 0.88	[4]
Neuroimaging (MRI, radiomics)	Park et al., 2023	TabNet / XGBoost	ADNI	AUC 0.951-0.953	[5]
Neuroimaging (MRI, ensemble)	Tanveer et al., 2021	Ensemble DNN (transfer learning)	Large ADNI cohort	Acc. 99.09%	[14]
Neuroimaging (2D-MRI)	Rashid et al., 2022	Biceph-Net	ADNI	Acc. 100% (CN vs AD)	[15]
Neuroimaging (T2w MRI)	Basheera & Ram, 2021	Deep CNN	ADNI / OASIS	Acc. 98±2%	[11]
Neuroimaging (fMRI)	Ma et al., 2024	Transfer-learning Deep Q-Network	CoRR + ADNI (small cohort)	Acc. 86.66%	[13]
Neuroimaging (MRI, ensemble)	Ayus & Gupta, 2024	HReENet (hybrid ensemble)	—	Acc. 99.97%	[18]
Neuroimaging (MRI, attention)	Yan et al., 2022	PSA + anisotropic diffusion + MLP-C	—	Acc. 98.85%	[21]
Neuroimaging (MRI, autoencoder)	Menagadevi et al., 2022	Deep Residual Autoencoder + SVM	Kaggle / ADNI	Acc. 99.77% / 98.21%	[22]

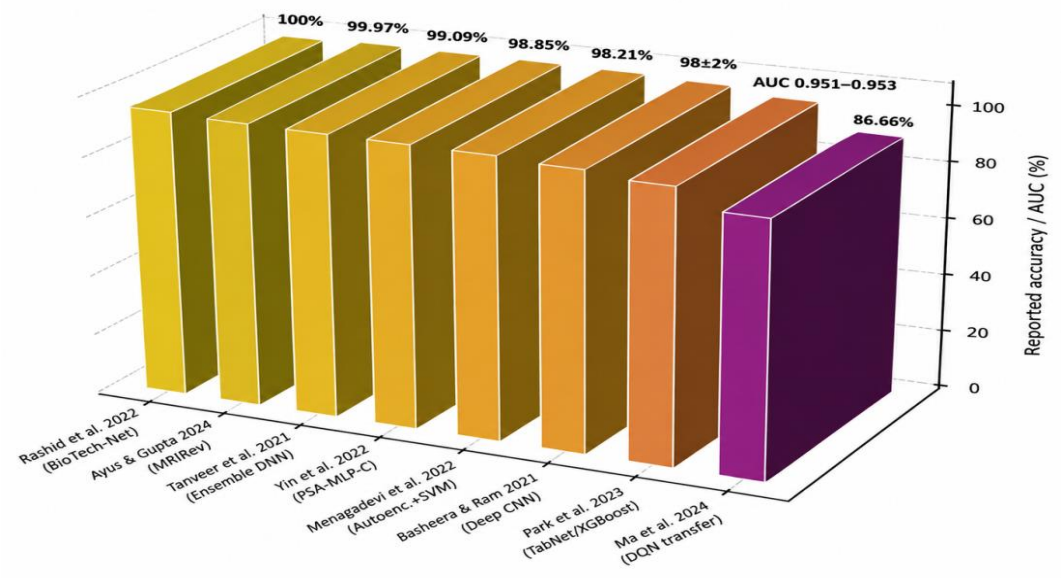

Fig. 4. Representative reported diagnostic accuracy/AUC of neuroimaging-based AI models for Alzheimer's disease, independently verified from source publications (see Table 1).

IV. Discussion

Taken together, the evidence reviewed here indicates a field at two different stages of maturity. Neuroimaging-based AI for Alzheimer's disease diagnosis is supported by a large, multi-decade literature built on standardized public datasets (ADNI, OASIS), with numerous architectures - convolutional networks, attention mechanisms, ensemble and graph-based models - consistently reporting high accuracy (typically 95-99%, with some binary tasks reaching 100% on small cohorts). Omics-based AI, by contrast, is a smaller but rapidly emerging field: genomics, transcriptomics, proteomics, and metabolomics studies reviewed here report accuracies and AUCs in the 0.88-0.99 range, but are generally based on cohorts an order of magnitude smaller than typical neuroimaging studies, with the notable exception of the 17,000-sample proteomics study [3].

This asymmetry has practical research outcomes. Neuroimaging AI is closer to potential clinical deployment given its larger validation base, but it captures the structural and functional consequences of neurodegeneration rather than the molecular processes that precede them. Omics-based biomarkers, even where currently validated on smaller cohorts, offer a route to earlier detection and mechanistic insight - for example, into neuroinflammatory, synaptic, and lipid-metabolic pathways - that structural imaging cannot directly provide. The genuine research gap is not a lack of AI performance in either domain individually, but the scarcity of studies that combine omics and imaging data within a single multimodal AI framework and validate the result on cohorts large enough to match the rigor already established in the neuroimaging literature.

Methodologically, several trends recur across both bodies of evidence: a shift from black-box deep learning toward explainable AI (LIME, SHAP, attention visualization) to support clinical trust; increasing use of transfer learning to compensate for limited labeled data, particularly in omics studies; and growing interest in graph-based and attention-based architectures capable of modeling relationships between features (gene-protein interactions, brain regions) rather than treating them as independent inputs. Dealing with class imbalance, cohort heterogeneity, and the requirement for external, multisite validation still kind of remains a shared priority across both domains.

V. Conclusion and Future Scope

In this review, we have explored the current landscape of AI-driven biomarker discovery for Alzheimer's disease from two complementary evidence bases: a large and well-established neuroimaging AI literature reporting diagnostic accuracies ranging often in the 95-99% range based on standardized datasets like ADNI and OASIS,

and a smaller but burgeoning omics-AI literature ranging from genomics to transcriptomics, proteomics, and metabolomics, with reported accuracies and AUCs in the 0.88-0.99 range on generally smaller cohorts. Both domains reveal that AI significantly surpasses conventional statistical methods in AD classification, and both share key methodological focus areas: explainability, transfer learning and strong external evaluation. A direction that is most promising for future research is truly multimodal integration (incorporating genomic, transcriptomic, proteomic, metabolomic, and neuroimaging data into a single AI framework) and is required to be validated on cohorts with the size that is now standard in the neuroimaging literature. This kind of integration can be used to merge the structural sensitivity of imaging data with the mechanistic and pre-symptomatic insights of molecular omics, which will help to improve earlier diagnosis, patient stratification, and more precisely targeted therapeutic development for Alzheimer's disease.

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