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**Research Article**

# APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN THE DIAGNOSIS OF NEURODEGENERATIVE CHANGES IN ALZHEIMER'S DISEASE

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**Abstract**

Neurodegenerative diseases, particularly Alzheimer's disease, remain one of the greatest challenges of modern medicine due to late clinical manifestation and lack of effective curative therapies. Traditional diagnostic methods, including neuropsychological tests and standard neuroimaging, are limited in detecting subtle early changes. Artificial intelligence, especially machine learning and deep learning, has demonstrated significant potential in improving early diagnosis, classification, and prediction of disease progression. Convolutional neural networks applied to MRI and PET data enable automated feature extraction and accurate differentiation between Alzheimer's disease, mild cognitive impairment, and healthy controls. Integrative multimodal approaches that combine imaging, cerebrospinal fluid biomarkers provide higher diagnostic sensitivity and specificity compared to unimodal analyses. Despite the advantages of AI in efficiency, scalability, and early detection, challenges remain regarding generalisability, interpretability, cost, and clinical implementation. This review highlights the current applications of AI in Alzheimer's disease diagnostics, contrasts them with classical methods, and discusses methodological limitations, ethical aspects, and perspectives for future integration into clinical practice.

**Keywords:** Alzheimer's disease, Artificial intelligence, Machine learning, Deep learning, Convolutional neural networks, Neuroimaging, Biomarkers, Predictive models

## INTRODUCTION

Neurodegenerative disorders, including Alzheimer's disease (AD), Parkinson's disease (PD), and other dementias, represent a major global health burden due to aging populations and the lack of curative treatments [1]. These conditions are characterized by progressive neuronal loss, cognitive decline, and functional impairment, often becoming clinically evident only after substantial neurobiological damage has occurred [2]. Early diagnosis remains one of the greatest challenges, as traditional clinical assessments and routine imaging modalities such as structural MRI or PET can typically detect neurodegeneration only at advanced stages [3]. Artificial intelligence (AI), particularly machine learning and deep learning algorithms, has emerged as a transformative tool capable of analyzing high-dimensional imaging data and identifying subtle disease-related features invisible to human observers [4].AI-based approaches have achieved strong performance in classifying Alzheimer's disease and in predicting progression from mild cognitive impairment, especially when multimodal imaging data are combined [2,5].Such techniques not only improve diagnostic accuracy but also enable earlier detection, which is crucial for timely therapeutic interventions and clinical trial enrollment [3,5].
Moreover, AI facilitates the rapid processing of large-scale neuroimaging datasets, reducing diagnostic delays and alleviating healthcare system burdens [4,6].Publicly accessible initiatives such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) provide standardized imaging datasets that support robust AI model training and validation across diverse populations, increasing generalizability and clinical applicability [7].

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Given the critical diagnostic challenges in neurodegeneration and the demonstrated potential of AI in neuroimaging, a comprehensive review of current applications, methodological strengths, limitations, and future directions is essential [1,4,5].

### Convolutional neural networks (CNN) for MRI analysis

CNNs have become a fundamental class of deep learning models in medical imaging because their layered architecture closely mirrors the hierarchical structure of information present in brain MRI images [6]. In neurodegeneration, CNN models trained on T1-weighted structural images are widely used for AD/MCI/HC classification and conversion prediction, but the literature highlights problems with method comparability and the risk of validation errors, which requires rigorous evaluation protocols [8]. In practice, 2D, 2.5D (triplanar) and 3D variants are used; 3D approaches make better use of the spatial context of the entire brain, although they are more computationally expensive [9]. Triplanar models combine predictions from networks trained in the axial, sagittal and frontal planes, achieving high effectiveness in segmenting changes relevant to vascular ageing and neurodegeneration, such as white matter hyperintensities [10]. Early work using 3D-CNNs (e.g., VGG/ResNet modifications) showed that it is possible to classify AD/MCI/HC without manual feature design, based solely on whole-brain T1-MRI [11]. Subsequent multicentre analyses with external validation indicated that 3D-CNNs can match classical methods (e.g. SVM), but performance declines when transferred to new cohorts and protocols, highlighting the need for cross-validation [12].

The effectiveness of CNNs depends significantly on pre-processing (including field inhomogeneity correction, intensity normalisation, registration and brain extraction), so the pipeline should be defined and reproducible [13]. Validation must be conducted at the subject level and data leakage (e.g.,

leakage between 2D sections of the same patient) must be strictly avoided, as this distorts the results and hinders comparisons between studies [8]. To increase clinical transparency, explainability methods such as Grad-CAM are commonly used to visualise the areas of the brain that most influence the model's decision [14]. Recent work shows that Grad-CAM maps generated for AD classification on MRI often correspond to areas of atrophy and support the clinical interpretation of predictions [15].In Alzheimer's disease research, independent saliency maps and relevance analyses repeatedly emphasise the hippocampus and temporal structures, which is consistent with the neurobiology of the disease [16]. Differences between scanners and protocols cause "domain shift," so harmonisation of multi-centre MRI data is crucial for model generalisation and reliable evaluation [17]. New methods, such as DeepComBat, combine statistical approaches and deep learning, effectively reducing the site/scanner effect while preserving the biological signal in neuroimaging features [18].

## Artificial intelligence in the diagnosis of Alzheimer's disease

Alzheimer's disease (AD) is the most common cause of dementia and one of the greatest public health challenges in ageing populations [19]. It is characterised by progressive loss of neurons and synapses, leading to cognitive deficits, memory impairment and irreversible loss of independence [20]. Despite significant advances in biomarker research, early and accurate diagnosis remains difficult, as classical clinical and imaging methods usually detect changes only at a moderate or advanced stage [21].

## Early diagnosis supported by AI

Artificial intelligence (AI), including machine learning (ML) and deep learning (DL), is revolutionising the approach to AD diagnosis by enabling the analysis of large-scale, multidimensional biomarker, imaging and clinical data sets [22]. Early applications included ML algorithms such as support vector machines (SVM), which allowed patients to be classified based on structural MRI images with high accuracy [23]. For example, Klöppel et al. demonstrated that SVM algorithms can distinguish individuals with AD from healthy controls (HC) with accuracy comparable to that of expert radiologists [24]. The development of deep learning has led to the use of convolutional neural networks (CNNs) and autoencoders for the analysis of whole-brain MRI and PET data, which has significantly increased the effectiveness of classification and prediction [25]. Research by Basai et al. demonstrated that single T1 MRI scans analysed in a deep neural network could distinguish between AD, MCI and healthy individuals with high accuracy, without the need for manual feature extraction [26]. Similarly, Wen et al. indicated in a systematic review that CNNs outperform classical ML algorithms in the diagnosis of AD, especially in tasks involving the prediction of conversion from MCI to AD [8].

## Multimodal and integrative models in the diagnosis of Alzheimer's disease

Models based on multiple data modalities, integrating brain imaging, biochemical biomarkers and genetic information to obtain a more accurate and early diagnosis, are playing an increasingly important role in the diagnosis of Alzheimer's disease (AD) [27]. Numerous studies indicate that different types of biomarkers provide complementary information about AD disease processes, e.g. structural magnetic resonance imaging (MRI) reflects neuronal loss, positron emission tomography (PET) reveals metabolic disorders or amyloid deposition, and fluid biomarkers directly reflect biochemical pathologies [28]. Combining these multiple data sources within artificial intelligence systems allows the limitations of individual markers to be overcome – studies have shown that models that simultaneously consider MRI, PET, fluid biomarkers (e.g., amyloid-β, tau in cerebrospinal fluid) and genetic information (e.g., the presence of the APOE ε4 allele) achieve greater diagnostic sensitivity and specificity compared to unimodal models [28]. A classic example of this is the Alzheimer's Disease Neuroimaging Initiative (ADNI), which aimed to collect correlated MRI, PET, CSF biomarker and genotype data to improve methods for detecting MCI and early AD. This approach has enabled the creation of numerous integrative models validated on a large cohort [29]. Early studies have already demonstrated clear benefits of data fusion: Zhang et al. combined MRI, FDG-PET and CSF biomarkers from the ADNI database, achieving 93% accuracy in classifying AD vs. healthy controls, while the best single modality yielded ~86% [30]. Similarly, for distinguishing MCI from healthy subjects, ~76% vs 72% was achieved for the multimodal model vs the best single biomarker, respectively [30]. These results have been confirmed in many subsequent studies - combining MRI, PET and fluid biomarkers consistently outperforms single-modality approaches [28,31]. A meta-analysis of the results of such studies clearly showed that multimodal classification methods significantly improve the diagnostic accuracy of AD compared to approaches based on a single type of data [27,31].

Genetic data are an important component of integrative models, with *APOE ε4* being of particular significance. The presence of the APOE4 allele, the strongest genetic risk factor for AD, is sometimes included as a feature in AI models, which further increases their predictive power [28]. For example, it has been shown that among people with MCI, the ε4 allele correlates significantly with faster conversion to dementia and including APOE4 status in a multimodal model allows for better identification of converters than using imaging alone [28]. In one study comparing MCI patients, the APOE4 genotype was found to be the most effective single predictor of progression, but only a model combining APOE with MRI, PET and CSF achieved the highest diagnostic accuracy, surpassing all single models [28]. These results confirm the added value of genetic information in integrative models, especially in the context of predicting the further course of the disease.

Deep learning has played a key role in the development of multimodal models, enabling the automatic extraction of complex patterns from different types of data and their effective fusion [27]. Unlike classical methods, which often relied on manual feature extraction from each type of biomarker and their simple combination (so-called *early fusion* through feature concatenation), deep neural networks are capable of learning a common multimodal representation, extracting hidden relationships between modalities. For example, Suk et al. used a Deep Boltzmann Machine to combine MRI and PET images, achieving ~95% accuracy in distinguishing AD from healthy subjects [31]. In the latest approaches, e.g. in the model proposed by Zhang et al., a

*cross-modal attention* mechanism was used, which allows the network to learn interactions between modalities (sMRI, FDG-PET, CSF) and strengthen the relationships between them, resulting in better use of their diagnostic complementarity [32]. Multimodality contributes not only to better classification of the patient's condition "here and now", but also to better prediction of the course of the disease over time. Predicting which patients with mild cognitive impairment (MCI) will develop AD-type dementia and which will remain stable is a critical issue, and here too, integrative approaches outperform single biomarkers [29,33]. The simultaneous inclusion of markers of neurodegeneration (MRI), amyloid/tau pathology (PET or CSF) and risk factors (APOE4, cognitive tests) allows for a more complete picture of the disease process, increasing the reliability of predictions [33]. For example, Lee et al. used a deep model integrating MRI scans, serial CSF biomarker measurements and cognitive test results simultaneously – they achieved ~81% accuracy in predicting conversion from MCI to AD, while a similar model based on a single type of data achieved ~75% [34]. Importantly, the multimodal approach improves not only overall accuracy but also the sensitivity of detecting future conversions (capturing more actual future dementia patients) without reducing specificity [33,34]. The examples presented clearly show that the fusion of multimodal data using artificial intelligence algorithms leads to a marked improvement in both the differential diagnosis of AD and the prediction of disease progression. The multimodal approach allows for a more comprehensive assessment of patients with cognitive impairment, which translates into increased accuracy in the diagnosis of AD and better prediction of its course, paving the way for earlier therapeutic intervention in those at highest risk. Each study cited here confirms that combining data from different biomedical domains is key to further improving diagnostic tools for Alzheimer's disease [28,31,34].

## Discussion – comparison of diagnostic approaches – classical methods vs AI

### Diagnostic accuracy and progression prediction

Traditional diagnosis of Alzheimer's disease (AD) is based on clinical assessment and neuropsychological tests, which allow for the identification of probable AD among patients with dementia with approximately 88% diagnostic accuracy [35]. Standard clinical criteria are highly sensitive (~98%) but moderately specific (approx. 69%) relative to the neuropathological gold standard [35]. Classic MRI, CT and PET analyses are also commonly used to detect changes typical of AD, but their interpretation requires an experienced specialist and may overlook subtle early changes [36]. Artificial intelligence (AI)-based methods, both classical machine learning and deep neural networks, have been shown in studies to be more effective in distinguishing AD. For example, deep learning models analysing MRI can identify early AD with over 90% accuracy by analysing the size of the areas of the brain responsible for memory, surpassing traditional visual assessment [37].

Similarly, AI algorithms analysing simple biomarkers, e.g. the level of d-glutamate responsible for memory and mental performance, detected early AD changes with over 85% accuracy [37]. Importantly, advanced AI models not only classify disease status, but are increasingly able to predict progression, e.g., the conversion of mild cognitive impairment (MCI) to Alzheimer's dementia. Using baseline imaging and clinical data, learning algorithms can achieve ~80% accuracy in predicting which patients with MCI will develop AD dementia over the next few years [38]. In comparison, in classical clinical practice, the prediction of progression is based mainly on risk factors (e.g., the presence of APOEε4, the severity of cognitive deficits) and is more probabilistic than individual. Studies indicate that AI models (e.g., recurrent neural networks) can detect patterns in sequences of cognitive test results and MRI images, achieving an AUC of approximately 0.9 in predicting the conversion of MCI to AD [39].

### Interpretability of results

A significant limitation of advanced AI models is their limited interpretability compared to classical methods. The result of a neuropsychological test or an MRI image evaluated by a radiologist is relatively transparent, e.g. a low score on the clock test indicates executive function impairment, and visible hippocampal atrophy explains memory problems. In contrast, deep learning algorithm decisions are often a "black box" – it is difficult to explain which data features determined the classification result. The inability to reliably explain the model's decisions raises mistrust among clinicians and hinders the integration of AI into practice [40]. In response to these concerns, *XAI* (explainable AI) is being developed, e.g. feature importance assessment methods (SHAP, LIME) or activation maps for images, but the interpretability of deep models remains limited [40,41]. It therefore seems that the development of "white box" ML algorithms, e.g. using simpler, understandable models or hybrid approaches combining domain knowledge with machine learning, will be crucial for clinical acceptance. Until AI predictions are transparent and consistent with medical knowledge, their usefulness will remain limited[41].

### Cost and availability

Traditional diagnostic methods vary in terms of cost and availability. Basic cognitive tests are inexpensive and do not require advanced equipment – they are conducted by a doctor or psychologist in an office, which makes them widely available. However, more specialised procedures, such as MRI or cerebrospinal fluid (CSF) testing, generate significant costs and are not always available outside academic centres. PET scans (e.g. using amyloid radiotracers) are very expensive and limited to specialisedcentres, and lumbar punctures to determine CSF biomarkers are sometimes rejected by patients. AI methods can partially reduce the cost barrier to AD diagnosis. Firstly, SI allows the use of cheaper tests as an alternative, e.g. analysis of patterns in blood data or cognitive tests by an algorithm can replace more expensive and invasive procedures such as PET or PMR [37]. For example, it has been shown that AI models can use blood metabolic profiles to identify people with early AD with high sensitivity, which may reduce the need for more expensive biomarker confirmation [37,41].

Secondly, AI increases the efficiency of available resources. Automatic analysis of hundreds of MRI scans per day can relieve radiologists, shortening queues and reducing healthcare costs [36]. Nevertheless, it should be emphasised that training AI models initially requires significant investment (computing equipment, data storage and annotation) and data science

specialists. Implementing such a system in a hospital involves investment in IT infrastructure and staff training. From the perspective of a single patient, the use of an algorithm (e.g. to analyse a single MRI) generates a minimal unit cost; the largest expenses are still the MRI or PET scan itself, which remain necessary if the AI is based on them. It is worth noting that the availability of AI-based methods also depends on access to digital data – facilities without PACS systems or digitised results will find it difficult to implement such solutions. Currently, traditional methods are almost universally available (every neurologist has cognitive tests at their disposal), while AI tools are only just emerging in pilot projects. Another barrier is the limited access to dementia diagnosis specialists on a global scale. Many countries lack neuropsychologists and geriatricians, so diagnosticians rely on simplified screening tests. In such conditions, simple, inexpensive AI tools (e.g., cognitive testing applications or cloud-based MRI image analysis) could increase the availability of diagnostics, provided that they are properly validated [42].

**Complexity of implementation and inter-cohort validation**

The introduction of AI methods into routine practice poses technical and scientific challenges. Machine-learned models are usually trained and tested on specific data sets (e.g. ADNI), which creates the risk of limited generalisability of results. Inter-cohort validation is absolutely necessary to confirm that the algorithm remains highly effective in different patient populations, with different imaging protocols or in other centres [40]. Unfortunately, many publications presenting high AI accuracy for AD do not test the model on independent external data, hence frequent concerns that the result is "over fitted" to the source data and will deteriorate in another hospital. Validation studies between different cohorts (e.g., testing an algorithm trained on ADNI on data from another country) are necessary, as well as prospective validation in real-world clinical settings. The complexity of implementation also concerns the integration of the AI system into the existing workflow. It is necessary to ensure the secure flow of data (images, test results) to the AI module, comply with data protection regulations (GDPR/HIPAA), and include the algorithm's result in the patient's documentation in an understandable way. Another challenge is acceptance by the medical community. There is resistance to entrusting some diagnostic decisions to a machine, especially if its recommendations are not transparent [36].

Doctors are also concerned about legal liability – it is unclear who is responsible for a possible misdiagnosis proposed by AI. Added to this are the potential biases of algorithms. If the model has been trained on an incomplete population, it may perform worse, for example, in people with different educational backgrounds or from different ethnic groups. All these issues make the implementation of AI much more complicated than the implementation of a new clinical scale. However, it is worth noting that as evidence of the effectiveness of AI emerges, it is proposed that these barriers be gradually overcome. The literature emphasises that if AI technology demonstrates a significant improvement in patient outcomes, then from an ethical point of view, the healthcare system should adapt it despite the initial difficulties. This is why further research into the generalisation and standardisation of algorithms and the development of guidelines regulating their use are so important.

**Clinical utility**

The ultimate test for any diagnostic method is its impact on patient care. Classic approaches are well established in practice: a neuropsychologist can not only diagnose dementia on the basis of tests, but also assess the cognitive profile (e.g. differentiating AD from front temporal dementia), while a neuroradiologist can indicate the probable aetiology of the changes on the basis of an MRI scan. However, AD diagnosis can be time-consuming and typically requires multiple visits and costly tests before it can be confirmed (e.g., MRI, PMR/PET assessment for amyloid/tau). AI tools can increase the clinical utility of AD diagnosis in several ways. Models that detect subtle neurodegenerative changes can signal the risk of AD at a very early stage, before the full clinical criteria are met [37]. This is particularly important in the era of AD-delaying therapies, which require early detection of changes and confirmation of amyloid aetiology. It also happens that the classical diagnostic approach has difficulty predicting the rate of progression in a particular patient, while models trained on longitudinal data can predict the dynamics of cognitive decline or the time to onset of dementia [39]. This can help in planning care and interventions (e.g., earlier initiation of cognitive rehabilitation for individuals at high risk of rapid decline). AI can support a clinician's decisions and serve as a second opinion by comparing a patient's data to thousands of other cases. For example, work on a multimodal model differentiating types of dementia has shown that combining clinician assessment and AI increases diagnostic accuracy compared to clinician assessment alone [42]. This suggests complementarity the algorithm can capture patterns missed by humans, and the clinician can verify their reliability in the clinical context. Nevertheless, the current clinical utility of AI models is limited. There is a lack of approved AI systems in AD diagnostic guidelines, and studies to date have focused primarily on effectiveness metrics, with less emphasis on assessing the impact on therapeutic decisions or patients' quality of life [40]. There is also a danger that the very high results achieved by AI in publications may not translate into real practice, e.g. a model with >90% accuracy in distinguishing AD vs. healthy individuals may prove less useful in more difficult clinical scenarios, such as differentiating AD from other dementias or mixed conditions.

In summary, AI-based approaches offer a promising complement to classical AD diagnostic methods, especially in terms of increasing diagnostic accuracy and predictive capabilities. However, their implementation requires further research to confirm their reliability in different populations, ensure interpretability, and gain acceptance from the medical community. It is crucial to demonstrate that the use of AI translates into a better prognosis for patients – if so, these tools may eventually become a standard part of AD diagnostics, coexisting with classical methods for optimal patient care.

**List of abbreviations**

AD - Alzheimer’s Disease
PD - Parkinson’s Disease
AI - Artificial Intelligence
ML - Machine Learning
DL - Deep Learning
MRI - Magnetic Resonance Imaging
PET - Positron Emission Tomography
ADNI - Alzheimer’s Disease Neuroimaging Initiative

CNN - Convolutional Neural Network
MCI - Mild Cognitive Impairment
HC - Healthy Controls
SVM - Support Vector Machine
CSF - Cerebrospinal Fluid
FDG-PET - Fluorodeoxyglucose Positron Emission Tomography
APOE ε4 - Apolipoprotein E epsilon 4
Grad-CAM - Gradient-weighted Class Activation Mapping
PMR - Płynmózgowo-rdzeniowy
CT - Computed Tomography
XAI - Explainable Artificial Intelligence
SHAP - SHapley Additive exPlanations
LIME - Local Interpretable Model-agnostic Explanations

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