THE ROLE OF ARTIFICIAL INTELLIGENCE IN ALZHEIMER'S DISEASE DETECTION: A DIGITAL TRANSFORMATION OF MEMORY LANE

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ABSTRACT

Alzheimer's disease (AD) is a prevalent neurological disorder with a significant global impact. Physicians conventionally use standard methods to diagnose AD, primarily relying on clinical assessments and professional judgment, along with a patient's medical history, to identify early symptoms or diagnose present AD. AD diagnostics have been strengthened with technological advances over time, such as neuroimaging and biomarker analysis. However, despite their advantages, these techniques face limitations in processing extensive radiological brain data. Artificial Intelligence (AI) offers unparalleled potential for early and precise diagnosis of Alzheimer's. Firstly, conventional methods for early AD detection are investigated, concentrating on their accessibility. Secondly, this review highlights novel AI-driven approaches that leverage machine learning models, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs), for diagnostic purposes. This review highlights the potential of these tools in transforming Alzheimer's early detection on a larger scale.

INTRODUCTION

By 2050, Alzheimer's disease (AD) cases are projected to reach 152 million globally (Breijyeh and Karaman, 2020). AD, the most prevalent form of dementia, is a neurodegenerative disorder causing progressive cognitive impairments and neuronal death. It is distinguished by amyloid-beta (Aβ) protein accumulation and neurofibrillary tangles in the brain (Nelson et al., 2009, p.774). Criteria have been devised to establish AD, including dementia, memory loss, impeded daily functioning, impaired language (aphasia), dysfunctional motor skills (apraxia), and loss of sight (agnosia) (Breijyeh and Karaman, 2020). In these cases, AD is probable if other neurological disorders can be ruled out. These benchmarks have become more specific as indicated by two clinical standards: (1) the presence of the protein amyloid detected by positron emission tomography (PET) and cerebrospinal fluid (CSF) scans, and (2) the detection of distinct protein markers of neuronal injury, including CSF tau, fluorodeoxyglucose (FDG) for metabolic tasks, and magnetic resonance imaging (MRI) tests for atrophy evaluations (McKhann et al., 2011, p.266).

Artificial Intelligence (AI) in neurology promises to enhance AD diagnosis and treatment timelines. AI is a system designed to perform tasks and develop solutions that address practical human needs. Machine learning (ML), a branch of AI, employs algorithms to analyse large datasets without explicit input (Cabrera-León et al., 2024, p.800). Artificial neural networks (ANN), a subset of machine learning, are a 'computational intelligence' algorithm that simulates neural pathways (Cabrera-León et al., 2024, p.800). This method is increasingly used to diagnose AD.

Early AD diagnoses enable preventative treatment to slow disease progression. However, current methods lack risk factor screening. Since cognitive deterioration is often overlooked as part of aging, individuals are typically diagnosed with advanced stages of AD (Angelucci et al., 2024). AI is emerging as a valuable tool for AD diagnosis and treatment, addressing the growing case numbers and future projections. ML databases can be trained to analyse demographic data including age, sex, and lifestyle factors to determine if an individual is at risk for AD. The technology can further analyse large medical datasets, including brain images, to identify AD in preliminary phases. Specifically, AI can scrutinise cerebral scans for structural and functional irregularities in distinct brain regions to differentiate the brain patterns between healthy individuals, AD patients, and other neurodegenerative disorders (Angelucci et al., 2024). This review explores conventional AD diagnostic techniques, demonstrating their limitations and ineffectuality. Subsequently, an exploration of the scope and sustainability of AI-based tools to diagnose AD is considered.

CONVENTIONAL METHOD FOR AD DIAGNOSIS

Before reviewing the sustainability of AI-based tools, it is necessary to consider the scope of current diagnostic tools that are contemporarily utilised. While early Alzheimer's diagnoses are clinically less accurate, early treatment is highly effective.

Therefore, research to find the most accurate tool to detect early-onset AD is a priority (Cabrera-León et al., 2024). Alzheimer's disease biomarkers, biological identifiers, distinguish healthy individuals from probable AD patients. There are no completely accurate biomarkers to diagnose AD. Only a postmortem autopsy or biopsy can provide a definitive confirmation of AD. However, researchers have established biomarkers whose presence is detected by diagnostic techniques to support an AD diagnosis or eliminate other neurodegenerative causes of the disease. As seen in Figure 1, the biomarkers are expressed with progressive brain phase development, from healthy brain scans to mild cognitive impairment (MCI) to AD (Cabrera-León et al., 2024, p.794)

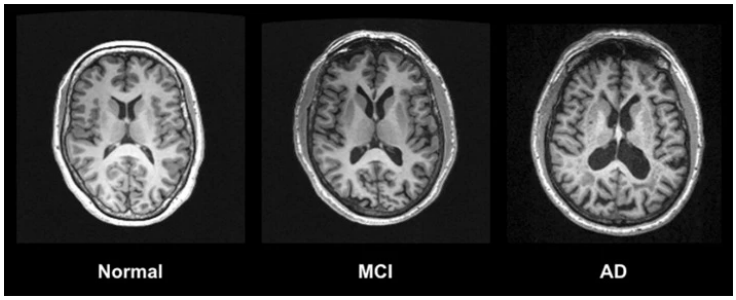

Figure 1: MRI scans of a brain (Chandra et al., 2019, p.1293-1302). Cross-section MRI scans show a progression from 'normal', to 'mild cognitive impairment (MCI)', to 'Alzheimer's disease (AD)' phases of the brain. Within MCI, brains can be considered 'early MCI' or 'late MCI'. There is progressive grey matter loss (appearing as the dark grey perimeter of the grooves) and increased white matter hyperintensities (visibly seen as increasing white spots) as the brain develops AD. Intermediate levels are found in the MCI brain scan.

Current methods include neuropsychological tests assessing daily functioning, cognitive abilities, and routine behavior to detect AD. Non-specialists can administer this inexpensive method. However, these tests often fail to consider confounding variables, such as cultural and socioeconomic differences, varying baseline cognitive levels, and a lack of sensitivity to early-stage symptoms of AD (Zamrini et al., 2004, p.687). A lumbar puncture test is another tool used to obtain cerebrospinal fluid (CSF) invasively, a biological fluid in the brain and spinal cord, to analyse protein molecular markers (Cabrera-León et al., 2024, p.799). Specific CSF biomarkers include accumulated amyloid beta peptide 42 (Aβ42), Aβ42:Aβ40 ratio, apolipoprotein E4 (APoE4), and tau concentrations in the early phases of AD. Though promising, obtaining CSF biomarkers is highly invasive. Additionally, the lumbar puncture may cause radiating pain, long-term post-puncture headaches, and associated psychological stress/fear. Finally, the test's cost and accessibility limit its utility (Vrahatis et al., 2023).

Another method to diagnose early-onset AD uses biosensors for biofluid detection, which convert biological symptoms into measurable factors. Biosensors are specific for Aβ42 amyloid at varying concentrations (Vrahatis et al., 2023). Biomarker-based techniques consist of mass spectrometry (MS), magnetic resonance imaging (MRI), immunohistochemistry (IHC), enzyme-linked immunosorbent assay (ELISA), computed tomography (CT), and positron emission tomography (PET). MRI and PET imaging techniques are preferred for early AD detection due to being non-invasive (Shui et al., 2018, p.14). However, they are limited by high costs, insensitivity to calcium buildups, inconsistent antibody reactivity resulting in biased interpretation, time-consuming processes that induce false positives, and low spatial resolution (Shui et al., 2018, p.15). Considering these limitations, it is paramount to evaluate more accurate and less invasive methods for early AD detection methods.

MACHINE LEARNING TECHNIQUES

AI serves as a valuable supplemental diagnostic tool because of its ability to process large multimodal datasets. Datasets such as the Alzheimer's Disease Neuroimage Initiative (ADNI) can be used to validate AD biomarkers. Additionally, the Open Access Series of Imaging Studies (OASIS) shares neuroimaging data to foster accessibility (Khojaste-Sarakhsi et al., 2022).

As depicted in Figure 2, ML mechanisms are divided into subcategories. Supervised learning (SL) contains trained AI systems using pre-labeled data (outcome/diagnosis information) such as neuroimaging. The databases determine the common characteristics predictive of the pre-labeled outcome, such as healthy brain or AD diagnoses. Unsupervised learning (UL) utilises unlabeled information to group the data by shared features or anomalies. Deep learning (DL) uses SL and UL to manipulate data from ANNs that mechanically appraise large raw datasets without external input. Reinforcement learning (RL) employs AI-driven algorithms that learn through trial and error, applying feedback quantified as negative or positive through punishments or rewards, to maximise reward signals (Hui et al., 2023, p.40).

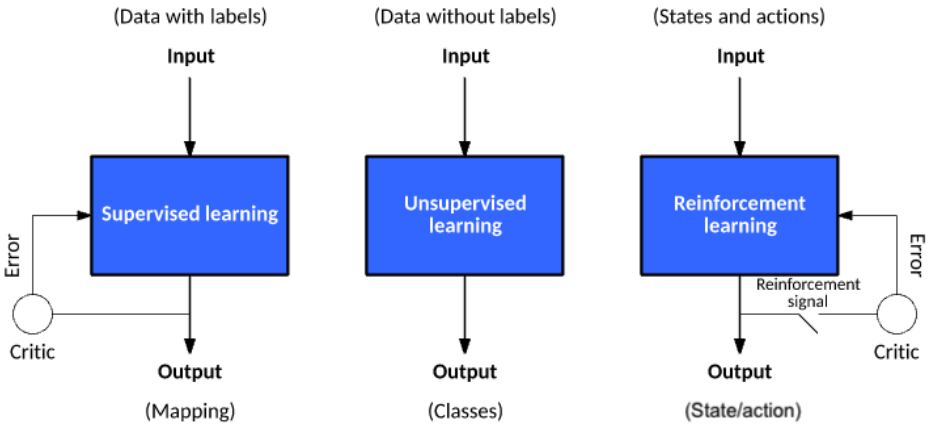

Figure 2: Machine learning categorisation (Rahman et al., 2024) ML categories consist of supervised learning (SL), unsupervised learning (UL), and reinforcement learning (RL).

AI-BASED AD DETECTION TECHNIQUES

Advances in AI have created new possibilities in healthcare. Combining these distinct domains revolutionises medical efficacy, enhances early disorder detection, and validates accurate diagnoses to improve patient outcomes. Imaging techniques including CTs, MRIs, and PET images, play a crucial role in producing copious amounts of brain data that needs to be interpreted, a task done by AI through making AD classifications, as seen in Figure 3. AI models are designed to process early-stage biomarkers, such as brain morphology changes or indications of cognitive decline, to identify patterns that precede symptoms of AD. AI enables accurate, precise, and timely detection, setting new standards for Alzheimer's diagnoses and improving treatment pathways (Pinto-Coelho, 2023).

Within the AI algorithm categories, each subsection can be further classified depending on their characteristics. SL networks, including convolutional neural networks, deep neural networks, deep polynomial networks, and recurrent neural networks, employ labelled data to identify features and make predictions, focusing on instant rewards. In contrast, UL networks, constituting auto-encoder and restricted Boltzmann machine, decode unlabelled data for AD biomarker analysis (Ebrahimighahnavieh et al., 2020). The RL paradigm balances exploration to maximise rewards (Pinto-Coelho, 2023).

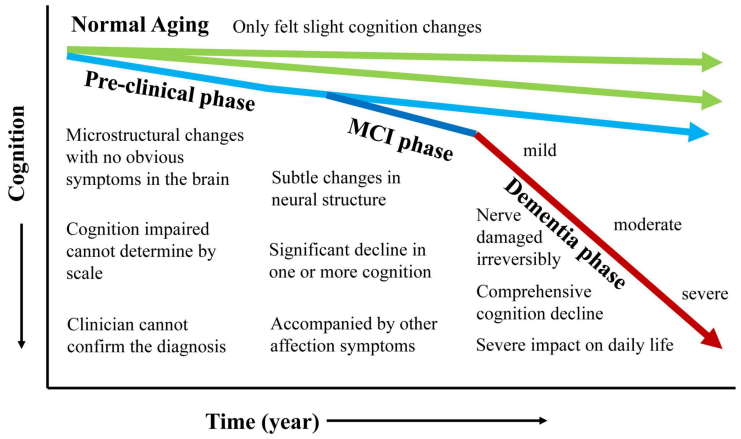

Figure 3: Progression of AD (Zhou et al., 2023) AI models take inputted data and categorise its output into distinct classifiers: cognitively normal (CN), early mild cognitive impairment (EMCI), mild cognitive impairment (MCI), late mild cognitive impairment (LMCI), or AD. AI models are built to determine the classifiers of known AD case diagnoses from datasets, to be trained for accurate application to future unknown cases.

CONVOLUTIONAL NEURAL NETWORKS (CNN)

CNNs, inspired by the brain's visual cortex, are deep models designed to analyse 2D/3D image inputs by extracting patterns from convolutional layers that create a feature map. These layers extract commonalities, such as cortical thinning or brain atrophy, from AD MRIs. While some studies formulate their own CNN framework, traditional CNN researchers use clinically

validated structures such as LeNet, VGGNet, GoogLeNet, and ResNet, for highly accurate image-based classifications (Ebrahimighahnavieh et al., 2020).

A study by Wee et al. (2019) advanced the CNN model benchmark by producing a spectral graph-CNN model containing cortical thickness calculations with transfer learning, where one algorithm's learning is standardised to another novel model's tasks. This framework identified cortical thickness, a potential biomarker for AD, to successfully classify patients within an AD stage. The model further learned to adapt its findings across populations by training using a Caucasian dataset and effectively generalising to an Asian-based dataset. The spectral graph-CNN framework reported classification accuracies of 85.8% (CN vs. AD) and 79.2% (EMCI vs. AD). Additionally, the graph-CNN predicted EMCI conversion to AD with 75% accuracy. Incorporating cortical geometry, the model reported prevailing accuracy compared to traditional CNNs concerning scalability and generalisability. By demonstrating the importance of cortical thinning geometry and transfer learning in neural networks, the study highlights a future ability to apply AI to all demographics without needing novel, population-specific classifier models. However, further research may substantiate its validity across widespread, diverse datasets (Wee et al., 2019).

AI has a high capacity to process whole-genome medical data to identify early signs of AD, specifically genomic structural changes, to acquire population-level genetic variants. This data analysis is crucial in providing personalised medicine based on one's genetic predispositions, making individualised preventative care a possibility (Vilhekar and Rawekar, 2024). Additionally, through brain scans, ANNs can identify functional deformities in brain regions to differentiate AD and healthy brain scans (Angelucci et al., 2024). Odusami et al. (2022) developed a model using pre-trained ResNet18 and DenseNET210, pre-trained CNN models, to identify features from brain networks in MRI images and classify AD stages. Analytically, the model achieved 98.86% accuracy (the overall correctness) and 95% precision (the extent of correct predictive classifications) in identifying early mild cognitive impairment (EMCI) cases in a five-way classification with a 98.89% recall (rate of data samples correctly classified) for EMCI, indicating a complete accuracy in identifying early AD with no unaccounted-for cases.

Compared to other models from the literature, the Odusami et al. (2022) model presented the most accurate results. This approach is one of the first scholarly studies to integrate the output of two pre-trained models diagnosing AD (Odusami et al., 2022). These results underscore the effectiveness of CNN models in accurately diagnosing EMCI patients from an existing dataset. Pre-trained AI systems reduce reliance on extensive AD-specific training datasets, enhancing accessibility for researchers with smaller datasets. Similarly, using MRI images removes the invasiveness of conventional techniques, making this method safer for diagnostic purposes. However, the model could better capture differences between EMCI and LMCI diagnoses by including a multimodal design, a method of combining different types of data to make more accurate predictions. Additionally, the high accuracy associated with specific datasets could indicate overfitting, wherein the model memorises the training data, resulting in flawed accuracy when applied to novel datasets or different imaging conventions.

DEEP NEURAL NETWORKS (DNN), DEEP POLYNOMIAL NETWORKS (DPN), AND RECURRENT NEURAL NETWORKS (RNN)

DNNs incorporate multiple stacked layers. In research, DNNs can combine layers to produce complex networks and extract abstract patterns and relationships from data (Fathi et al., 2022). For example, Lu et al. (2018) developed a novel model, combining multimodal information from MRI and fluorodeoxyglucose PET (FDG-PET) images within a DNN framework. Using ADNI records, the study predicted MCI progression to AD. The multi-modal model classified the dataset with an 86.4% accuracy.

Additionally, the study demonstrated 94.23% sensitivity in diagnosing individuals with potential AD. The DNN framework achieved high accuracy in detecting prodromal MCI (the period between initial symptomatic onset and full manifestation of AD) conversion cases up to three years before the change, outperforming single-modality classifiers in the literature and exceeding other multi-modal methods. These findings exhibit the sustainability and longevity of a DNN framework in early AD diagnosis. However, without transfer learning, as presented in the Wee et al. (2019) model, the model's efficacy with new, diverse data comes into question (Lu et al., 2018).

DPNs, another supervised deep learning model, model complex variable relationships (polynomial interactions) from input data, making this a benchmark for high-functioning feature extraction (Fathi et al., 2022). RNNs, with their memory-based programming, are designed to manage time series data (recorded consistently over specified periods) and sequential data from images. This AI framework compiles past information stores and accumulates them in its memory, storing long-term data (Ebrahimighahnavieh et al., 2020). Despite their potential, these models are unable to amalgamate spatiotemporal information, a challenge that should be addressed in future studies.

AUTO-ENCODER (AE) AND RESTRICTED BOLTZMANN MACHINE (RBM)

UL AEs contain two parts: an encoder and a decoder. The encoder compresses data into a simpler format, enclosing key characteristics obtained from the inputs. The decoder reformats the original data from the represented information. RBM models derive input variables from hidden illustrations (Ebrahimighahnavieh et al., 2020).

Suk et al. (2016) presented a novel method to identify patterns in resting-state functional MRI (rsfMRI) scans using functional computational networks and state-space modeling to diagnose early AD cases in MCI. The study employs a deep AE with RBMs in a non-linear hierarchy to find brain relationship patterns and a state-space Hidden Markov Model to map neuronal associations. Achieving an accomplished diagnostic accuracy of 72.58% and 81.08% compared to existing trailblazing datasets, such as ADNI2 cohort and in-house cohort, the study's framework proves to be a sustainable model in diagnosing MCI and AD. The model parallels the time-varying functional dynamics of brain network interactions within the cohort data to detect early AD and reduce misdiagnoses (Suk et al., 2016).

REINFORCEMENT LEARNING

Compared to the other ML categories, RL differentiates itself by learning from punishments inherent within its programming to magnify prospective rewards. However, this technique's applicability and efficacy are limited to reduced feature sets from datasets and difficulties in processing hand-crafted feature design information from images, typically seen in conventional ML mechanisms (Hui et al., 2023).

Zhang et al. (2021) developed a multimodal deep RL framework for AD detection, integrating compressed sensing MRI (CS-MRI) into high-quality MRI (HQ-MRI) using the RL model, to improve patient outcomes. The model was designed to improve image quality and interpret the scans for common pathological features. The model was trained with clinical factors such as age, APoE4 (a biomarker for AD), gender, and mini-mental state examination (MMSE) scores. It achieved a high accuracy of 95.6% ± 2.5% from the ADNI dataset. Addressing concerns from past studies, this model successfully reproduced these results in the AIBL and NACC datasets, interpreting key biomarkers of AD presence such as amyloid degradation, atrophy in critical brain lobes, and Tau protein aggregation. The model highlights the potential of APoE4 as a target for treatments, as seen by the increased accuracy from the model when testing with the APoE4 state compared to without it (with = 94.9% > without = 94.7%) (Zhang et al., 2021).

LIMITATIONS OF AI

While AI methodologies for early AD detection are advancing, there are limitations to their applicability and sustainability. AI models are constrained by existing datasets, limiting accurate AD stage classification and real-life applications with unknown datasets. Another limitation of this research is that AI models are only as robust as their training. For example, Zhang et al. (2021) focused only on healthy and AD patients, limiting their model's scope and scalability. Confounding factors, such as missing data, generalisability, and small sample sizes, limit AI adoption in clinical settings. While studies such as Lu et al. (2018) achieve precise classification in controlled environments, dynamic clinical setting application of existing frameworks requires further research and validation.

Another limitation is the large datasets all ML techniques require for accurate classification. Due to patient confidentiality, hospitals, clinics, and other institutions limit public data sharing. Similarly, ethical concerns arise regarding the distribution of patient data, a lack of privacy and security, and AI accountability. While ethical policies may constrict the information acquired for AI models, resulting in inaccurate model designs and data overfitting, the lack of universal guidelines surrounding the moral and ethical use of AI encourages its misuse. This is a larger discussion that requires a balance between innovation and improved healthcare with evaluations for safety and AI-driven efficacy in healthcare (Khan et al., 2023, p.733).

Constricted inputted data can lead to biased AI output, particularly due to the underrepresentation of ethnic minorities, causing the algorithm to develop racial uninformed biases. Wee et al. (2019) applied racially diverse datasets and observed similar AD diagnosis success rates across ethnicities. Researchers should implement multi-ethnic training datasets to eliminate bias. Since AI frameworks learn independently, they may contrive stereotypes themselves, a struggle for AI development (Khan et al., 2023, p.733).

CONCLUSION

This review highlights AI's potential for early AD detection over conventional techniques. Emphasising the importance of AI in research brings about a discussion on the efficacy and applicability of AI in improving standards of healthcare. The studies in this review all commonly express how conventional methods are outperformed by AI models in accurately and precisely detecting early AD, a hallmark of transformation and science. Ethical guidelines should be implemented to maintain accountability and transparency within the field. Additionally, AI-based algorithms used in clinical settings require approval before being used for actual patient treatment and diagnosis-related decision-making. The specificity of AI frameworks should be compared to standard diagnostic tests to establish the most accurate solutions (Khan et al., 2023).

In conclusion, AI offers a new potential for early detection of AD, allowing a future possibility of implementing early treatments, providing earlier chances to plan for the future, and promoting accessible and scalable research. AI models, especially CNN-based models, act as tools to intervene at the earliest stage possible. As AI models evolve, their clinical utility could accelerate early AD detection, enabling patients to timely interventions by slowing down disease progression. With that said, AI is a tool, not a solution in and of itself. With future advances, AI has the potential to analyse large-scale datasets acquired from conventional imaging techniques to identify signs of early AD onset, becoming a cornerstone for preventative treatments and early AI diagnosis accessibility, changing the scale of this disease worldwide.

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