

Research Article

The Application of Artificial Intelligence in the Treatment of Alzheimer's disease


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Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, memory loss, and behavioural changes, significantly impacting patients' quality of life and placing a substantial burden on healthcare systems worldwide. Despite extensive research, effective treatments to halt or reverse its progression remain elusive. Traditional diagnostic and therapeutic approaches often fall short in early detection and personalized intervention. This paper explores the transformative potential of Artificial Intelligence (AI) and Machine Learning (ML) methods in revolutionizing the treatment of Alzheimer's disease. It used various AI methodologies, their application in early diagnosis, personalized treatment strategies, drug discovery, and disease progression monitoring. It discussed specific algorithms, illustrate their use with examples, present current research findings, and conclude with the challenges and future directions of AI in combating this complex disease.

1. Introduction

Alzheimer's disease is the most common cause of dementia, affecting millions globally [1, 2]. Its insidious onset and progressive nature make early and accurate diagnosis crucial for potential interventions, though current treatments primarily focus on symptom management. The complexity of AD, involving multiple genetic and environmental factors, diverse pathological pathways (e.g., amyloid plaques, tau tangles, neuroinflammation), and varied patient responses to treatments, presents significant challenges for conventional medical approaches [3–5].

The advent of Artificial Intelligence, particularly Machine Learning, offers a paradigm shift in addressing these challenges. AI's ability to process and analyze vast, complex, and heterogeneous datasets including medical images (MRI, PET), genetic information, electronic health records, cognitive test scores, and biomarker data enables the identification of subtle patterns and correlations often imperceptible to human analysis [4]. This capability holds immense promise for improving every stage of AD management, from early detection and risk stratification to personalized treatment and the accelerated discovery of novel therapeutics. This paper aims to provide a comprehensive overview of how AI is being leveraged to reshape the landscape of Alzheimer's treatment [6–10].

2. Different Methods of Machine Learning

Machine Learning (ML) is a subfield of AI that empowers systems to learn from data, identify patterns, and make decisions with minimal human intervention. Various ML techniques are being applied in AD research:

2.1. Supervised Learning

Supervised learning algorithms learn from labeled datasets, where input data is paired with corresponding output labels. The goal is to learn a mapping from inputs to outputs, which can then be used to predict labels for new, unseen data.

Classification: Used to categorize data into predefined classes (e.g., AD, Mild Cognitive Impairment (MCI), and Healthy Control (HC)) [11].

- **Support Vector Machines (SVMs):** Effective for classification and regression tasks, particularly with high-dimensional data. SVMs find an optimal hyper plane that best separates data points into different classes. In AD, SVMs have been used to classify AD from MCI or HC based on neurology based imaging features (e.g., cortical thickness, hippocampus volume) and other biomarkers.
- **Logistic Regression:** A statistical model used for binary classification. It estimates the probability of an instance belonging to a particular class. Can be used for predicting progression from MCI to AD.
- **Random Forests:** An ensemble learning method that constructs a multitude of decision trees during training and outputs the class that is the mode of the classes (classification) or mean prediction (regression) of the individual trees. Robust against over fitting and can handle various data types.

Regression: Used to predict a continuous output value based on input features.

- **Linear Regression:** Models the relationship between a scalar dependent variable and one or more independent variables.
- **Ridge/Lasso Regression:** Regularized linear regression methods that help prevent over fitting by adding a penalty term to the cost function, particularly useful with high-dimensional genomic or proteomic data.

2.2. Unsupervised Learning

Unsupervised learning algorithms work with unlabeled data, aiming to discover hidden patterns or intrinsic structures within the data [12].

Clustering: Groups similar data points together.

- **K-Means Clustering:** Partitions data into K clusters, where each data point belongs to the cluster with the nearest mean. Useful for identifying distinct patient subgroups within AD populations based on diverse biomarker profiles or disease progression trajectories.
- **Hierarchical Clustering:** Builds a hierarchy of clusters.

Dimensionality Reduction: Reduces the number of random variables under consideration, often by obtaining a set of principal variables.

- **Principal Component Analysis (PCA):** Transforms data into a new coordinate system such that the greatest variance by any projection of the data comes to lie on the first coordinate (called the first principal component), the second greatest variance on the second coordinate, and so on. Useful for reducing the complexity of high-dimensional neuro based imaging or genetic datasets while retaining essential information.
- **Auto encoders:** Neural networks that learn a compressed, dense representation (encoding) of the input data in an unsupervised manner. Can be used for anomaly detection and feature extraction from complex medical images.

2.3. Deep Learning

Deep learning (DL) is a subset of ML that uses artificial neural networks with multiple layers (deep neural networks) to learn complex representations of data. DL models have shown exceptional performance in tasks involving image, speech, and text data due to their ability to automatically learn hierarchical features [13].

- **Convolutional Neural Networks (CNNs):** Primarily used for image processing tasks. CNNs excel at extracting spatial features from medical images like MRI and PET scans, making them invaluable for AD diagnosis and prognosis by identifying subtle structural or metabolic changes in the brain.
- **Recurrent Neural Networks (RNNs) and Long Short-Term Memory (LSTM) Networks:** Designed for processing sequential data, such as time-series clinical data (e.g., patient cognitive scores over time, biomarker progression). LSTMs are particularly adept at capturing long-term dependencies in sequences.
- **Generative Adversarial Networks (GANs):** Composed of two neural networks, a generator and a discriminator, that competes against each other. GANs can generate synthetic data, which is useful for augmenting limited medical datasets or creating realistic simulations for training other AI models.
- **Transformer Networks:** Originally developed for natural language processing, transformers leverage self-attention mechanisms to weigh the importance of different parts of the input data. They are increasingly being explored for multimodal data integration and drug discovery.

2.4. Reinforcement Learning

Reinforcement learning (RL) is an area of ML concerned with how intelligent agents should take actions in an environment to maximize a cumulative reward. While less common in direct AD diagnosis, RL holds promise for optimizing treatment strategies and drug discovery by iteratively learning optimal approaches based on simulated patient responses.

3. Background of Alzheimer’s disease

Alzheimer’s disease is a chronic neurodegenerative disease that gradually worsens over time. It is characterized by the accumulation of abnormal protein aggregates in the brain: amyloid-beta plaques and neuro fibrillary tangles composed of hyperphosphorylated tau protein. These pathological hallmarks lead to neuronal dysfunction and death, resulting in brain atrophy and cognitive decline [14–17]. The following are the Key features of AD including the following:

- **Memory Loss:** Initially, short-term memory is affected, progressing to long-term memory impairment.
- **Cognitive Decline:** Difficulties with thinking, reasoning, problem-solving, language, and spatial awareness.
- **Behavioural and Psychological Symptoms:** Mood swings, agitation, depression, apathy, and psychosis can occur as the disease progresses.
- **Pathophysiology:**
 - **Amyloid-beta plaques:** Extracellular deposits of amyloid-beta protein.
 - **Neurofibrillary tangles:** Intracellular aggregates of hyperphosphorylated tau protein.
 - **Neuroinflammation:** Activation of glial cells (microglia and astrocytes) contributing to neuronal damage.
 - **Synaptic Dysfunction and Neuronal Loss:** Loss of connections between neurons and subsequent brain cell death, particularly in areas critical for memory and cognition like the hippocampus and cortex.
- **Risk Factors:** Age is the primary risk factor. Genetic factors (e.g., APOE $\epsilon 4$ allele), lifestyle factors (e.g., cardiovascular health, diet, exercise), and environmental exposures also play a role.
- **Diagnosis:** Traditionally based on clinical assessment, cognitive tests, and exclusion of other causes of dementia. Neuroimaging (MRI, PET) and cerebrospinal fluid (CSF) biomarkers (amyloid-beta 42, total tau, phosphorylated tau) are increasingly used for earlier and more definitive diagnosis. Blood-based biomarkers are an active area of research for less invasive diagnostic methods.
- **Treatment:** Current treatments are symptomatic, aiming to temporarily improve cognitive function or manage behavioural symptoms (e.g., cholinesterase inhibitors, memantine). Disease-modifying therapies are emerging (e.g., amyloid-targeting antibodies like Lecanemab, Donanemab) that aim to remove amyloid plaques, potentially slowing cognitive decline in early stages. However, their efficacy and accessibility are still under investigation.

The heterogeneity in disease presentation and progression among AD patients, coupled with the long asymptomatic phase, highlights the critical need for personalized approaches to diagnosis, prognosis, and treatment [18, 19].

4. Related work

This literature review explores diverse approaches to classifying Alzheimer’s disease, encompassing various viewpoints and methodologies.

Sarraf and Tofghi [20] proposed a novel approach using Convolutional Neural Networks (CNN) to classify Alzheimer’s disease structural MRI data. The authors achieved an accuracy of 98.84% in predicting Alzheimer’s disease from normal control brains using two CNN architectures: LeNet and Google Net. This study highlighted the significance of deep learning architectures in medical diagnostic imaging, particularly for brain disorders, offering promising opportunities for future research and clinical applications.

Korolev et al [21] introduced deep 3D CNN architectures for brain MRI classification. The small training dataset limitations were addressed through advanced deep learning techniques, and an accuracy of 80% was achieved for Alzheimer’s disease versus normal control classification. The study’s major advantages included its simplicity and elimination of feature generation requirements, enabling real-time MRI prediction without complex preprocessing.

Janghel and Rathore [22] suggested a deep learning-based approach for AD detection, employing the ADNI database with fMRI and PET images. The authors applied 3D to 2D conversion and image resizing before using the VGG-16 CNN architecture. The study achieved an average accuracy of 99.95% for fMRI and 73.46% for PET dataset classification, outperforming existing methods and improving CNN model performance.

Mukhtar and Farhan [23] proposed a CNN-based deep learning approach for predicting the conversion from MCI to AD using various features, including MRI, genetics, and neuropsychological assessment scores. The CNN model achieved an accuracy of 94% for predicting MCI to AD conversion. The proposed technique showed promise for assisting medical practitioners in the timely and accurate prognosis of AD, providing opportunities for early detection and intervention.

5. Proposed Method

Our proposed method leverages a multi-modal AI framework to enable personalized treatment strategies for Alzheimer’s patients. The core idea is to integrate diverse patient data points such as genomic, proteomic, neuroimaging, clinical, cognitive, and lifestyle—to create a holistic digital profile for each individual. AI algorithms will then analyze these profiles to predict disease progression, identify optimal therapeutic interventions, and monitor treatment response in real-time.

5.1. Data Acquisition and Pre-processing

The success of any AI model hinges on the quality and quantity of data. For AD, this involves:

MRI (structural, functional), PET (amyloid, tau, FDG-PET), fMRI. Pre-processing includes registration, normalization, segmentation, and feature extraction (e.g., brain volume, cortical thickness, white matter integrity, metabolic activity) [24].

Data pre-processing will involve:

- **Normalization:** Scaling numerical features to a standard range.

- **Imputation:** Handling missing data using appropriate techniques (e.g., mean, median, k-nearest neighbour's imputation).
- **Feature Engineering:** Creating new features from existing ones (e.g., ratios of biomarker levels, change in cognitive scores over time).
- **Data Harmonization:** Ensuring consistency across different data sources and cohorts.

5.2. AI Model Development

The framework will employ a combination of deep learning and traditional machine learning models tailored for specific tasks.

Early Diagnosis and Risk Prediction (CNNs, SVMs, Ensemble Methods):

- CNNs will analyze structural MRI and PET scans for subtle signs of brain atrophy, amyloid deposition, and metabolic changes that precede clinical symptoms. A multi-input CNN architecture can combine features from different imaging modalities.
- SVMs and ensemble methods (e.g., Gradient Boosting Machines like XGBoost, LightGBM) will integrate imaging features with genetic data, CSF/blood biomarkers, and clinical history to predict the likelihood of AD onset and progression from MCI to AD.
- **Example:** A CNN model trained on longitudinal MRI scans could learn to detect patterns of brain volume change that are indicative of early AD progression, even before significant cognitive decline is observed. This model could achieve high sensitivity and specificity in differentiating stable MCI from MCI converters.

Personalized Prognosis and Disease Trajectory Prediction (RNNs, LSTMs, Transformers):

- LSTMs or Transformer networks will analyze longitudinal patient data (time-series of cognitive scores, biomarker levels, medication adherence) to predict individual disease progression trajectories, including the rate of cognitive decline and the onset of specific symptoms.
- **Example:** An LSTM model can learn from a patient's historical cognitive test scores and biomarker fluctuations to predict their cognitive status 1, 3, or 5 years into the future, providing a more accurate prognosis than traditional clinical assessments. This personalized prediction can inform proactive care planning.

Drug Discovery and Repurposing (Graph Neural Networks, Generative Models):

- **Graph Neural Networks (GNNs):** Will model molecular structures and protein-protein interaction networks to identify novel drug targets and design new compounds. GNNs can learn complex relationships within biological networks relevant to AD pathogenesis.
- **Generative Models (GANs, Variation Auto encoders - VAEs):** Can be used to generate novel drug-like molecules with desired properties (e.g., blood-brain barrier permeability, target binding affinity) or to identify promising candidates from large chemical libraries.
- **Example:** A GNN could analyze the interaction network of proteins involved in amyloid-beta production and clearance, identifying key nodes that, when modulated, could significantly impact disease progression. This could lead to the discovery of new therapeutic targets. Furthermore, GANs could generate thousands of novel molecules that are optimized to bind to these targets, accelerating the lead optimization phase of drug discovery.

Personalized Treatment Response Prediction and Optimization (Reinforcement Learning, Predictive Analytics):

- RL agents can be trained in simulated environments that mimic patient responses to different drug regimens and non-pharmacological interventions. The agent learns optimal treatment sequences or combinations by maximizing a reward signal (e.g., slowed cognitive decline, improved quality of life).
- Predictive analytics using patient-specific data will forecast the likely efficacy and side effects of various treatments, allowing clinicians to tailor therapies for individual patients.
- **Example:** An RL model could suggest optimal timing and dosage of AD medications based on a patient's genetic profile, current cognitive status, and predicted response to different drug classes, aiming to maximize treatment benefits while minimizing adverse effects. This moves beyond a "one-size-fits-all" approach to truly personalized medicine.

6. Algorithm

The overarching algorithm for AI-driven personalized AD treatment can be outlined as follows:

1. Data Collection and Integration:

- Continuously collect multi-modal data: Neuroimaging (MRI, PET), Biomarkers (CSF, Blood), Genetic (SNP, WES), Clinical Records (EHR), Cognitive Test Scores, and Wearable Sensor Data.
- Establish secure, privacy-compliant data repositories (e.g., federated learning to protect patient privacy).

2. Data Pre-processing and Feature Engineering:

- Clean, normalize, and impute missing values across all datasets.
- Extract relevant features from raw data (e.g., volumetric measures from MRI, protein concentrations from blood, genetic variants).
- Engineer novel features that capture temporal dynamics or complex interactions between modalities.

3. Model Training and Validation:

For Diagnosis/Prognosis:

- Split data into training, validation, and test sets.
- Train diverse ML/DL models (CNNs for imaging, LSTMs/Transformers for time-series, SVMs/Ensemble for integrated features).

- Optimize model hyperparameters using cross-validation.
- Evaluate performance using metrics such as accuracy, sensitivity, specificity, AUC-ROC, and prediction error.
- Iteratively refine models based on validation performance.

For Drug Discovery:

- Train GNNs on molecular graphs and biological networks.
- Train generative models (GANs, VAEs) to design novel compounds.
- Use predictive models to screen and prioritize drug candidates based on desired properties (efficacy, safety, pharmacokinetics).

For Treatment Optimization:

- Develop a simulation environment reflecting AD progression and treatment responses.
- Train RL agents using various reward functions (e.g., minimizing cognitive decline, improving daily living activities).

4. Personalized Profile Generation:

- For each new patient, create a comprehensive digital profile by integrating all available multi-modal data.

5. Prediction and Recommendation:

Utilize the trained models to generate patient-specific predictions:

- **Diagnosis:** Current AD stage (e.g., MCI, mild AD, moderate AD).
- **Prognosis:** Predicted rate of cognitive decline, risk of progression to next stage, expected onset of specific symptoms.
- **Treatment Options:** Recommended drug therapies, non-pharmacological interventions (e.g., cognitive training, lifestyle modifications) based on predicted efficacy and side effects.
- **Drug Candidates (for researchers):** Identification of promising compounds or targets for further wet-lab validation.

6. Monitoring and Feedback Loop:

- Continuously monitor patient's response to treatment (e.g., through follow-up cognitive tests, new imaging, wearable data).
- Use new data to update the patient's digital profile and refine predictions.
- Provide feedback to the AI models, allowing for continuous learning and adaptation to new patterns and treatment outcomes. This is crucial for improving model accuracy over time, reflecting real-world complexities.

7. Examples of AI Applications in AD Treatment

7.1. Early Diagnosis through Imaging Biomarkers

- **Problem:** AD diagnosis often happens late, limiting intervention windows. Subtle changes in brain structure/metabolism can precede overt symptoms by years.
- **AI Solution:** Deep learning, particularly CNNs, can analyze vast datasets of MRI and PET scans.
- **Example:** A study trains a 3D CNN on a dataset like ADNI (Alzheimer's Disease Neuroimaging Initiative), comprising thousands of longitudinal MRI and FDG-PET scans from HC, MCI, and AD patients. The CNN learns intricate volumetric and metabolic patterns associated with different AD stages. When a new patient's scan is input, the model can classify them with high accuracy (e.g., 90-95% for AD vs. HC, 80-85% for MCI vs. HC, and predicting MCI conversion to AD). This allows for earlier identification of at-risk individuals, enabling earlier lifestyle interventions or clinical trial enrolment [17].

7.2. Predicting Disease Progression and Personalized Prognosis

- **Problem:** AD progression is highly variable among individuals, making it difficult to predict how quickly a patient will decline.
- **AI Solution:** RNNs or LSTM networks are well-suited for time-series data analysis.
- **Example:** An LSTM model is trained on longitudinal clinical data (e.g., MMSE scores, ADAS-Cog scores, and a panel of blood biomarkers collected annually over several years) from a cohort of MCI patients. The model learns individual trajectories of cognitive decline. For a newly diagnosed MCI patient, the LSTM can predict their likely cognitive score trajectory over the next 5 years, along with the probability of converting to AD within a certain timeframe. This personalized prognosis helps families prepare and clinicians tailor care plans more effectively.

7.3. Accelerating Drug Discovery and Repurposing

- **Problem:** Traditional drug discovery is time-consuming, expensive, and has a high failure rate, especially for complex diseases like AD.
- **AI Solution:** GNNs and generative models.
- **Example:** Researchers use a GNN to analyze a vast database of existing drugs and their interactions with hundreds of known and suspected AD-related protein targets (e.g., BACE1, tau, APOE). The GNN identifies drugs, originally approved for other conditions (e.g., diabetes, hypertension), that show high predicted binding affinity and favourable interaction profiles with AD targets. This "drug repurposing" approach drastically reduces the time and cost compared to developing new compounds from scratch. Additionally, generative models could design novel small molecules from scratch that specifically target difficult-to-drug proteins implicated in AD pathology, which are then synthesized and tested in vitro.

7.4. Optimizing Non-Pharmacological Interventions

- **Problem:** Non-pharmacological interventions (e.g., cognitive training, exercise, diet) are important but their optimal combination and intensity vary among individuals.
- **AI Solution:** Reinforcement Learning.
- **Example:** An RL agent is trained in a simulated environment representing an AD patient's cognitive and physical state, which responds to different interventions. The agent learns an optimal sequence of cognitive exercises, physical activity recommendations, and dietary adjustments for a specific patient, aiming to maximize their cognitive function and quality of life. For instance, based on real-time data from wearables and cognitive app usage, the RL model could recommend a specific type and duration of exercise on a given day, combined with a particular memory game, to best maintain cognitive function for that individual.

8. Results and Discussion

The application of AI in Alzheimer's disease treatment has shown promising results across various domains:

- **Improved Diagnostic Accuracy:** AI models, particularly deep learning on neuroimaging data, consistently outperform traditional methods in early AD detection and differentiation from other dementias or normal aging. Studies have reported accuracies exceeding 90% for AD vs. HC classification and significant improvements in predicting MCI conversion to AD (e.g., 80-85% accuracy several years before clinical diagnosis). This early detection is critical for potential disease-modifying interventions.
- **Enhanced Prognostic Capabilities:** AI-driven predictive models can accurately forecast individual disease trajectories, providing more precise prognoses and enabling proactive planning for patients and caregivers. The ability to predict the rate of decline and the emergence of specific symptoms allows for more timely and tailored interventions.
- **Accelerated Drug Discovery:** AI algorithms significantly shorten the drug discovery pipeline by rapidly screening vast chemical libraries, identifying novel drug targets, and repurposing existing drugs. This has already led to the identification of several promising therapeutic candidates and even some entering clinical trials. The ability to simulate molecular interactions and predict compound properties drastically reduces the experimental burden.
- **Personalized Treatment Approaches:** By integrating multi-modal data, AI facilitates the development of personalized treatment plans that account for individual genetic predispositions, biomarker profiles, and disease progression patterns. This move towards precision medicine maximizes treatment efficacy and minimizes adverse effects, improving patient outcomes.
- **Identification of Novel Biomarkers and Risk Factors:** AI's capacity to uncover subtle patterns in large datasets has led to the discovery of previously unrecognized biomarkers and risk factor combinations (e.g., certain co-occurring conditions, specific gene variants) for AD, opening new avenues for research and diagnostic development.

Challenges and Limitations

Despite these promising results, several challenges remain

- **Data Availability and Quality:** High-quality, diverse, and large-scale multimodal datasets are crucial. Data privacy concerns and the heterogeneity of data collection methods across institutions pose significant hurdles.
- **Interpretability and Explainability (the "Black Box" Problem):** Many powerful deep learning models are "black boxes," making it difficult to understand why they make certain predictions. In clinical settings, clinicians need to trust and understand the basis of AI recommendations. Developing interpretable AI models is a critical area of research.
- **Generalizability:** AI models trained on specific datasets may not perform equally well on new, unseen data from different populations or clinical settings due to variations in demographics, genetics, or imaging protocols.
- **Regulatory Approval and Clinical Integration:** Integrating AI tools into routine clinical practice requires rigorous validation, regulatory approval, and addressing ethical considerations related to data privacy, bias, and accountability.
- **Lack of Causal Inference:** While AI can identify strong correlations, establishing causal relationships (e.g., specific molecular changes causing cognitive decline) remains challenging and often requires complementary biological research.

9. Conclusions

Artificial Intelligence is rapidly transforming the landscape of Alzheimer's disease treatment, offering unprecedented opportunities for early and accurate diagnosis, personalized prognosis, accelerated drug discovery, and optimized patient management. By integrating diverse data types and leveraging advanced machine learning and deep learning techniques, AI can uncover subtle disease patterns, predict individual progression trajectories, and identify novel therapeutic targets, moving beyond traditional "one-size-fits-all" approaches.

While significant progress has been made, challenges related to data availability, model interpretability, and clinical validation must be addressed for widespread adoption. Future research should focus on developing robust, explainable, and generalizable AI models, coupled with a concerted effort to create comprehensive and standardized multi-modal datasets. As AI continues to evolve and integrate with biological and clinical research, it holds immense potential to unlock new insights into AD pathophysiology and pave the way for more effective, personalized treatments that significantly improve the lives of Alzheimer's patients and their families. The convergence of AI with precision medicine promises a new era in the fight against this devastating disease.

Article Information

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

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