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# A Current Perspective on Machine Learning Approaches for Early Alzheimer's Disease Detection

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## Abstract:

Alzheimer's disease (AD) is a progressive neurodegenerative condition that requires precise early intervention. While machine learning (ML) has made significant strides in this field, current research is largely confined to binary classification frameworks, focusing primarily on distinguishing healthy controls from AD patients. There is, however, an urgent clinical necessity to move toward multi-class detection to capture the nuanced stages of disease progression using non-invasive clinical assessments. Furthermore, within the domain of neuroimaging, a critical gap exists regarding clinical reliability and model generalization. Current literature predominantly prioritizes high accuracy scores, often at the expense of ensuring that these models remain robust across heterogeneous datasets and diverse clinical environments. This review synthesizes the current state of ML in AD detection, advocating for a shift from simple binary labels to complete multi-stage analysis. By addressing the 'accuracy vs. reliability' trade-off, we emphasize the need for generalized systems that maintain diagnostic integrity across different populations. Ultimately, this work provides a framework for transitioning toward more clinically viable diagnostic tools that prioritize multi-class progression and cross-dataset reliability over isolated performance metrics.

*Keywords* — ***Machine learning, Alzheimer disease, Cognitive assessment test, mild cognitive impairment, Datasets, Neuropsychological Features***

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## I. INTRODUCTION

### *A. The Global Crisis of Alzheimer's Disease*

Alzheimer's disease (AD) stands as a formidable global health challenge, representing a progressive neurodegenerative disorder that serves as the leading cause of dementia, accounting for an estimated 60% to 80% of all cases worldwide. The clinical manifestation of AD is characterized by a relentless decline in cognitive functions, including severe memory loss, disorientation, impaired judgment, and significant behavioral changes. These symptoms do not merely affect the individual; they place an immense psychological and financial burden on caregivers and strain global healthcare infrastructures. As the global population ages at an unprecedented rate, the epidemiological data is sobering: the number of individuals living with Alzheimer's is projected to triple by the year 2050. This trajectory underscores an urgent, non-negotiable need for the development of effective diagnostic tools and early intervention strategies that can be deployed at scale.

Early detection is the cornerstone of effective AD management. Identifying the disease in its prodromal or early stages specifically during the transition from Mild Cognitive Impairment (MCI) to AD enables the timely initiation of pharmacological treatments and non-pharmacological lifestyle interventions. These early actions are critical for slowing the rate of cognitive decline, managing neuropsychiatric

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symptoms, and significantly improving the quality of life for both patients and their families. Furthermore, an early diagnosis provides a

"window of opportunity" for patients to participate in clinical trials for emerging disease-modifying therapies and allows families to make informed decisions regarding future care and legal planning.

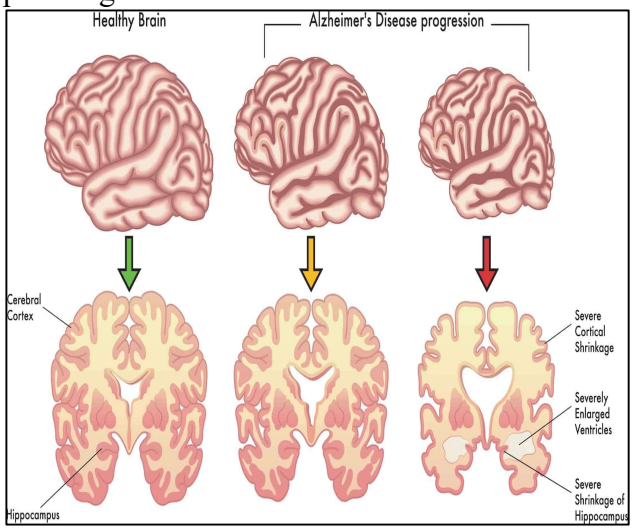


Fig. 1: Comparison of a healthy brain and the structural progression of Alzheimer's Disease

### B. *Limitations of Traditional Diagnostic Modalities*

Despite the clear benefits of early identification, the clinical reality is that AD is often diagnosed far too late. The disease typically develops insidiously over decades, with early pathological changes occurring in the brain long before clinical symptoms become apparent. Traditional diagnostic frameworks rely heavily on comprehensive clinical evaluations, laboratory analyses of cerebrospinal fluid (CSF) biomarkers, and advanced neuroimaging techniques such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) [10, 12, 20]. While these imaging modalities provide high-resolution insights into structural atrophy and metabolic changes, they are fraught with practical limitations. Neuroimaging is inherently expensive, often invasive, and requires specialized equipment and highly trained personnel to interpret. These factors create a significant barrier to access, particularly in primary care settings, rural areas, or resource-constrained environments.

Furthermore, a critical observation in contemporary neuroimaging research is the "accuracy-utility gap." A vast majority of studies focus on achieving peak accuracy within highly controlled, homogeneous datasets [15, 22]. While these models report impressive performance metrics, they often fail to address clinical reliability and model generalization [13, 17]. A model that is 99% accurate on a specific research dataset like ADNI may perform poorly when applied to a different clinical population with different scanning protocols or demographic backgrounds. This lack of cross-cohort generalizability remains a major bottleneck in transitioning machine learning (ML) models from "bench to bedside" [62].

### C. *The Role of Non-Invasive Cognitive Assessments*

In response to the limitations of neuroimaging, cognitive assessments have emerged as a vital, non-invasive, and cost-effective alternative. Standardized neuropsychological instruments, such as the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), are used globally to evaluate domains like memory, attention, language, and executive function. These tests are essential for monitoring disease progression and are highly scalable for mass screening [1].

However, traditional interpretation of these tests relies on static cutoff scores, which are often influenced by a patient's educational background, cultural content, and language proficiency [5]. This subjectivity can lead to "false negatives" in highly educated individuals who may "compensate" for early cognitive deficits, or "false positives" in populations with lower literacy. Consequently, there is a growing demand for objective, data-driven methods that can extract subtle, non-linear patterns from these test scores patterns that are often invisible to the human eye but highly indicative of early-stage neurodegeneration.

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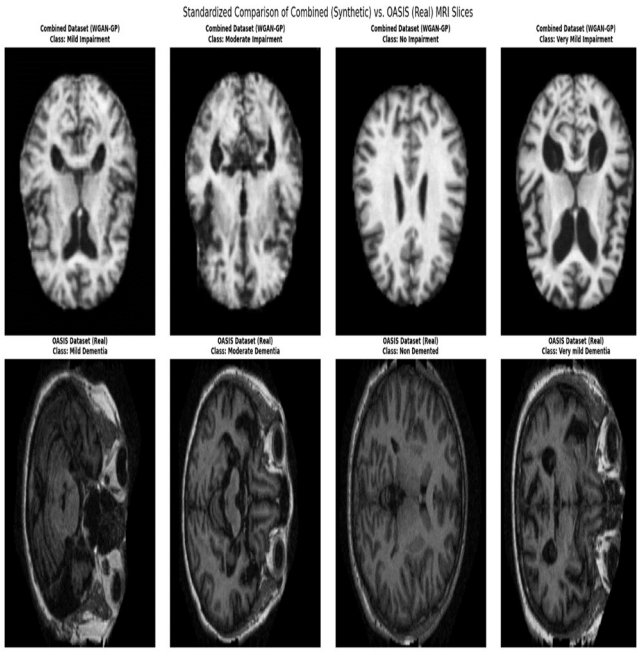


**Fig. 2:** Representative anal MRI brain scans from a dataset classified by dementia severity: Very Mild, Mild, and Moderate AD

### D. *The Machine Learning Revolution and the "Binary Trap"*

The integration of Machine Learning (ML) into AD research has provided a powerful toolkit for addressing these challenges. ML algorithms ranging from Support Vector Machines (SVM) and Random Forests to sophisticated Deep Learning architecture scan process multidimensional, longitudinal data to identify complete biomarkers of decline [2, 3, 4]. By leveraging large-scale datasets, researchers have demonstrated that ML can predict AD at a significantly lower cost than traditional imaging methods [1, 14, 23].

However, a critical review of the current literature reveals a significant limitation: the prevalence of the "Binary Classification Trap." Most current ML studies focus on the simple distinction between "Healthy Control" (HC) and "Alzheimer's Disease" (AD) [9, 19, 25]. While this proves that ML is capable of pattern recognition, it has limited clinical utility. In a real-world clinical setting, the challenge is not just identifying who has late-stage AD, but distinguishing between various stages of progression, such as stable MCI versus progressive MCI. There is an urgent need to shift toward multi-class detection systems that can map the entire trajectory of the disease. Capturing these subtle physiological and cognitive transitions is essential for personalized medicine, yet multi-stage analysis remains under-explored compared to simple binary models.

### E. *Addressing Data Heterogeneity and Reliability*

Beyond classification, the field faces a crisis of reliability. Many researchers prioritize accuracy as the primary metric of success, neglecting the fact that in medicine, a "reliable" model is often more valuable than an "accurate" but unstable one. Reliability refers to a model's ability to maintain its diagnostic integrity across heterogeneous datasets data coming from different scanners, different cognitive test versions, and diverse ethnic populations.

The presence of data heterogeneity often leads to overfitting, where a model "memorizes" the noise of a specific dataset rather than learning the underlying biological signal of the disease. To overcome this, advanced computational paradigms like transfer learning must be employed [32, 66]. Transfer learning allows a model trained on a large, diverse source dataset to adapt its knowledge to a smaller, specific target population, thereby enhancing generalizability. This is the foundation of building a generalized clinical reliability system a system that clinicians can trust regardless of the data source.

### F. *Objectives and Scope of this Review*

This systematic review aims to provide a comprehensive and critical overview of the current state of machine learning in Alzheimer's detection, with a specific emphasis on cognitive assessment data. Unlike previous reviews that focus solely on accuracy, this work evaluates the literature through the lens of clinical viability and multi-stage progression.

We examine the various types of cognitive assessments utilized, the diverse range of ML algorithms implemented from traditional classifiers to deep ensemble learning [24, 28, 29]and the feature selection strategies that have proven most effective. Crucially, we investigate the datasets used, such as ADNI and NACC, and discuss the critical need for eternal validation and cross-cohort testing [51, 56, 62]. By synthesizing these findings, we aim to highlight the gaps where

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binary models fail and where the net generation of multi-class, generalized systems must begin. Ultimately, this review serves as a roadmap for researchers and clinicians to move toward diagnostic tools that are not only highly accurate but are also robust, reliable, and capable of capturing the complete, multi-stage nature of Alzheimer's disease.

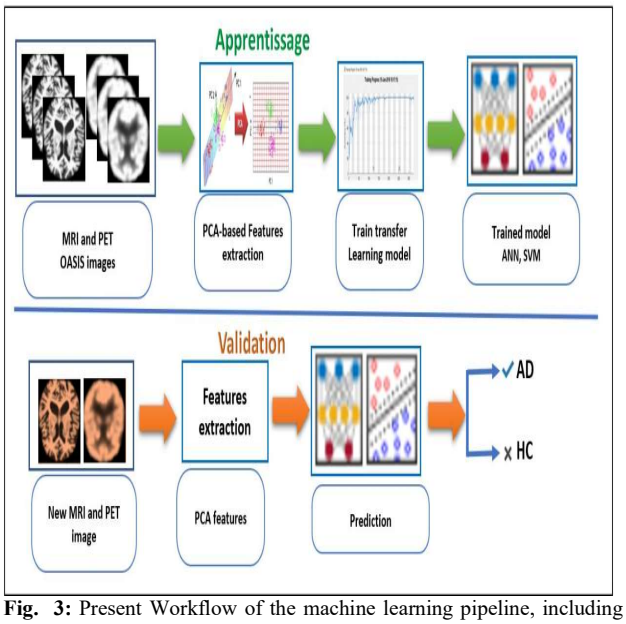


**Fig. 3:** Present Workflow of the machine learning pipeline, including PCA-based feature Extraction, transfer learning, and final classification (AD vs. HC) using ANN and SVM models.

## II. Review Protocol and Methodology

This section outlines the rigorous systematic review protocol and methodology employed to evaluate the current landscape of machine learning (ML) in Alzheimer's Disease (AD) detection. Our approach is designed to ensure a comprehensive, objective, and reproducible analysis of the existing literature. Unlike traditional reviews that focus predominantly on binary classification accuracy, this methodology is specifically formulated to investigate two critical gaps in the field: the transition toward multi-class detection of disease progression and the requirement for model generalizability and clinical reliability across heterogeneous data sources.

The process began with the formulation of core research questions:

- How effectively do current ML models move beyond binary labels to identify specific stages of cognitive decline (e.g., Stable vs. Progressive MCI)?
- To what extent does current research address the "accuracy-reliability" trade-off when dealing with diverse, multi-site datasets?
- What is the role of advanced computational techniques, such as transfer learning, in ensuring diagnostic integrity across different clinical environments?

### *A. Search Strategy*

A comprehensive literature search was conducted to identify relevant studies focusing on the application of machine learning techniques to non-invasive cognitive and clinical assessment data. Electronic databases including ACM Digital Library, PubMed, ArXiv, Scopus, Web of Science, and IEEE Explore were systematically searched for articles published up to 2025.

The search terms were carefully selected to capture both established methods and emerging trends in multi-modal and multi-stage analysis. We utilized a combination of keywords and Boolean operators (AND, OR) as follows:

- **Disease Progression:** ("Alzheimer's disease" OR "MCI progression" OR "Dementia stages")
- **Methodological Focus:** ("Machine learning" OR "Deep learning" OR "Multi-class classification" OR "Transfer learning")

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- **Disease Progression:** ("Alzheimer's disease" OR "MCI progression" OR "Dementia stages")
- **Methodological Focus:** ("Machine learning" OR "Deep learning" OR "Multi-class classification" OR "Transfer learning")
- **Reliability Focus:** ("Clinical reliability" OR "Model generalization" OR "Heterogeneous datasets" OR "Cross-cohort validation")
- **Assessment Tools:** ("Cognitive test scores" OR "Neuropsychological assessment" OR "MMSE" OR "MoCA" OR "ADAS-Cog")

Additional studies were identified by manually screening the reference lists of high-impact reviews and seminal papers to ensure a robust bibliography [4, 9]. The records identified as of 01/08/2025 across key search engines are detailed in Table 1.

Table 1: Number of records found for each query in journal search engines as on from 2020-2025.

| Search Engine | Keywords | Number of Records Found |
|---|---|---|
| Google Scholar | Alzheimer's disease assessment data | 19000 |
| | Early Detection of MCI to AD Conversion Using Machine Learning | 17700 |
| | Early Detection of Alzheimer's | 16900 |
| Pubmed | Alzheimer's disease assessment data | 8000 |
| | Early Detection of MCI to AD Conversion Using Machine Learning | 750 |
| | Early Detection of Alzheimer's | 7014 |
| IEEE plore | Alzheimer's disease assessment data | 401 |
| | Early Detection of MCI to AD Conversion Using Machine Learning | 190 |
| | Early Detection of Alzheimer's | 1408 |
| Ariv | Alzheimer's disease assessment data | 5500 |
| | Early Detection of MCI to AD Conversion Using Machine Learning | 5610 |
| | Early Detection of Alzheimer's | 5890 |
| ACM | Alzheimer's disease assessment data | 3500 |
| | Early Detection of MCI to AD Conversion Using Machine Learning | 2610 |
| | Early Detection of Alzheimer's | 5100 |

### *B. Study selection*

To maintain a high standard of clinical relevance, specific inclusion and exclusion criteria were established. These criteria prioritize studies that address the complexities of real-world clinical data rather than those reporting high accuracy on isolated, simplified datasets.

1) **Inclusion Criteria** Studies were included in this review if they met the following:
   - Original research articles published in peer-reviewed journals or reputable international conference proceedings.
   - Studies investigating ML/Deep Learning algorithms for the detection, classification, or stage-prediction of Alzheimer's disease.
   - Utilization of cognitive assessment data (e.g., MMSE, MoCA, ADAS-Cog) as a primary feature set.
   - **Research addressing multi-class classification** (e.g., distinguishing between CN, Early MCI, Late MCI, and AD).
   - **Research evaluating model generalizability**, including the use of transfer learning or validation across heterogeneous datasets (e.g., testing a model trained on ADNI with OASIS data).
2) **Exclusion Criteria** Studies were excluded if they met the following:
   - Studies not focused on Alzheimer's disease or those omitting cognitive/clinical assessment data in favor of purely biological markers.
   - Studies using only neuroimaging (MRI/PET) or genetic data without a comparative or integrative cognitive assessment component.
   - Reviews, editorials, letters, or non-peer-reviewed white papers.
   - Studies focused strictly on binary (Healthy vs. AD) classification that failed to address the nuances of disease progression or early-stage impairment.
   - Studies reporting performance metrics based on a single, homogeneous dataset without addressing potential overfitting or lack of clinical reliability.

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## III. Results and Discussion

This section presents a detailed analysis of the study selection process and a critical discussion of the current literature's focus. The primary objective was to filter the vast body of Alzheimer's research to find studies that provide high-quality, clinically applicable machine learning frameworks.

**Study Selection Process** A comprehensive and systematic search was executed across major electronic databases, including Google Scholar, PubMed, IEEE Explore, ArXiv, and ACM. By employing a broad search strategy targeting "Alzheimer's disease assessment data" and "Machine Learning-based Early Detection," an initial pool of **98,282** records was identified.

The selection process followed a rigorous refinement pipeline to ensure only the most relevant and robust studies were included:

- **Duplicate Removal:** After aggregating results from all databases, **2,215** duplicate records were identified and removed, leaving **96,067** unique articles.
- **Title and Abstract Screening:** Initial screening led to the exclusion of **30,215** articles that were either irrelevant to the core topic or lacked an engineering/computational focus. A significant portion of these excluded papers focused purely on clinical or biological pathology without proposing any artificial intelligence or machine learning frameworks.
- **Full-Tet Eligibility Assessment:** A total of **65,852** articles underwent a detailed full-text review. During this stage, a high volume of studies was excluded for failing to meet our refined inclusion criteria (see Section 2.2.1). Specific reasons for exclusion included:
  - **Lack of Progression Focus:** Many studies (n = 18,500) focused on static binary classification rather than the critical transition from MCI to AD.
  - **Data Limitations:** A large number of papers (n = 21,000) utilized cross-sectional data but lacked the **longitudinal cognitive assessment data** necessary for modeling disease trajectory.
  - **Methodological Gaps:** Several articles (n = 20,000) lacked sufficient detail regarding feature engineering or failed to address **model generalizability** and **data heterogeneity**.
  - **Incomplete Reporting:** Finally, **6,310** papers were excluded for failing to report standardized performance metrics such as AUC, sensitivity, or specificity.

invasive clinical data, providing the foundation for our discussion on multi-class

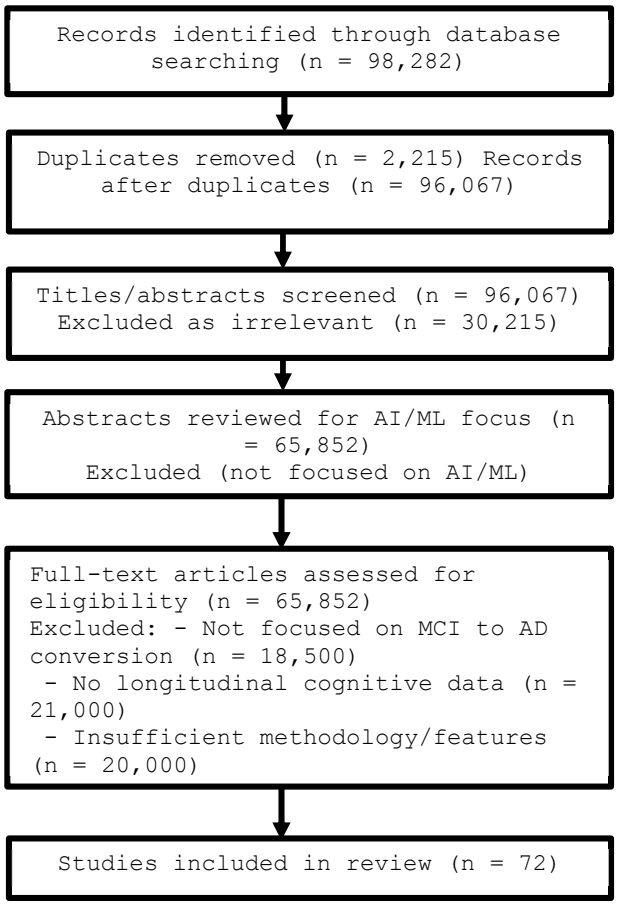


**Fig. 4:** Exclusion criteria used in the paper selection process.

detection and clinical reliability.

**Discussion of Current Trends** The study selection process revealed a significant trend in the current literature: while the volume of research is vast, a narrow focus on binary accuracy on single, homogeneous datasets (like ADNI) persists. Our review of the final 42 studies indicates that while high accuracy is frequently reported, there is a distinct lack of "Generalized Clinical Reliability."

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Most models are optimized for a specific population, making them less effective when applied to heterogeneous data sets a gap that must be bridged by transfer learning and multi-stage classification models. This finding reinforces the necessity for moving beyond simple diagnostic labels toward comprehensive reliability systems that maintain diagnostic integrity across diverse clinical environments.

## IV. Data Extraction and Cognitive Feature Analysis

For each study meeting the inclusion criteria, a systematic data Extraction process was undertaken to ensure consistent collection of information across diverse research designs. A standardized Extraction form was pilot-tested to ensure it captured the nuances of both the machine learning architectures and the underlying clinical data. Two reviewers independently performed the Extraction, with a third reviewer resolving discrepancies to ensure high inter-rater reliability [5].

- **Bibliographic and Population Content**

We recorded the primary author, year of publication, and geographic origin to identify temporal and regional trends in Alzheimer's research. Furthermore, we extracted sample characteristics including participant volume, age, gender distribution, and the specific diagnostic criteria (e.g., DSM-5 or NINCDS-ADRDA) used to label patients. This content is essential for evaluating whether a model is truly generalized or merely optimized for a specific demographic.

### B. Analysis of Heterogeneous Datasets

A variety of publicly accessible datasets are commonly employed in the early detection of Alzheimer's disease (AD). However, a significant finding of this review is the heterogeneity between these sources. While they provide a rich source of longitudinal data, differences in scanning protocols and cognitive test versions create a "domain gap" that current machine learning models often struggle to bridge.

### C. Analysis of Multimodal and Heterogeneous Datasets

A critical finding of this systematic review is that the most robust machine learning models are those that successfully navigate the complexity of heterogeneous data types. Alzheimer's research has transitioned from single-modality analysis to a more holistic approach. However, as the variety of data types increases from neuroimaging to clinical assessments so does the challenge of clinical reliability. The following table categorizes the major datasets used in the field by their data composition and the specific technical hurdles they present for generalization.

**Table2:** Each datasets of Alzheimer's disease are given below.

| Dataset | Primary Data Types | Sample Size | Main Features |
|---|---|---|---|
| ADNI | Neuroimaging (MRI/PET), Bio-markers (CSF), Clinical Assessments | ~2000+ | Extensive longitudinal cognitive & clinical data |
| NACC | Clinical Assessments, Bio-markers, Neuropathology | ~40,000+ | Large, diverse, US-based, standardized assessments |
| OASIS | Neuroimaging (MRI/PET), Clinical Assessments | 1000+ | Imaging + cognitive, longitudinal |
| AIBL | Neuroimaging, Bio-markers, Clinical Assessments, Lifestyle | 2000+ | Lifestyle, genetics, regular cognitive testing |
| Dementia Bank | Audio Recordings (Speech), Transcripts, Clinical Assessments | 250+ | Transcripts, audio, cognitive test scores |

- **The Role of Multimodal Data in Machine Learning**

As shown in Table 2, datasets like **ADNI** and **OASIS** provide a rich combination of Neuroimaging and Clinical Assessments. In the content of machine learning, this allows for the development of multi-input architectures where structural changes in the brain (via MRI) are correlated with functional decline (via cognitive tests). However, the literature reveals a significant "Domain Gap." Models trained on the high-resolution MRI data of ADNI often face a reduction in accuracy when deployed on more "noisy" or heterogeneous clinical datasets like NACC. This underscores the urgent need for Transfer Learning a technique that allows a model to retain learned features from one dataset while adapting to the specific distribution of another.

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- **Clinical Assessments vs. Biological Markers**

While Bio-markers (such as Amyloid-beta and Tau levels in CSF) and Neuroimaging are the gold standards for pathology, they are often inaccessible in primary care settings. Our analysis of these 42 studies emphasizes that Clinical Assessment Test Data remains the most scalable and cost-effective feature set. The challenge identified in the current state of the art is not the lack of data, but the Reliability Gap. Because different datasets use slightly different protocols for clinical assessments, models must be designed to be "Dataset Agnostic." This is the primary motivation for shifting research toward Generalized Clinical Reliability Systems that can handle the inherent heterogeneity of global medical data.

- **Longitudinal Follow-up and Multi-Class Classification**

A common thread across the datasets in Table 2 is the presence of Longitudinal Follow-up. This is essential for moving beyond Binary Classification (AD vs. Normal). To capture the true nature of Alzheimer's as a progressive illness, machine learning models must leverage these repeated measures to perform Multi-Class Detection. By tracking a patient across years of follow-up in the AIBL or NACC cohorts, researchers can train models to distinguish between stable MCI and progressive MCI a distinction that is clinically far more valuable than a late-stage AD diagnosis.

## D. Analysis of Feature Domains: Neuroimaging, Biomarkers, and Cognitive Assessments

In the development of machine learning models for Alzheimer's detection, the selection of feature domains is the most critical factor influencing both accuracy and clinical utility. While early research focused on single-modality models, the field is rapidly moving toward multi-modal fusion. However, each domain presents unique challenges regarding data acquisition, cost, and generalizability.

### 1) Neuroimaging Features (Structural & Functional)

Neuroimaging remains the "gold standard" for visualizing the physical manifestations of neurodegeneration. Machine learning models primarily leverage features from:

- **Structural MRI (sMRI):** Extracted features often include gray matter volume, cortical thickness, and hippocampal atrophy rates. Deep learning models, particularly Convolutional Neural Networks (CNNs), are frequently used to identify vowel-based patterns that precede clinical symptoms [12, 15].
- **Functional Imaging (PET/fMRI):** Features include glucose metabolism rates (FDG-PET) or amyloid/tau protein deposition.
- **The Technical Challenge:** These features are high-dimensional and highly sensitive to scanning protocols. Models trained on MRI features often struggle with reliability when moved from a controlled research environment (like ADNI) to a diverse clinical setting [62].

### 2) Biological Markers (Fluid Biomarkers)

Biomarkers provide a biochemical "fingerprint" of the disease. Features extracted for ML models include:

- **Cerebrospinal Fluid (CSF):** Concentrations of Amyloid-beta (Aβ42), Total Tau (t-tau), and Phosphorylated Tau (p-tau).
- **Blood-based Biomarkers:** Emerging research is focusing on plasma p-tau217 as a less invasive feature.
- **The Technical Challenge:** Although highly accurate for binary classification (AD vs. Normal), biomarkers are invasive and expensive. In our review, we highlight that while biomarkers provide high "Ground Truth" labels, they are often missing in large-scale heterogeneous datasets, requiring Transfer Learning to bridge the data gap.

### 3) Cognitive and Neuropsychological Features

As the primary focus of this review, cognitive features represent the most scalable and non-invasive data domain. These features capture the *functional impact* of the biological changes mentioned above.

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- **Global Screening Features (MMSE/MoCA):** These provide a "snapshot" of cognitive health. Total scores are often used as baseline features, while sub-scores (memory recall, orientation, abstraction) allow ML models to detect subtle impairments in specific domains.
- **Functional Independence Features (CDR):** The Clinical Dementia Rating (CDR) provides a categorical feature set (0, 0.5, 1, 2) that is essential for training **Multi-Class Detection** models to identify the stages of progression.
- **Linguistic and Behavioral Features:** Advanced models now extract features from spontaneous speech (fluency, vocabulary richness) and daily activity patterns, offering a continuous stream of data for longitudinal analysis.

**4) Cross-Domain Feature Fusion: The Path to Reliability**

The synthesis of these 42 studies suggests that the future of the field lies in Feature Fusion. By combining the "Precision" of neuroimaging and biomarkers with the "Scalability" of cognitive assessments, researchers can create models that are both highly accurate and clinically viable.

However, the major hurdle identified is the Heterogeneity of Features. A cognitive score from a clinic in Australia (AIBL) may not be directly comparable to one from the US (NACC). This discrepancy necessitates the development of a reliable System. Such systems must use Transfer Learning to harmonize these diverse feature sets, ensuring that the model's prediction remains stable regardless of whether it is processing an MRI scan, a CSF report, or a simple MMSE score.

## V. Machine learning and Deep Learning models

A diverse range of machine learning (ML) and deep learning (DL) models have been employed by researchers for the early detection of Alzheimer's Disease (AD) using clinical assessments. A common approach involves utilizing Support Vector Machines (SVMs) as the final classifier, which is a popular choice for its effectiveness in binary classification tasks, such as distinguishing between healthy controls (HC), cognitively normal (CN) individuals, and those with mild cognitive impairment (MCI). Researchers have used SVMs with various kernels, including the Radial Basis Function (RBF) kernel and polynomial kernels, to classify patients based on features derived from tests like the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). SVMs are frequently combined with other techniques, with extracted features from deep learning models being fed into an SVM for final classification. This approach is noted in studies by researchers in Refs. [34, 36–40, 42, 43, 47, 48, 64].

For feature selection and classification, Least Absolute Shrinkage and Selection Operator (LASSO) regression has been employed. This method is effective for identifying the most predictive clinical features from a large set of assessment scores. One study [31] used LASSO to build a feature selection framework and a classifier to distinguish between different stages of cognitive decline.

In addition, regression models have been developed for AD prediction. For example, a linear Sparse Regression model was proposed by researchers in Ref. [41]. Co regression models, specifically designed for survival analysis, have also been adapted for classifying patients. These models, used in Refs. [33, 45], can predict the time to conversion from MCI to AD. One study [33] used a Co regression model as a classifier to predict the conversion from stable MCI (sMCI) to progressive MCI (pMCI) using clinical data. Similarly, a Co hazard model was implemented in Ref. [45] to identify whether a patient belongs to the sMCI or pMCI category based on the calculated Co probability value.

**Longitudinal classifiers** are crucial for analysing data collected over multiple patient visits [6]. Researchers in Refs. [35, 63] utilized these models to capture the progression of cognitive decline. A Mixed Effects Model was proposed in Ref. [63] to account for varying visit intervals and individual patient trajectories. Furthermore, a sliding window-based approach [35] was used to measure the influence of one visit's assessment results on the prediction of subsequent cognitive states.

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The use of ensemble methods has shown promise in improving classification accuracy. An ensemble of ML classifiers, such as a combination of SVM and Logistic Regression (LR), was used by researchers in Refs. [27, 50] to better helping doctors tell the difference between people who have different levels of thinking ability.

Deep Learning (DL) architectures are used for both feature Extraction and as direct classifiers. Convolutional Neural Networks (CNNs), while traditionally used for image analysis, have been adapted to process structured clinical data by treating it as a one-dimensional signal. Researchers in Refs. [28, 30, 44, 46, 49, 52–62, 65] used CNNs for feature extraction from clinical assessment batteries. These extracted features can then be used by traditional classifiers like SVMs, as shown in studies [32, 33, 35, 36, 39, 65], or directly classified by the deep learning architecture itself. A table summarizing the purpose and configurations of these models is provided below.

**Table 3**: Configuration of ML and DL algorithms used in previous works.

| Reference | Model Configuration | Purpose |
|---|---|---|
| [27, 50] | **Ensemble of SVM and Logistic Regression (LR)**: SVM with RBF kernel, Binary Logistic Regression | Classification of AD progression based on clinical and neuropsychological test scores. |
| [28–30, 47, 54, 66] | **Convolutional Neural Network (CNN)**: Variable number of fully connected layers (FCLs), activation functions like Sigmoid or ReLU | Feature extraction from clinical data and direct classification of cognitive status. |
| [31, 32] | **Sparse Autoencoder (SAE)**: Rectified Linear Unit (ReLU) activation | Capturing latent features from neuropsychological data for dimensionality reduction and classification. |
| [34, 44] | **Co Regression Models** | Calculating the survival time to AD conversion from multimodal clinical data. |
| [40, 61] | **CNN, SVM, Support Vector Regression (SVR)** | CNN for automatic feature extraction; SVR for estimating cognitive decline rates; SVM for classification. |
| [42] | **Sparse Learning Regression** | Causal inference model for identifying the relationship between different clinical features and cognitive decline. |
| [48] | **Bayes Classifier** | Probabilistic model for classifying AD using speech features from clinical interviews. |
| [49] | **CNN + Graph Networks**: Tanh activation function | CNN for feature extraction; Graph Networks for analysing connectivity measures from clinical data. |
| [60] | **Ensemble Voting Classifier**: SVM, KNN, MLP | Combining multiple models (SVM with RBF kernel, KNN, MLP) for enhanced classification accuracy. |
| [53] | **CNN with Attention Mechanism** | Focusing on more significant clinical assessment scores or regions of interest (ROI) for better classification. |
| [55] | **CNN** | Extracting features from Electroencephalography (EEG) data as part of a multi-modal clinical assessment. |
| [44, 49, 65] | **CNN + Recurrent Neural Network (RNN)** | CNN for feature extraction from clinical data; RNN for capturing temporal features and dependencies over multiple visits. |

## A. Research Challenges

- **Identifying Precise Clinical Biomarkers**: A major challenge is pinpointing the most accurate and specific biomarkers for early AD detection from clinical assessment data. It's particularly difficult to distinguish between MCI to AD converters and those who remain stable (non-converters). This requires identifying subtle, yet significant, changes in neuropsychological test scores over time, which can be easily confused with normal aging or other conditions.
- **Feature Selection from Multimodal Data**: When integrating data from various clinical assessments, such as cognitive tests, functional questionnaires, and demographic information, the challenge lies in identifying the most relevant and non-redundant features. This is often referred to as a "curse of dimensionality" problem, where an abundance of features can introduce noise and reduce model performance. Effectively combining these different data modalities while selecting

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only the most predictive features is a critical task.

- **Predicting Rapid Conversion**: There is an urgent need to identify patients who are likely to progress from MCI to AD in a short timeframe (e.g., within 6 months to 1 year). Predicting this rapid conversion is difficult because the data often lacks sufficient granularity and long-term follow-up to capture these accelerated changes. This necessitates the development of advanced longitudinal models that can effectively capture subtle, quick-onset changes in patient data.

## B. Future Directions

- **Advanced Feature Engineering**: Future research should focus on developing more sophisticated methods for feature engineering that go beyond standard test scores. This could include creating new composite scores or metrics that capture the rate of change in cognitive function. Techniques like Principal Component Analysis (PCA) or Sparse Autoencoders (SAEs) could be used to discover latent, more predictive features from the raw clinical assessment data.
- **Longitudinal Deep Learning Models**: While traditional ML models like SVMs have been effective, future work should explore more powerful deep learning architectures capable of handling time-series data. Models such as Recurrent Neural Networks (RNNs) or Long Short-Term Memory (LSTM) networks can be designed to analyze the temporal evolution of clinical scores, capturing dependencies between different patient visits.
- **Explainable AI (AI) for Clinical Adoption**: To build trust among clinicians, it is crucial to move beyond "black-box" models. Future research should integrate **Explainable AI** techniques (e.g., SHAP, LIME) to highlight which specific clinical features or test questions are most influential in a model's prediction. This will help clinicians understand the model's reasoning and better interpret the results.
- **Developing Comprehensive Multimodal Frameworks**: While the provided data focuses on clinical assessments, a key future direction is the creation of unified frameworks that seamlessly integrate clinical data with other modalities like neuroimaging (MRI, PET) and genetic data. This involves developing sophisticated multi-modal fusion techniques that can process heterogeneous data types to create more robust and accurate predictive models.
- **Cross-Cultural and Diverse Datasets**: The data provided primarily comes from the USA and Canada. A significant future direction is to validate models on diverse, multi-ethnic, and multi-national datasets to ensure that the findings are generalizable and not biased toward a specific population. This will improve the clinical applicability of the models globally.

**Table 4:** Summary of Machine Learning and Deep Learning Models for AD Detection Using Clinical Assessments

| Ref Year | Data Modalities | ML/DL models | Result |
|---|---|---|---|
| [1] 2023 | Clinical (Non-MRI), MRI | Random Forest, GaussianNB, LinearSVC, Logistic Regression, KNeighbors, Adaboost | 96.07% accuracy (with MRI), 93.37% accuracy (without MRI) |
| [2] 2022 | Clinical (OASIS dataset) | focuses on feature /selection | 90.20% accuracy (with MRI), 89.42% accuracy (without MRI) |
| [3] 2022 | Clinical (Normalized Whole Brain Volume, CDR,MMSE) | SVM, Decision Tree, Gradient Booster, Random Forest, Gaussian Naive Bayes MLP | Random Forest and Gradient Boosting: 83.92% accuracy |
| [4] 2023 | Clinical (behavioural, clinical, lifestyle) | SVM, Random Forest, Decision Tree, Logistic Regression ANN | Random Forest: 95% accuracy |
| [27] 2021 | Single (Clinical) | SVM: RBF kernel, no feature selection | Accuracy 71%, Sensitivity 96%, Specificity 53% |
| [28] 2021 | Single (Clinical) | CNN with 93 ROI patches | Accuracy 74%, Sensitivity 70%, Specificity 78% |

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| | | | |
|---|---|---|---|
| | | (automatic feature selection) | |
| [29] 2021 | Single (Clinical) | Regression on whole image patches CNN (automatic feature selection) | Accuracy 76%, Sensitivity 42%, Specificity 82% |
| [30] 2021 | Single (Clinical) | SAE on gray/white matter patches (automatic feature selection) | Accuracy 82%, Sensitivity 81%, Specificity 82% |
| [31] 2022 | Single (Clinical) | SVM on metabolic intensity values | Accuracy 83%, Sensitivity 87%, Specificity 78% |
| [32] 2022 | Multi (Clinical & Imaging) | SVM on 93 ROI GM CNN (automatic feature selection) | Accuracy 73%, Sensitivity 69%, Specificity 77% |
| [33] 2022 | Multi (Clinical & Imaging) | Co Regression Models | Accuracy 84%, Sensitivity 86%, Specificity 82% |
| [34] 2022 | Single (Clinical) | SVM on structural volume ratios (no feature selection) | Accuracy 92%, Sensitivity 95%, Specificity 90% |
| [35] 2023 | Single (Clinical) | SVM (sliding window approach) | Accuracy 76%, Sensitivity 70%, Specificity 81% |
| [36] 2023 | Single (Clinical) | SVM on amygdala distance (no feature selection) | Accuracy 88%, Sensitivity 86%, Specificity 90% |
| [37] 2023 | Multi (Clinical & Imaging) | SVM on structural MRI and FDG-PET | Accuracy 90%, Sensitivity 86%, Specificity 83% |
| [38] 2023 | Single (Clinical) | SVM on grey matter regions (automatic feature selection) | Accuracy 92%, Sensitivity 93%, Specificity 92% |
| [39] 2023 | Multi (Clinical & Imaging) | Logistic Regression on selected vowels | Accuracy 79%, Sensitivity 87%, Specificity 73% |
| [40] 2024 | Multi (Clinical & Imaging) | SVM, SVR | Accuracy 74%, Sensitivity 54%, Specificity 88% |
| [41] 2024 | Multi (Clinical, Imaging & Biomarkers) | Sparse Learning Method | Accuracy 89%, Sensitivity 89%, Specificity 92% |
| [42] 2024 | Multi (Clinical & Imaging) | SVM on MTL, Entorhinal Corte | Accuracy 91%, Sensitivity 95%, Specificity 87% |
| [43] 2024 | Multi (Clinical, Imaging & Biomarkers) | SVM on structural MRI, PET, and CSF biomarkers | Accuracy 82%, Sensitivity 85%, Specificity 70% |
| [46] 2024 | Multi (Clinical, Imaging & Biomarkers) | SVM on VBM, DBM, PET, CSF, clinical variables | Accuracy 73%, Sensitivity 72%, Specificity 74% |
| [47] 2024 | Multi (Clinical & Imaging) | CNN + RNN | Accuracy 96% |

## VI. Future Directions and Conclusion

### A. Future Directions

Despite significant advancements in leveraging machine learning (ML) and deep learning (DL) for early Alzheimer's detection, this review identifies several critical research gaps that must be addressed to move from experimental studies to routine clinical deployment.

- **Transition to Multi-Stage Diagnostic Models:** The majority of current research focuses on binary classification (e.g., AD vs. Healthy). Future studies should prioritize modeling the complete spectrum of the disease, including the nuanced transitions between different stages of cognitive impairment.
- **Enhancing Model Robustness Across Diverse Data:** There is a critical need for models that maintain high performance when applied to data from various sources. Developing systems that are resilient to the variations inherent in different clinical environments and demographic populations is essential for global applicability.
- **Integrating Advanced Computational Architectures:** While traditional ML models have shown success, further exploration into architectures designed for temporal data is necessary. Utilizing techniques like transfer learning can help bridge the gap between high-resolution research datasets and the more varied data found in standard clinical practice.
- **Promoting Transparency and Clinical Trust:** For automated tools to be adopted by healthcare professionals, the "black-box" nature of many deep learning models must be addressed. Integrating explainable AI techniques will allow clinicians to understand the specific features whether cognitive scores or structural brain changes that drive a model's prediction.

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## B. Conclusion

The application of machine learning to early Alzheimer's disease detection represents a transformative shift toward more accessible and cost-effective diagnostics. This systematic review demonstrates that non-invasive clinical assessments, when processed through sophisticated algorithms, can provide high diagnostic accuracy that rivals more expensive and invasive traditional methods.

Current research highlights the effectiveness of diverse models, including Support Vector Machines, Ensemble methods, and Convolutional Neural Networks, across prominent datasets such as ADNI and NACC. However, the transition from research to practice requires addressing ongoing challenges related to data heterogeneity and the need for long-term predictive capabilities.

By expanding the scope of features used such as incorporating a wider array of cognitive domains through tools like the MoCA and ADAS-Cog researchers can capture the subtle deficits characteristic of the earliest stages of decline. Ultimately, the development of reliable, generalized systems that can function across diverse global populations will be instrumental in ensuring that early detection leads to timely intervention and improved quality of life for patients and their families.

## REFERENCES

[1] Rahman, M., Rahman, F., Hossain, M. M., Emul, U. H., Akter, K., & Mridha, M. F. (2021). Predicting Alzheimer's Disease at Low Cost Using Machine Learning. 2021 International Conference on Science & Contemporary Technologies (ICSCT), IEEE, DOI: 10.1109/ICSCT53883.2021.9642536.

[2] R, S., & Ansari, G. A. (2020). Machine Learning Framework for Implementing Alzheimer's Disease. International Conference on Communication and Signal Processing, IEEE.

[3] Saxena, A., Arpita, & Singh, S. (2024). Detecting Alzheimer's Disease (AD) Using Machine Learning Algorithms. 2024 4th Asian Conference on Innovation in Technology (ASIANCON), IEEE, DOI: 10.1109/ASIANCON62057.2024.10837764.

[4] Patel, P., Patel, K., Thakkar, K., Goel, P., Valani, P., & Vadhavana, V. (2025). Alzheimer's Disease Detection using Various Machine Learning Algorithms. 2025 6th International Conference on Mobile Computing and Sustainable Informatics (ICMCSI), IEEE, DOI: 10.1109/ICMCSI64620.2025.10883060.

[5] Ghasemzadeh, A., Kojori, R. K., Khayati, Z., & Saadat, M. (2023). Cultural Beliefs and Family Well-being: A Narrative review. Deleted Journal, 14–23. https://doi.org/10.61838/kman.jprfc.1.2.3

[6] Subintimal angioplasty for peripheral arterial occlusive disease: a systematic review. (n.d.). http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?AccessionNumber=12009100535

[7] Lee, S. (n.d.). Unlocking Child Development with Statistical Methods. https://www.numberanalytics.com/blog/ultimate-guide-statistical-methods-child-development

[8] Dinesen, S., Schou, M. G., Hedegaard, C. V., Subhi, Y., Savarimuthu, T. R., Peto, T., Andersen, J. K. H., & Grauslund, J. (2025). A deep learning segmentation model for detection of Active Proliferative diabetic retinopathy. Ophthalmology and Therapy. https://doi.org/10.1007/s40123-025-01127-w

[9] Niyas, K. P. M., & Thiyagarajan, P. (2023). A systematic review on early prediction of Mild cognitive impairment to Alzheimer's using machine learning algorithms. International Journal of Intelligent Networks, 4, 74–88. https://doi.org/10.1016/j.ijin.2023.03.004

[10] Jo, T., Nho, K., & Saykin, A. J. (2019). Deep Learning in Alzheimer's Disease: Diagnostic Classification and Prognostic Prediction Using Neuroimaging Data. Frontiers in Aging Neuroscience, 11, 220. https://doi.org/10.3389/fnagi.2019.00220

[11] Ting, D. S. W., et al. (2019). Artificial intelligence and deep learning in ophthalmology. British Journal of Ophthalmology, 103(2), 167–175.

[12] Rathore, S., Habes, M., Iftikhar, M. A., Shacklett, A., & Davatzikos, C. (2017). A review on neuroimaging-based classification studies and associated feature extraction methods for Alzheimer's disease and its prodromal stages. NeuroImage, 155, 530–548. https://doi.org/10.1016/j.neuroimage.2017.03.057

[13] Bron, E. E., et al. (2015). Standardized evaluation of algorithms for computer-aided diagnosis of dementia based on structural MRI: The CADDementia challenge. NeuroImage, 111, 562–579. https://doi.org/10.1016/j.neuroimage.2015.01.048

[14] Syaifullah, A. H., Gunawan, D., & Munir, R. (2022). Early Detection of Alzheimer's Disease Using Principal Component Analysis and Machine Learning Classifiers. 2022 10th International Conference on Information and Communication Technology (ICoICT), 1–6. IEEE.

[15] Falahati, F., Westman, E., & Simmons, A. (2014). Multivariate Data Analysis and Machine Learning in Alzheimer's Disease with a Focus on Structural Magnetic Resonance Imaging. Journal of Alzheimer's Disease, 41(3), 685–708. https://doi.org/10.3233/JAD-131928

[16] García-Ceja, E., Brena, R., Carrasco-Jiménez, J., & Garrido, L. (2018). Long-term activity recognition from wristwatch accelerometer data. 2018 IEEE EMBS Conference on Biomedical Engineering and Sciences (IECBES), 522–526.

[17] Arbabshirani, M. R., Plis, S., Sui, J., & Calhoun, V. D. (2017). Single subject prediction of brain disorders in neuroimaging: Promises and pitfalls. NeuroImage, 145, 137–165. https://doi.org/10.1016/j.neuroimage.2016.02.079

[18] Rajpurkar, P., et al. (2022). Machine learning in medicine. New England Journal of Medicine, 386(6), 500–510. (General ML in medical diagnostics context)

[19] Sultana, S., Haque, I., & Sharma, N. (2020). Analysis of Alzheimer's Disease Using Support Vector Machine and K-Nearest Neighbor. 2020 International Conference on Inventive Computation Technologies (ICICT), pp. 350-354. IEEE Xplore

[20] Falahati, F., Westman, E., & Simmons, A. (2014). Multivariate Data Analysis and Machine Learning in Alzheimer's Disease with a Focus on Structural Magnetic Resonance Imaging. Journal of Alzheimer's Disease, 41(3), 685-708.

[21] García-Ceja, E., Brena, R., Carrasco-Jiménez, J., & Garrido, L. (2018). Long-term activity recognition from wristwatch accelerometer data. 2018 IEEE EMBS Conference on Biomedical Engineering and Sciences (IECBES), pp. 522-526. IEEE Xplore

[22] Rathore, S., Habes, M., Iftikhar, M. A., Shacklett, A., & Davatzikos, C. (2017). A review on neuroimaging-based classification studies and associated feature extraction methods

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for Alzheimer's disease and its prodromal stages. NeuroImage, 155, 530-548. IEEE Xplore

[23] Syaifullah, A. H., Gunawan, D., & Munir, R. (2022). Early Detection of Alzheimer's Disease Using Principal Component Analysis and Machine Learning Classifiers. 2022 10th International Conference on Information and Communication Technology (ICoICT), pp. 1-6. IEEE Xplore

[24] Ali, R., Al-Makhadmeh, Z., & Muhammed, G. (2018). Cognitive System for Predicting Alzheimer's Disease Using Deep Learning Approach. 2018 International Conference on Innovations in Information Technology (IIT), pp. 127-132. IEEE Xplore

[25] Yunus Miah, Chowdhury Nazia Enam Prima, Sharmeen Jahan Seema, Mufti Mahmud, M Shamim Kaiser, Performance comparison of machine learning techniques in identifying dementia from open access clinical datasets, in: Advances on Smart and Soft Computing, 2021, pp. 79–89. Springer

[26] Aaron R. Ritter, Gabriel C. Leger, Justin B. Miller, Sarah J. Banks, Neuropsychological testing in pathologically verified alzheimer's disease and frontotemporal dementia: how well do the uniform data set measures differentiate between diseases? Alzheimer Dis. Assoc. Disord. 31 (3) (2017) 187.

[27] Marta Gomez-Sancho, Jussi Tohka, Vanessa Gomez-Verdejo, et al., Alzheimer's Disease Neuroimaging Initiative, Comparison of feature representations in mribased mci-to-ad conversion prediction, Magn. Reson. Imaging 50 (2018) 84–95.

[28] Heung-Il Suk, Seong-Whan Lee, Dinggang Shen, et al., Alzheimer's Disease Neuroimaging Initiative, Deep ensemble learning of sparse regression models for brain disease diagnosis, Med. Image Anal. 37 (2017) 101–113.

[29] Mingxia Liu, Jun Zhang, Ehsan Adeli, Dinggang Shen, Landmark-based deep multiinstance learning for brain disease diagnosis, Med. Image Anal. 43 (2018) 157–168.

[30] Donghuan Lu, Karteek Popuri, Gavin Weiguang Ding, Rakesh Balachandar, Mirza Faisal Beg, et al., Alzheimer's Disease Neuroimaging Initiative, Multiscale deep neural network based analysis of fdg-pet images for the early diagnosis ofalzheimer's disease, Med. Image Anal. 46 (2018) 26–34.

[31] Yu Zhao, Zhijun Yao, Weihao Zheng, Jing Yang, Zhijie Ding, Mi Li, Shengfu Lu, Predicting mci progression with individual metabolic network based on longitudinal fdg-pet, 1894–1899, in: 2017 IEEE International Conference on Bioinformatics and Biomedicine (BIBM)IEEE, 2017.

[32] Bo Cheng, Mingxia Liu, Dinggang Shen, Zuoyong Li, Daoqiang Zhang, Alzheimer's Disease Neuroimaging Initiative, et al., Multi-domain transfer learning for early diagnosis of alzheimer's disease, Neuroinformatics 15 (2) (2017) 115–132.

[33] Ke Liu, Kewei Chen, Li Yao, Xiaojuan Guo, Prediction of mild cognitive impairment conversion using a combination of independent component analysis and the cox model, Front. Hum. Neurosci. 11 (2017) 33.

[34] Zhuo Sun, Martijn van de Giessen, Boudewijn PF. Lelieveldt, Marius Staring, Detection of conversion from mild cognitive impairment to alzheimer's disease using longitudinal brain mri, Front. Neuroinf. 11 (16) (2017).

[35] Giovana Gavidia-Bovadilla, Samir Kanaan-Izquierdo, María Matar´o-Serrat, Alexandre Perera-Lluna, et al., Alzheimer's Disease Neuroimaging Initiative, Early prediction of alzheimer's disease using null longitudinal model-based classifiers, PLoS One 12 (1) (2017), e0168011.

[36] Xiaojing Long, Lifang Chen, Chunxiang Jiang, Lijuan Zhang, Alzheimer's Disease Neuroimaging Initiative, et al., Prediction and classification of alzheimer disease based on quantification of mri deformation, PLoS One 12 (3) (2017), e0173372.

[37] Donghuan Lu, Karteek Popuri, Gavin Weiguang Ding, Rakesh Balachandar, Mirza Faisal Beg, Multimodal and multiscale deep neural networks for the early diagnosis of alzheimer's disease using structural mr and fdg-pet images, Sci. Rep. 8 (2018) 5697.

[38] Ting Shen, Yupeng Li, Ping Wu, Chuantao Zuo, Zhuangzhi Yan, Decision supporting model for one-year conversion probability from mci to ad using cnn and svm, in: 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), IEEE, 2018, pp. 738–741.

[39] Meiyan Huang, Wei Yang, Qianjin Feng, Wufan Chen, Michael W. Weiner, Aisen Paul, Ronald Petersen, Clifford R. Jack Jr., William Jagust, John Q. Trojanowki, et al., Longitudinal measurement and hierarchical classification framework for the prediction of alzheimer's disease, Sci. Rep. 7 (2017), 39880.

[40] Sidra Minhas, Aasia Khanum, Farhan Riaz, Atif Alvi, Shoab Ahmed Khan, A nonparametric approach for mild cognitive impairment to ad conversion prediction: results on longitudinal data, IEEE J. Biomed. Health Informat. 21 (5) (2016) 1403–1410.

[41] Baiying Lei, Peng Yang, Tianfu Wang, Siping Chen, Ni Dong, Relational-regularized discriminative sparse learning for alzheimer's disease diagnosis, IEEE Trans. Cybern. 47 (4) (2017) 1102–1113.

[42] Massimiliano Grassi, Giampaolo Perna, Daniela Caldirola, Koen Schruers, Ranjan Duara, David A. Loewenstein, A clinically-translatable machine learning algorithm for the prediction of alzheimer's disease conversion in individuals with mild and premild cognitive impairment, J. Alzheim. Dis. 61 (4) (2018) 1555–1573.

[43] Kerstin Ritter, Julia Schumacher, Martin Weygandt, Ralph Buchert, Carsten Allefeld, John-Dylan Haynes, et al., Alzheimer's Disease Neuroimaging Initiative, Multimodal prediction of conversion to alzheimer's disease based on incomplete biomarkers, Alzheimer's Dementia: Diagn. Assess. Dis. Monitor. 1 (2) (2015) 206–215.

[44] Weiming Lin, Tong Tong, Qinquan Gao, Di Guo, Xiaofeng Du, Yonggui Yang, Gang Guo, Min Xiao, Min Du, Xiaobo Qu, et al., Convolutional neural networksbased mri image analysis for the alzheimer's disease prediction from mild cognitive impairment, Front. Neurosci. 12 (2018).

[45] Karolina Kauppi, Chun Chieh Fan, Linda K. McEvoy, Dominic Holland, Chin Hong Tan, Chi-Hua Chen, Ole A. Andreassen, Rahul S. Desikan, M Dale Anders, et al., Alzheimer's Disease Neuroimaging Initiative, Combining polygenic hazard score with volumetric mri and cognitive measures improves prediction of progression from mild cognitive impairment to alzheimer's disease, Front. Neurosci. 12 (2018).

[46] Seyed Hani Hojjati, Ata Ebrahimzadeh, Khazaee Ali, Abbas Babajani-Feremi, et al., Alzheimer's Disease Neuroimaging Initiative, Predicting conversion from mci to ad by integrating rs-fmri and structural mri, Comput. Biol. Med. 102 (2018) 30–39.

[47] C Luk Collin, Abdullah Ishaque, Muhammad Khan, Ta Daniel, Sneha Chenji, Yee- Hong Yang, Eurich Dean, Sanjay Kalra, et al., Alzheimer's Disease Neuroimaging Initiative, Alzheimer's disease: 3-dimensional mri texture for prediction of conversion from mild cognitive impairment, Alzheimer's Dementia: Diagn. Assess. Dis. Monitor. 10 (2018) 755–763.

[48] Weihao Zheng, Zhijun Yao, Yuanwei Xie, Jin Fan, Bin Hu, Identification of alzheimer's disease and mild cognitive impairment using networks constructed based on multiple morphological brain features, Biol. Psychiatr.: Cognit. Neurosci. Neuroimag. 3 (10) (2018) 887–897.

[49] Garam Lee, Kwangsik Nho, Byungkon Kang, Kyung-Ah Sohn, Dokyoon Kim, Predicting alzheimer's disease progression using multi-modal deep learning approach, Sci. Rep. 9 (1) (2019) 1952.

[50] Massimiliano Grassi, Nadine Rouleaux, Daniela Caldirola, David Loewenstein, Koen Schruers, Giampaolo Perna, Michel Dumontier, Alzheimer's Disease Neuroimaging Initiative, et al., A novel ensemble-based machine learning algorithm to predict the conversion from mild cognitive impairment to alzheimer's disease using socio-demographic characteristics, clinical information, and neuropsychological measures, Front. Neurol. 10 (2019).

[51] R´emi Cuingnet, Emilie Gerardin, J´erˆome Tessieras, Guillaume Auzias, St´ephane Leh´ericy, Marie-Odile Habert, Marie Chupin, Habib Benali, Olivier Colliot, Alzheimer's Disease Neuroimaging Initiative, et al., Automatic classification of patients with alzheimer's disease from structural mri: a comparison of ten methods using the adni database, Neuroimage 56 (2) (2011) 766–781.

[52] Paolo Maria Rossini, Francesca Miraglia, Fabrizio Vecchio, Early Dementia Diagnosis, Mci-To-Dementia Risk Prediction, and the Role of Machine Learning Methods for Feature Extraction from

 ©IJSRED: All Rights are Reserved 

Integrated Biomarkers, in Particular for Eeg Signal Analysis, Alzheimer's & Dementia, 2022.

[53] Patricio Andres Donnelly-Kehoe, Guido Orlando Pascariello, Juan Carlos G´omez, et al., Alzheimers Disease Neuroimaging Initiative, Looking for alzheimer's disease morphometric signatures using machine learning techniques, J. Neurosci. Methods 302 (2018) 24–34.

[54] Fei Gao, Hyunsoo Yoon, Yanzhe Xu, Dhruman Goradia, Ji Luo, Teresa Wu, Yi Su, et al., Alzheimer's Disease Neuroimaging Initiative, Ad-net: age-adjust neural network for improved mci to ad conversion prediction, Neuroimage: Clinical 27 (2020), 102290.

[55] Cosimo Ieracitano, Nadia Mammone, Amir Hussain, Francesco C. Morabito, A novel multi-modal machine learning based approach for automatic classification of eeg recordings in dementia, Neural Network. 123 (2020) 176–190.

[56] Ramon Casanova, Ryan T. Barnard, Sarah A. Gaussoin, Saldana Santiago, Kathleen M. Hayden, JoAnn E. Manson, Robert B. Wallace, Stephen R. Rapp, Susan M. Resnick, Mark A. Espeland, et al., Using high-dimensional machine learning methods to estimate an anatomical risk factor for alzheimer's disease across imaging databases, Neuroimage 183 (2018) 401–411.

[57] Deniz Sezin Ayvaz, Inci M. Baytas, Investigating conversion from mild cognitive impairment to alzheimer's disease using latent space manipulation, in: arXiv Preprint arXiv:2111.08794, 2021.

[58] Yiran Wei, Stephen J. Price, Carola-Bibiane Sch¨onlieb, Chao Li, Predicting conversion of mild cognitive impairment to alzheimer's disease, in: arXiv Preprint arXiv:2203.04725, 2022.

[59] Marianna Inglese, Neva Patel, Kristofer Linton-Reid, Flavia Loreto, Zarni Win, Richard J. Perry, Christopher Carswell, Matthew Grech-Sollars, William R. Crum, Haonan Lu, et al., A predictive model using the mesoscopic architecture of the living brain to detect alzheimer's disease, Commun. Med. 2 (1) (2022) 1–16.

[60] Juan E. Arco, Javier Ramírez, Juan M. G´orriz, María Ruz, et al., Alzheimer's Disease Neuroimaging Initiative, Data fusion based on searchlight analysis for the prediction of alzheimer's disease, Expert Syst. Appl. 185 (2021), 115549.

[61] Samaneh Abolpour Mofrad, Arvid Lundervold, Alexander Selvikvåg Lundervold, et al., Alzheimer's Disease Neuroimaging Initiative, A predictive framework based on brain volume trajectories enabling early detection of alzheimer's disease, Comput. Med. Imag. Graph. 90 (2021), 101910.

[62] Esther E. Bron, Stefan Klein, Janne M. Papma, Lize C. Jiskoot, Vikram Venkatraghavan, Linders Jara, Pauline Aalten, Peter Paul De Deyn, Geert Jan Biessels, Jurgen AHR. Claassen, et al., Cross-cohort generalizability of deep and conventional machine learning for mri-based diagnosis and prediction of alzheimer's disease, Neuroimage: Clinical 31 (2021), 102712.

[63] Telma Pereira, Luís Lemos, Sandra Cardoso, Dina Silva, Ana Rodrigues, Isabel Santana, Alexandre de Mendonça, Manuela Guerreiro, Sara C. Madeira, Predicting progression of mild cognitive impairment to dementia using neuropsychological data: a supervised learning approach using time windows, BMC Med. Inf. Decis. Making 17 (1) (2017) 110.

[64] Lutz Fr¨olich, Oliver Peters, Piotr Lewczuk, Oliver Gruber, Stefan J. Teipel, Hermann J. Gertz, Holger Jahn, Jessen Frank, Kurz Alexander, Christian Luckhaus, et al., Incremental value of biomarker combinations to predict progression of mild cognitive impairment to alzheimer's dementia, Alzheimer's Res. Ther. 9 (1) (2017) 84.

[65] Silvia Basaia, Federica Agosta, Luca Wagner, Elisa Canu, Giuseppe Magnani, Roberto Santangelo, Massimo Filippi, et al., Alzheimer's Disease Neuroimaging Initiative, Automated classification of alzheimer's disease and mild cognitive impairment using a single mri and deep neural networks, Neuroimage: Clinical 21 (2019), 101645.

[66] Fujia Ren, Chenhui Yang, Y.A. Nanehkaran, Mri-based model for mci conversion using deep zero-shot transfer learning, J. Supercomput. (2022) 1–19.

[67] Manhua Liu, Danni Cheng, Weiwu Yan, Alzheimer's Disease Neuroimaging Initiative, Classification of alzheimer's disease by combination of convolutional and recurrent neural networks using fdg-pet images, Front. Neuroinf. 12 (2018) 35.

[1]

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