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Artificial Intelligence and Machine Learning in Early Detection and Prediction of Mild Cognitive Impairment (MCI): A Comprehensive Review

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Abstract: Mild Cognitive Impairment (MCI) is in an intermediate state between normal aging and dementia, the early detection of which is particularly important for early treatment and better prognosis. Recent developments in Artificial Intelligence (AI) and Machine Learning (ML) have indeed considerably improved the capabilities of detecting subtle cognitive, behavioral and neurobiological alterations linked to MCI. In this comprehensive review, we analyze the recent AI and ML methods employed in predicting MCI as well as detecting MCI and cover implementations of artificial intelligence assisted disease detection from supervised learning, unsupervised learning to deep learning models across various heterogeneous datasets like neuroimaging, cognitive assessment scores, speech patterns, genetic biomarkers data a-3 nd digital behavioral data. Mild Cognitive Impairment (MCI) is in an intermediate state between normal aging and dementia, the early detection of which is particularly important for early treatment and better prognosis. Recent developments in Artificial Intelligence (AI) and Machine Learning (ML) have indeed considerably improved the capabilities of detecting subtle cognitive, behavioral and neurobiological alterations linked to MCI. In this comprehensive review, we analyse the recent AI and ML methods employed in predicting MCI as well as detecting MCI and cover implementations of artificial intelligence assisted disease detection from supervised learning, unsupervised learning to deep learning models across various heterogeneous datasets like neuroimaging, cognitive assessment scores, speech patterns, genetic biomarkers data a-3 nd digital behavioral data.

This review also points out obstacles—such as data inconsistency, small dataset sizes, bias in algorithms, and difficulty in interpreting models—that impede clinical application. Nonetheless, existing trends suggest significant potential for AI-driven systems to assist healthcare providers, improve screening processes, and facilitate real-time monitoring via digital health instruments. In the end, AI and machine learning present hopeful opportunities for early identification, prognosis, and prevention of mild cognitive impairment, aiding in more effective long-term management of cognitive health.

Keywords: *Artificial Intelligence, Machine Learning, Mild Cognitive Impairment, Early Detection, Prediction Models, Neuroimaging.*

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I. INTRODUCTION

Having mild cognitive impairment (MCI) increases the likelihood of acquiring Alzheimer's disease (AD), a stage between dementia and normal aging. Memory loss that is somewhat worse than what is normally anticipated with normal aging but does not yet fulfill the criteria for dementia 1 characterizes this preclinical period, which is called moderate cognitive impairment. In 2021, 57 million people were impacted by dementia, according to the World Health Organization. Within the next 30 years, experts anticipate a fourfold increase in this figure. A recent systematic analysis including 66 studies confirmed a prevalence of around 15% for MCI overall. The same research also found that between

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the ages of 60 and 80, the frequency of MCI rises by 10%. It is common for people to have mild cognitive impairment (MCI) as they age, a transitional state between the more severe deterioration seen in dementia (especially Alzheimer's disease) and the natural aging process. Disabilities in thinking, reasoning, and memory that are measurable but not severe enough to significantly hinder daily functioning characterize this condition. 4 It is critical to identify MCI early on because timely treatment may improve patients' quality of life, slow disease progression, and ease clinical decision-making. However, conventional diagnostic methods like clinical assessments, neuropsychological testing, and neuroimaging sometimes have issues with subjectivity, high cost, and the delayed identification of minor cognitive abnormalities. 5 A number of game-changing technologies, including AI and ML, have recently surfaced in the healthcare industry. Advanced analytical capabilities provided by these technologies allow for the discovery of complex patterns in large, multidimensional datasets. The use of these technologies opens up new possibilities for improving the accuracy, timeliness, and dependability of MCI diagnosis and prediction. 6 When it comes to identifying early signs of cognitive decline, machine learning models like decision trees, ensemble methods, support vector machines, and deep learning frameworks have proven to be incredibly effective. These models analyze data from a wide range of sources, including EEG signals, genetic markers, electronic health records, speech patterns, MRI and PET scans, and behavioural data from digital devices. 7The integration of AI and ML in MCI research is driven by the need for non-invasive, cost-effective, and scalable diagnostic approaches that can be used to different populations. Predictive models trained on longitudinal datasets may evaluate minute changes over time, allowing clinicians to estimate the development from mild cognitive impairment to Alzheimer's disease. Furthermore, AI-enabled systems can automate complex image processing, decrease diagnostic variability, and assist personalized treatment approaches by identifying patient-specific risk factors. 8 Despite significant advancements, there are still challenges to using AI and ML for MCI diagnosis and prediction. These include concerns with dataset heterogeneity, model interpretability, ethical considerations, and the need for clinical validation. But more and more studies show that they can revolutionize cognitive healthcare and early diagnosis paradigms.9 New advances in neuroimaging analytics lend credence to the idea of using AI for early identification of MCI. Neuroimaging is crucial for understanding the brain changes associated with cognitive impairment, both anatomically and functionally. Intricate patterns distributed throughout the brain may easily go unnoticed by conventional image analysis methods that depend on predefined region-of-interest procedures or manual segmentation.10 Autonomous feature extraction from high-dimensional imaging data allows AI-based image analysis, particularly deep convolutional neural networks, to identify MCI rapidly and reliably. Through the use of these methods, biomarkers such as cortical thinning, hippocampus shrinkage, ventricular enlargement, and disrupted connectivity have been identified in critical brain networks associated with memory, executive function, and attention. Functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scans have also been enhanced by advancements in artificial intelligence, enabling for more precise mapping of metabolic abnormalities, amyloid accumulation, and abnormal connectivity patterns. 11 The use of biomarkers related to language and speech to evaluate cognitive function is an exciting new area of research.12 Many aspects of cognitive processes, including memory, processing speed, attention, and executive function, may be gleaned from spoken language. Natural language processing (NLP) and artificial intelligence (AI) models may analyze patterns in narrative, visual description, or spontaneous speech to identify moderate cognitive impairment (MCI) in its early stages. Indicators such as a lack of vocabulary diversity, increased pauses, difficulty recovering words, and simplified syntax are the main focus of these assessments. This extensive study examines the present state of artificial intelligence and machine learning methods for the early diagnosis and prediction of myocardial infarction (MCI), assesses their relative merits, and proposes avenues for further investigation to enhance the precision of diagnostics and their practical use in clinical settings. 13

II. MILD COGNITIVE IMPAIRMENT (MCI)

A clinical condition known as mild cognitive impairment (MCI) is defined as a noticeable decrease in cognitive ability that goes beyond what is typical with age, but is not severe enough to greatly impact everyday functioning. Persons with MCI nonetheless manage to carry out most of their daily tasks on their own, despite the fact that they have noticeable difficulties with memory, focus, language, and solving problems. Mild cognitive impairment (MCI) is considered a stepping stone between normal aging and advanced neurodegenerative diseases like Alzheimer's and dementia. People with mild cognitive impairment are more likely to develop dementia than those with normal cognitive function; however, this does not always happen to all people with MCI. 14.

➢ *Classification of Mild Cognitive Impairment (MCI).*

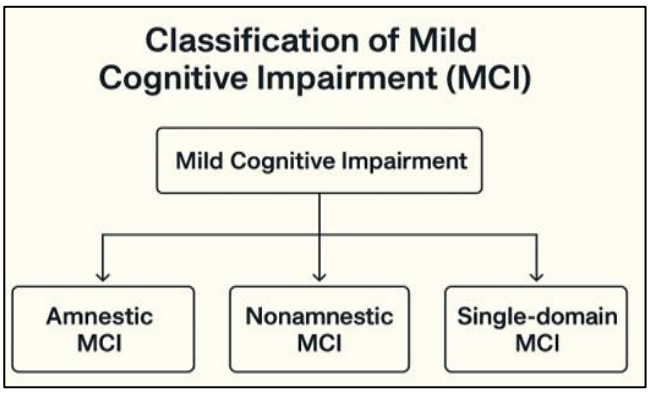

Fig 1(A) Classification of Mild Cognitive Impairment (MCI).

- *Amnestic Mild Cognitive Impairment (aMCI).*

Amnestic mild cognitive impairment (aMCI) is a subtype of mild cognitive impairment, the most prominent and serious of which is a memory impairment. Learning new

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knowledge, recalling recent events, or gaining new skills proves to be more challenging than expected for those with aMCI, even when other cognitive functions like as language, logic, and attention may largely remain unaltered.

Clinical examinations are necessary to determine if a patient with amnestic mild cognitive impairment may continue independently handle their daily activities, but only if their memory problems are severe enough. A higher chance of developing Alzheimer's disease is strongly connected with aMCI, making this subtype very important. fifteen, sixteen.

➢ *Non-Amnestic Mild Cognitive Impairment (naMCI).*

A kind of mild cognitive impairment called non-amnestic mild cognitive impairment (naMCI) is defined by measurable decline in cognitive abilities in areas other than memory, including executive functioning, attention, language, and visuospatial skills. Unlike amnestic MCI, the primary drawbacks of naMCI do not include significant memory loss.

People with non-amnestic MCI are still able to do most things on their own, even if they may have trouble with things like planning, judgment, understanding visual information, and paying attention. Dementia with Lewy bodies (DLB), vascular dementia, and frontotemporal dementia (FTD) are non-Alzheimer's dementias that are more often associated with this kind of mild cognitive impairment (MCI).17

III. CLINICAL ASSESSMENT CHALLENGES

Identifying mild cognitive impairment (MCI) at an early stage is crucial for preventing or delaying the progression of Alzheimer's disease and other forms of dementia. Although artificial intelligence (AI) and machine learning (ML) techniques offer superior predictive abilities compared to traditional methods, their effectiveness, reliability, and use in clinical settings are limited by several challenges in clinical evaluation. These challenges stem from the difficulties of incorporating AI models into healthcare systems, constraints within diagnostic processes, and the inconsistencies found in cognitive assessments.18

➢ *Clinical Diagnosis Subjectivity and Variability*

Conventional clinical diagnoses of Mild Cognitive Impairment (MCI) primarily rely on:

- Neuropsychological evaluations (such as MMSE, MoCA, etc.)
- Assessment by physicians
- Self-reports from patients

➢ *Challenges*

- Variability among clinicians: Different physicians may interpret symptoms in various ways.
- Subjective evaluation: Cognitive tests can produce inconsistent outcomes based on the patient's mood, effort, literacy level, or the testing environment.19

➢ *Heterogeneity of MCI Presentation*

MCI is not a singular, uniform condition.

- *Variability Includes:*

✓ Amnestic versus non-amnestic MCI
✓ Single-domain compared to multi-domain impairment
✓ Varying rates of progression

- *Impact on AI Models:*

✓ Algorithms face challenges in generalizing across diverse symptoms.
✓ Clinical datasets do not encompass all MCI subtypes, which diminishes model robustness.

The absence of standardized clinical definitions complicates the development and validation of models.21

➢ *Limited Sensitivity of Cognitive Tests*
- *Standard Assessment Tools Such as:*

✓ MMSE
✓ MoCA
✓ Clock Drawing Test may not effectively identify very early cognitive changes.

- *Problems:*

✓ Ceiling effects (high-functioning individuals may seem "normal")
✓ Insensitivity to subtle declines in memory or executive function
✓ Cultural and language biases

ML models that rely on these tests inherit their limitations, which reduces detection accuracy in real-world populations.22

➢ *Lack of Large, High-Quality, Clinically Verified Datasets*

AI/ML systems necessitate extensive datasets with dependable labels. However:

- *Challenges:*

✓ Clinical MCI diagnosis is costly, time-consuming, and frequently inconsistent.
✓ Most datasets (e.g., ADNI) consist of well-controlled research samples rather than real-world patients.
✓ Data imbalance: very few patients transition from MCI to dementia.
✓ Privacy and ethical issues restrict data sharing.

- *This Impacts:*

✓ Training effectiveness
✓ Model generalization
✓ Reproducibility of results.23

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IV. ROLE OF ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN MCI DETECTION

Artificial intelligence (AI) and machine learning (ML) have become revolutionary tools for the early detection and prediction of mild cognitive impairment (MCI), which often precedes dementia and Alzheimer's disease.AI/ML algorithms are capable of identifying concealed patterns within extensive and complex datasets significantly faster and more accurately than conventional diagnostic methods, which often overlook subtle cognitive changes in their initial stages.24

➢ *Typical Algorithms for Machine Learning*

- Support Vector Machines (SVM): Ideal for high-dimensional features in limited datasets.
- Random Forests (RF): They effectively handle heterogeneous data and are both robust and interpretable.
- Logistic regression serves as a fundamental statistical method for comparison.
- k-Nearest Neighbors (k-NN): This simpler method was utilized in early studies.25

➢ *Support Vector Machines (SVMs)*

One common and effective machine learning approach in the field of Mild Cognitive Impairment (MCI) study is Support Vector Machines (SVMs). These models are particularly useful for computer-aided diagnosis and neuroimaging data-based forecasting. They help in identifying which mild cognitive impairment (MCI) patients are at risk for developing Alzheimer's disease (AD) and in differentiating MCI patients from healthy controls (HC).

➢ *Function and use in MCI*

- Categorization: SVMs are predominantly employed as classifiers in MCI. They categorize individuals into predefined groups (e.g., MCI vs. HC or MCI converters vs. non-converters) by examining complex, high-dimensional data, like characteristics derived from structural or functional Magnetic Resonance Imaging (MRI) scans.
- Predictive Modeling: SVMs can create models that estimate a patient's prognosis, such as the likelihood that an MCI patient will develop AD dementia, by training on datasets from initiatives like the Alzheimer's Disease Neuroimaging Initiative (ADNI).
- Managing High-Dimensional Data: SVMs excel in handling datasets that encompass numerous features.26

➢ *K-Nearest Neighbors (k-NN)*

One kind of supervised machine learning, the K-Nearest Neighbors (k-NN) algorithm, is extensively used for the diagnosis and prediction of Mild Cognitive Impairment (MCI), which is often regarded as an early stage of Alzheimer's disease (AD). Using inputs like neuroimaging and genetic data, k-NN aids in this context in differentiating between healthy people, those with MCI, and AD patients.

- Convolutional Neural Networks (CNNs): Highly effective for analyzing MRI/PET images and identifying structural changes in the brain.
- Recurrent Neural Networks (RNNs), LSTMs: Employed for longitudinal data such as cognitive scores over time.
- Autoencoders: Detect latent features associated with cognitive impairment.
- Transformers: Emerging models for the multimodal integration of neuroimaging and non-imaging data.

V. AI APPLICATIONS IN MCI EARLY DETECTION

➢ *Magnetic Resonance Imaging (MRI)*

Magnetic Resonance Imaging (MRI) is a non-invasive technology for neuroimaging that combines high magnetic fields and radio waves to obtain complete pictures of the brain's structure and function. It plays a significant role in recognizing and assessing Mild Cognitive Impairment (MCI) and Alzheimer's disease, since it may detect subtle changes in the brain far before clinical symptoms show.

➢ *Positron Emission Tomography (PET).*

Positron Emission Tomography (PET) is an advanced neuroimaging method used to examine the brain's metabolic processes and molecular changes. In the realm of Mild Cognitive Impairment (MCI), PET plays a crucial role in detecting early biomarkers associated with neurodegeneration, even before structural changes in the brain become apparent.

➢ *Prediction of MCI Conversion to Dementia*

As people age, the likelihood of experiencing cognitive decline increases. With the ongoing rise in life expectancy, the number of individuals affected by cognitive impairment is also expected to grow. Mild cognitive impairment (MCI) is a phase where people encounter challenges in remembering specific details.

➢ *Longitudinal Data Modeling*

Longitudinal data modeling in Mild Cognitive Impairment (MCI) entails utilizing data gathered from the same individuals across various time points to monitor disease progression, identify biomarkers, and forecast the future risk of transitioning to Alzheimer's disease (AD). These methodologies have demonstrated superiority over single-timepoint (cross-sectional) analyses by effectively capturing the dynamic nature and individual trajectories of the disease.

- *Key Concepts*

✓ Longitudinal Data: Repeated measurements (e.g., cognitive scores, MRI scans, biomarkers) obtained from the same subjects over time.
✓ MCI Heterogeneity: MCI is a heterogeneous condition; some individuals progress to AD, while others remain stable, and some may even revert to normal cognition. Longitudinal models assist in identifying these distinct subtypes and their unique progression patterns.

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- ✓ Prediction of Progression: A primary objective is to predict which MCI patients are most likely to advance to AD (MCI converters or MCIc) as opposed to those who remain stable (MCI non-converters or MCInc), facilitating earlier, targeted interventions.

- *Common Modeling Methods*

Longitudinal Data in MCI Research is Modeled Using Both Classic Statistical Methods and Innovative Machine Learning Approaches:

✓ *Models Using Linear Mixed Effects (LME):*

Analysis of data with missing or irregularly timed elements makes heavy use of these statistical models. Group variations in atrophy rates may be better understood when they are able to distinguish between population-average trends and individual-specific deviations (random effects) in measurements like hippocampus volume or entorhinal cortex thickness.

✓ *Machine Learning Using Long Short-Term Memory (LSTM):*

A specialized kind of RNN that is very good at processing sequential input and capturing intricate relationships between different times. In comparison to more conventional approaches, models that use a combination of demographics, neuropsychological testing, and neuroimaging to predict the development of mild cognitive impairment (MCI) to Alzheimer's disease (AD) have shown much better accuracy.27

➢ *Multimodal Fusion Models*

One independent risk factor for cerebral ischemia is intracranial arterial stenosis (ICAS), the most common kind of which is middle cerebral artery (MCA) stenosis. Cognitive impairments may develop as a consequence of brain shrinkage and neurodegeneration brought on by intracranial ischemia injury caused by chronic constriction of brain arteries. As a transitional state between healthy aging and dementia, mild cognitive impairment (MCI) occurs. A battery of tests, including the AD8, the MoCA, and the MMSE, are used to diagnose mild cognitive impairment (MCI). The diagnostic outcomes could differ among these scales since they evaluate cognitive function using somewhat varied standards and methodologies. In addition, the assessor's biases and experiences might impact the scoring criteria and results of these scales, which could result in missing or wrong diagnoses.Characteristics and manifestations of MCI vary across demographic subsets. Age, cultural background, and degree of education are some of the factors that might affect how accurate assessment results are. In order to ensure early identification and prompt treatment, it is necessary to investigate sophisticated diagnostic and analytical procedures for MCI. This research bears great therapeutic value. Multimodal magnetic resonance imaging (MRI) has allowed for the discovery of more objective disease indicators for computer-assisted MCI diagnosis, thanks to developments in imaging technology. When you have a structural MRI of the brain, you can see where the white and gray matter have shrunk. By using blood oxygen level-dependent (BOLD) signals, which are an indirect measure of brain activity, resting-state functional magnetic resonance imaging (rs-fMRI) may identify deficits in brain function in individuals with mild cognitive impairment (MCI). White matter fiber tract integrity and orientation may be investigated using diffusion tensor imaging (DTI), which tracks the Brownian motion of water molecules in brain tissues to reflect tissue architecture and pathological alterations.White matter characteristics, such as anisotropy scores (FA) and mean diffusivity (MD), change significantly between healthy persons and patients with MCI. There are limits to depending on a single modality to discover imaging signals and comprehend illness features, notwithstanding the benefits of these approaches. By integrating complementing data from several modalities, multimodal MRI improves illness diagnosis via the identification of subtle structural brain alterations. Consequently, a number of research on MCI have brought together functional and structural connection networks, showing that multimodal imaging-derived network properties are useful for MCI diagnosis. One example is the use of hyper-graph-based sparse canonical correlation analysis (HGSCCA) to combine several modalities, including as genetic, epigenomic, and neuroimaging data, in order to uncover relevant biomarkers associated to MCI. For conversion employing imperfect multi-modal neuroimaging data, Joint Neuroimaging Synthesis Representation Learning (JSRL) is suggested since it outperforms several sophisticated algorithms for MCI cross-database synthesis. Feature selection methods, such as an integrated multi-modal multi-classification prediction model, have also been created to precisely diagnose and forecast the development of MCI. The suggested feature selection technique using a multikernel support vector machine (MK-SVM) demonstrated better classification capabilities than the most recent multimodality-based methods. Using rs-fMRI and DTI, another research built a functional brain network (FBN) and a structural brain network (SBN). We achieved diagnosis accuracies surpassing 84.80% when discriminating between normal controls and patients with subjective cognitive impairment with MCI by combining these structural and functional connectivity indicators with an automated weighted centralized multitasking learning framework. This provides strong evidence that networks formed by multimodal imaging might be very useful in MCI diagnosis and classification. 28.

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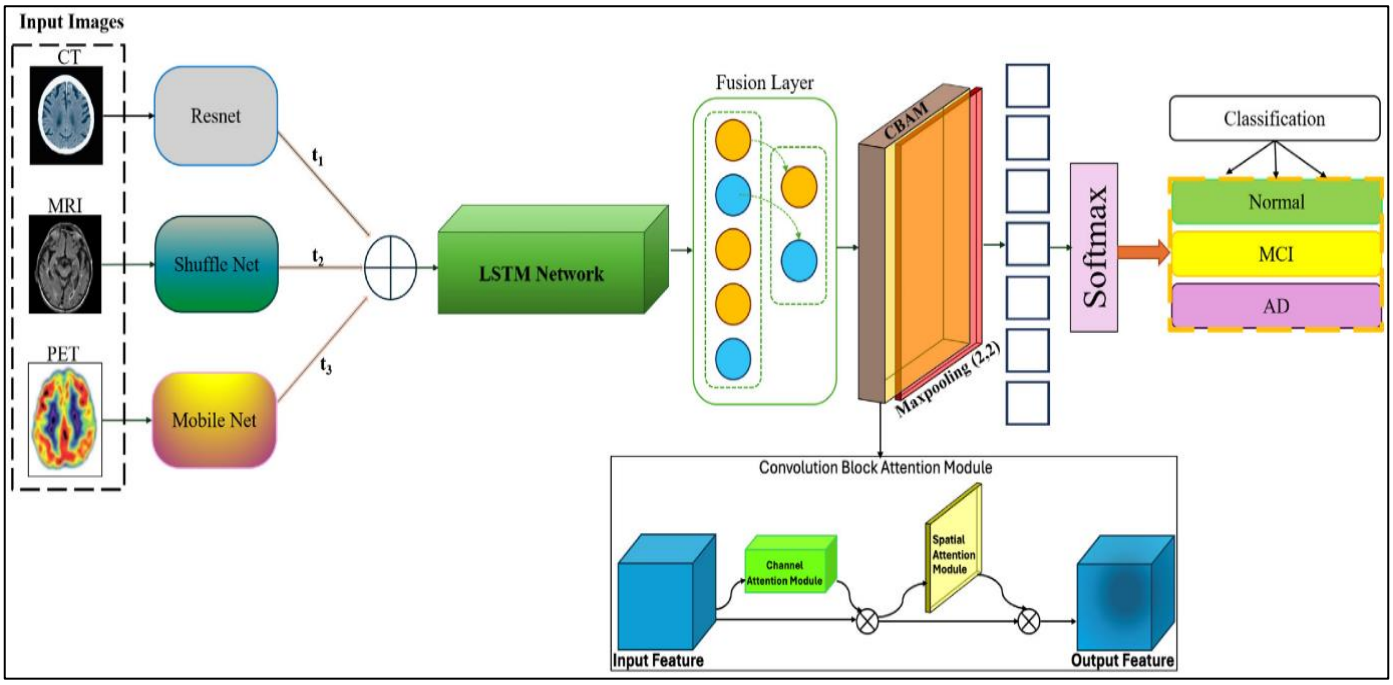

Fig 2 Multimodal Fusion Models

➢ *Datasets Commonly Used:*

- *ADNI (Alzheimer's Disease Neuroimaging Initiative):*

In 2004, a multi-center study called the Alzheimer's Disease Neuroimaging Initiative (ADNI) began with the goal of creating and validating imaging, genetic, clinical, and biochemical biomarkers that could be used to detect and track mild cognitive impairment (MCI) and Alzheimer's disease (AD) at an early stage. Participants range from healthy older adults to those with mild cognitive impairment (MCI) and Alzheimer's disease (AD)—thousands of people are being tracked in this longitudinal study. This joint effort between the NIH and prominent academic and pharmaceutical institutions integrates data from a wide range of sources, including magnetic resonance imaging (MRI) and positron emission tomography (PET) scans, cognitive and neuropsychological tests, biomarkers found in cerebrospinal fluid (CSF), blood samples, and genetic information. Thanks to this linkage, scientists can track the evolution of diseases quite precisely.Due to the fact that all datasets are publicly accessible to academics worldwide, ADNI is among the most significant and frequently used databases in the fields of machine learning and neuroscience. A number of areas have benefited substantially from ADNI, including the creation of AI-based diagnostic tools, the understanding of early AD pathology, and the creation of prediction models to identify individuals at high risk of dementia (31). Studying healthy older persons, those with moderate cognitive impairment (MCI), and those with Alzheimer's disease, the Alzheimer's Disease Neuroimaging Initiative (ADNI) covers a wide range of topics over the course of several years and locations. Various clinical and psychometric tests, as well as magnetic resonance imaging (MRI), (18F)-fluorodeoxyglucose positron emission tomography (FDG PET), and biomarkers from cerebrospinal fluid (CSF) and urine are collected at various intervals. We will ensure that all collected data is linked and accessible to the wider scientific community. The purpose of this study is to provide an account of the MRI techniques used by ADNI. The ADNI MRI core established requirements that were used to guide the development of the protocols. A substantial effort was made to evaluate 3D T1-weighted sequences for morphometric analysis. A small-scale clinical investigation examined many versions of this sequence after they were optimized for the relevant manufacturing platforms. In order to detect disease, the ADNI research uses a technique that involves using B1-calibration pictures when needed, sequential 3D magnetization prepared rapid gradient echo (MP-RAGE) scans, and an axial proton density-T2 dual contrast fast spin echo/turbo spin echo (FSE/TSE).30

- *Open Access Series of Imaging Studies (OASIS):*

As part of its mission, the Open Access Series of Imaging Studies (OASIS) aims to make available to researchers brain imaging datasets at no cost. Similar to the Alzheimer's Disease Neuroimaging Initiative (ADNI), this initiative intends to compile and openly share these datasets to aid future progress in scientific and clinical neuroscience. More than 400 adults, some with dementia and others without, were included in the first OASIS collection, which included cross-sectional MRI data. This study introduces a longitudinal dataset consisting of magnetic resonance imaging (MRI) scans of elderly persons, some of whom have Alzheimer's disease (AD) and others of whom do not. Thorough quality checks, detailed documentation, example postprocessed photos, complete anonymization, multiple access choices, continuous support, and flexible data use regulations are all part of the dataset's preparation and release, which follows the same rigorous standards as the initial launch. A total of 150 participants, ranging in age from 60 to 96, are included in the dataset. Of these, 64 have been clinically diagnosed with mild to severe AD and were assessed using the Clinical Dementia Rating (CDR) scale on their first visit. The data is collected by longitudinal magnetic

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resonance imaging (MRI).Also, fourteen patients were found to have Alzheimer's disease after earlier scans had ruled them out as having the disease. Everyone used the same scanner and followed the same procedures while collecting data. Although the usual variances associated with aging were taken into account, participants were screened to exclude individuals who may have mental or neurological disorders that might lead to dementia. Consequently, a number of elderly people dealt with diabetes, while others developed hypertension due to aging. Both the AD and non-AD groups had comparable sample characteristics. Biomarkers that suggest moderate cognitive impairment (MCI) including proteins like Aβ1-42 and tau that can be detected in cerebrospinal fluid (CSF), along with neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) that can be found in both cerebrospinal fluid (CSF) and brain tissue.

VI. BIOMARKERS IN CEREBROSPINAL FLUID (CSF)

Alzheimer's disease is characterized by reduced levels of Aβ1-42 and elevated tau proteins (both total tau and p-tau), which can help identify MCI patients who are at a higher risk of progressing to AD. The combination of tau and Aβ1-42 has been shown to be highly effective in accurately detecting MCI converters.

Neurofilament light chain (NfL) and GFAP: Patients with MCI exhibited increased levels of NfL and GFAP in their cerebrospinal fluid (CSF) compared to controls, which could indicate neuroaxonal injury and astroglial pathology.

➢ *Biomarkers in Blood.*

- NfL and GFAP: These biomarkers can also be measured in the blood, providing a less invasive option for screening and diagnosis. Studies show they can accurately predict progression to AD dementia.
- Other proteins: Research is ongoing to identify other useful blood-based biomarkers, such as specific amyloid and tau proteins. 32

➢ *Imaging Biomarkers.*

- FDG-PET: This is a type of positron emission tomography (PET) scan that measures glucose metabolism in the brain. Positive FDG-PET results are considered a strong predictor of dementia in individuals with MCI.
- Amyloid-PET: This scan can directly visualize amyloid plaques in the brain. 33

➢ *Machine Learning for Medical Diagnosis*

Machine learning (ML) algorithms are emerging as a valuable tool for integrating various biomarkers to facilitate the early detection, diagnosis, and prediction of dementia. These ML models are capable of processing vast datasets and uncovering intricate patterns that might elude human experts. Additionally, ML algorithms can combine information from diverse sources, including neuroimaging, genetics, and clinical data, to create models that accurately forecast the onset and progression of dementia. Research indicates that ML algorithms can enhance the precision of diagnosing and predicting dementia.

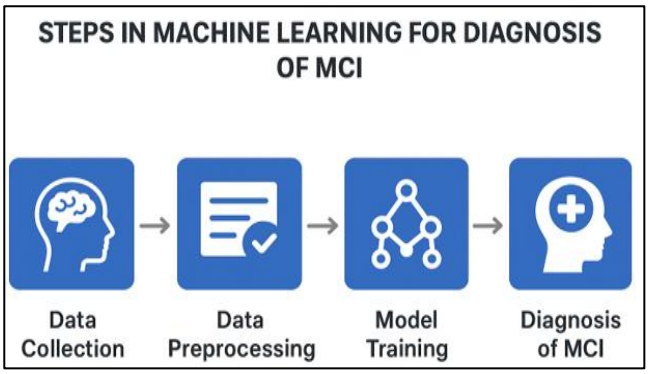

Fig 3 (A) Steps in Machine Learning for Diagnosis

Personalized therapy options customized to a patient's unique biomarker profile and illness development may be aided by machine learning (ML), as opposed to traditional approaches that depend on individual biomarkers. Machine learning algorithms can assess trends in imaging, genetic data, and biomarker testing to identify patients' optimal treatments and predict which therapies will be most effective.34 Treatment accuracy and effectiveness can be improved with this strategy, which might improve outcomes and quality of life for people with dementia and Alzheimer's disease. In general, ML algorithms make it easier to analyze several datasets simultaneously in order to find hidden relationships and patterns. Supervised learning, unsupervised learning, semi-supervised learning, and reinforcement learning are the four main ways that ML algorithms are usually classified, depending on their role.Through the introduction of novel and very efficient methods for study design and assessment, machine learning is revolutionizing the process of knowledge generation in the scientific community. This is particularly true in relation to the Four V's of big data: volume, velocity, variety, and veracity. This effectiveness is a direct result of healthcare organizations making the most of their available resources to collect massive volumes of high-quality data. It is possible to make machine learning analysis and modeling more adaptable and scalable for continuous growth and improvement by carefully optimizing the processes that generate large amounts of scientific data. Machine learning research strategies that utilize fluid biomarker data aim to improve large-scale diagnosis of conditions ranging from mild cognitive impairment (MCI) to Alzheimer's disease (AD) by filling in the gaps in cost-efficiency optimization of resource utilization.

There is no denying that ML opens up exciting new avenues for data science. But there is a lot of fear about developing medical apps that use ML models in the medical field. This concern arises from the fact that trust concerns are caused by the lack of transparency in these models, which gets more difficult to understand and trace as ML algorithms become more sophisticated. The whole ML algorithm's calculation is considered a "black box" since it cannot be understood or deciphered. Even the academics who create the algorithms have no idea what goes on inside these "black

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box" models when they are fed data; no one can say for sure how they arrive at a certain result. Not all ML algorithms can explain their reasoning behind producing a certain result or conclusion; this is especially true with neural network-based algorithms, which are widely employed.Here, a new subfield of machine learning called explainable artificial intelligence (XAI) is rapidly expanding, with the goal of bringing more transparency to the modeling process by shedding light on the underlying metrics and principles that these "black box" algorithms use to make decisions. Consequently, XAI is becoming more important in machine learning-driven applications, particularly in the field of medical diagnostics. If we want to build machine learning (ML) tools that can better diagnose Alzheimer's disease (AD) and mild cognitive impairment (MCI) using fluid biomarkers or multimodal data, we need to make sure that the model is explainable from all relevant angles, in line with its theoretical and experimental foundations. This study intends to conduct a comprehensive literature evaluation on the topic of dementia research using machine learning and fluid biomarkers in order to make the most of ML's capabilities in this area. The purpose of this study is to shed light on where our understanding of the relationships between biomarkers is lacking, to highlight research questions that need answering, and to provide suggestions for how to structure future investigations. A comprehensive literature review is an important first step in achieving the goal of integrating machine learning with fluid biomarker research, which has great promise for improving our knowledge of the pathobiology of dementia.35

➢ *Identification of Studies*

The databases Scopus and PubMed Central were searched by us. Because of its prominence and breadth of coverage in the biological and life scientific domains, PubMed Central, the electronic archive of the United States National Institutes of Health, was chosen. Also used was Scopus, a database of citations and abstracts from peer-reviewed publications. We used precise keywords arranged into four groups (including related and synonyms) to conduct a thorough literature search and guarantee reliable results: First, mild cognitive impairment (MCI) and second, diagnosis; third, machine learning (ML), artificial intelligence (AI), algorithms, and deep learning; and fourth, fluid biomarkers (FBG), amyloid-beta, blood, serum, plasma, urine, progranulin, neurofilament, and cerebrospinal fluid. Article titles, abstracts, or keywords have to include at least one term from each category in order for the search method to work. We narrowed our scope to publications published between 2012 and 2023 so that we could focus on more current investigations.36

➢ *Selection of Studies*

The co-authors have reviewed all of the abstracts. Then, the co-authors reached a consensus after reviewing the complete texts of the abstracts that were chosen to determine whether they were eligible. The two databases mentioned earlier were first searched using the chosen keywords and Boolean operators. The database's characteristics were then used to filter articles according to inclusion and exclusion criteria. After then, we looked at the remaining publications' titles to see whether they were applicable to our research and if they used any biomarkers other than neuroimaging, such as genetic, clinical, or fluid data. Similarly, we went over the abstracts of these papers. After much deliberation, we chose which articles would be included in this evaluation. Figure 1 is a flow diagram showing the process and its outcomes. The total number of records found via database searches is the starting point for the PRISMA flow diagram of the systematic literature search. It goes on to list the records that were first reviewed and then the ones that were later removed, often because it was evident from their titles or abstracts that they did not qualify for inclusion. The figure then goes on to display the total number of full-text publications that were considered for eligibility, the total number that were eliminated along with the reasons given, and finally, the total number of studies that were included. In order to guarantee that the systematic review is credible, this open method is crucial.37

➢ *Inclusion and Exclusion Criteria*

Studies were considered if they met two criteria: (i) they were global in scope and (ii) they used machine learning and fluid biomarkers to analyze samples of mild cognitive impairment; and (iii) the algorithm was validated. Such studies could have been empirical, quantitative, longitudinal, follow-up, neuroimaging, randomized controlled trials, quasi-randomized controlled trials, or cross-sectional studies.

➢ *Categorization of Studies*

A table was created to arrange the information from each research. The table included all relevant citation elements such as the authors, title, DOI, and year of publication. Every article's abstract, cohort size and origin, machine learning methods, top algorithm performance, features, amount of features, and validation technique were meticulously recorded. The papers were arranged in descending order of the characteristics used after each one was examined. The use of supervised machine learning methods was a common thread among the included papers in this meta-analysis. An algorithm learns to provide predictions or judgments using labelled input-output pairs in supervised learning, the most prevalent machine learning approach. This method involves training the model using data that contains input characteristics that are paired with labels for the output. By understanding the connection between inputs and outputs, the algorithm should be able to forecast results for previously unknown data. The fact that supervised machine learning is applicable to regression and classification problems is vital to understand.Each study's data was methodically entered into a table together with all pertinent citation details, such as authors, DOI, title, and publication year. Abstract, cohort size, origin, machine learning algorithms, leading algorithm performance, features, amount of features, and validation technique were some of the key information noted from each paper. The characteristics used to classify the papers were determined after each one was reviewed. The use of supervised machine learning methods was a common thread among the included papers in this meta-analysis. The majority of machine learning algorithms learn to generate predictions or choices via supervised learning, which involves labeling input-output pairs. This technique involves training the model using data that contains input

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characteristics and labels for the outputs. In order for the algorithm to be able to forecast results for previously unknown data, it must first comprehend the connection between inputs and outputs. Keep in mind that supervised machine learning is versatile enough to work with both regression and classification problems.One of the main algorithms used for regression tasks is linear regression, which predicts the target variable by minimizing the squared error sum. Another is ridge regression, which uses L2 regularization to address overfitting. Decision trees that have been modified for regression predict continuous values instead of categories. Finally, neural networks that have been optimized for regression predict continuous outputs in a way similar to classification neural networks. Taken together, the definitions provided allow us to classify all of the examined publications using supervised machine learning (ML) techniques (see Table 1). Figure 2 shows the supervised learning procedure for biomarker-based medical diagnosis. Collecting biomarkers from a cohort is the first step in supervised ML. The data must first be preprocessed by eliminating outliers, filling in missing values, and normalizing it. After that, the data is split into two sets: one for training the algorithms and the other for assessment and validation. It is possible to diagnose new patients using the selected most effective model.38

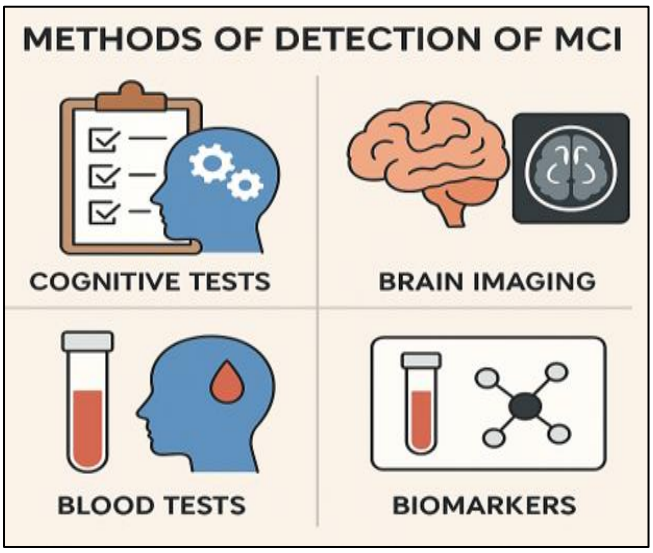

Fig 4 (A) Steps in Detection of MCI

➢ *Evaluation Metrics in Machine Learning*

It is critical to accurately assess the performance of machine learning models as they are being developed. We can gauge the efficacy of our models with the use of evaluation measures. Choosing the correct assessment measure is crucial for determining how well the model accomplishes our objectives, whether we are dealing with classification tasks, continuous result prediction, or data clustering. To help you determine the best assessment measure for your model, this article will explore many popular options.

- *Classification Metrics*

Predicting different types of data is the main goal of classification tasks. Here are some metrics that we use to evaluate categorization models:

✓ *Accuracy*

When measuring the efficacy of a classification model, accuracy is a crucial statistic to consider. The accuracy rate is the percentage of the model's predictions that turn out to be right. Although accuracy gives a picture, it is not always reliable, particularly when dealing with unbalanced datasets. A model that reliably predicts class A would achieve 90% accuracy but completely fail to detect any occurrences of class B in a dataset where class A accounts for 90% of the entries and class B for the remaining 10%. The danger of misclassifying samples from the minority class is often overlooked, leading to a misleading sensation of great performance, even when accuracy is desirable.39

✓ *Precision*

This metric measures how many of the model's favorable predictions turned out to be correct. In situations where the consequences of false positives are substantial, such as in medical diagnostics, where an inaccurate illness prognosis might result in serious consequences, this metric is vital. When the model predicts a favorable result, it is likely accurate because of its precision.

✓ *Recall*

The proportion of real-world examples that the model correctly identifies is measured by recall, which is sometimes called sensitivity. When the potential consequences of false positives exceed the costs of false negatives, this becomes crucial.

✓ *F1 Score*

The F1 score is useful for achieving a happy medium between recall and accuracy since it combines the two metrics into one single number, representing the harmonic mean of the two. Impressive achievement in both domains is indicated by a high F1 score. From zero to one, that's the score. Accuracy may be achieved with lesser recall and better precision, but it may miss a lot of cases. A better overall performance is indicated by a higher F1 score. In mathematical terms, it looks like:

✓ *Logarithmic Loss (Log Loss)*

By punishing the model when it correctly assigns low probability to categories, Log Loss measures the uncertainty in its predictions. To measure the model's prediction confidence, this metric is used in multi-class classification. Log Loss is calculated for N samples over M classes using the following formula:

The objective is to minimize Log Loss, as a lower value indicates higher prediction accuracy.

- *Area Under the Curve (AUC) and ROC Curve*

Jobs requiring binary categorization benefit from these. A higher AUC number implies that the model is more likely to give a positive instance a higher rank than a negative one, given that the two instances are randomly selected. Model performance is improved with larger AUC values, which may range from 0 to 1.

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- *True Positive Rate (TPR)*

An evaluation of the model's accuracy in identifying true positive instances is the True Positive Rate, which is sometimes called the sensitivity rate or recall. "How many actual positive examples did the model correctly identify?" is the question it seeks to answer.

- *True Negative Rate (TNR)*

Specificity, or the True Negative Rate, measures how many real negative situations the model correctly classifies as negative. "How many of all the actual negative instances did the model accurately label as negative?" is the question it seeks to answer.

- *ROC Curve*

The True Positive Rate (TPR) and the False Positive Rate (FPR) are shown in relation to each other across various categorization levels in this graph. It is possible to evaluate the compromise between sensitivity (TPR) and specificity (1 - FPR) at different threshold settings by analyzing the curve. An indication of the model's overall capability to differentiate between positive and negative classes is the Area Under the Curve (AUC).

- ✓ AUC = 1: Indicates a perfect model that always correctly identifies positives and negatives.
- ✓ AUC = 0.5: Indicates a model that performs no better than random chance.41

VII. FUTURE DIRECTIONS IN THE DETECTION OF MILD COGNITIVE IMPAIRMENT (MCI)

Future investigations into the detection of Mild Cognitive Impairment (MCI) are advancing towards the development of more accurate, accessible, and tailored diagnostic approaches by leveraging breakthroughs in artificial intelligence, digital health technologies, and various biomarkers. A primary objective is to create multimodal deep learning models that combine MRI, PET scans, genetic data, cognitive assessments, speech analysis, and lifestyle information to deliver a thorough assessment of an individual's cognitive state. These models are designed to offer earlier and more precise forecasts of MCI and its progression to Alzheimer's disease. Another promising avenue is the advancement of explainable AI (XAI), which aims to make diagnostic algorithms transparent and comprehensible, allowing clinicians to trust and validate the foundations of the predictions. Additionally, wearable devices, smartphones, and IoT monitoring systems will play a crucial role in real-time detection by continuously tracking subtle changes in behavior, movement, sleep, and speech, aiding in the early identification of cognitive decline outside clinical settings. Federated learning is also becoming popular as an effective approach to train AI models using data from multiple institutions while maintaining patient privacy, thereby improving model performance across diverse populations. Furthermore, future initiatives will likely concentrate on cost-effective, non-invasive biomarkers such as voice analysis, eye-tracking, gait recognition, and digital pen tests, making MCI screening more accessible, even in resource-constrained environments. Ultimately, integrating predictive models into standard clinical practice and developing personalized early intervention strategies will significantly enhance preventive care, paving the way for precision neurology and improved management of cognitive decline.

➢ *Transition from a Categorical to a Spectrum-Based Clinical Approach*

In order to better personalize treatment for patients, a Canadian care facility first created the idea of Mild Cognitive Impairment (MCI) in the 1950s. Research and therapeutic settings have increasingly begun to use this phrase to categorize persons. But recently, there has been a shift away from labeling people with moderate memory loss as having mild cognitive impairment (MCI) or not. Because of the challenges in differentiating between normal and damaged cognition and our limited knowledge of how cognitive impairment develops, this shift has taken place. Dementia and normal aging both include stages that might be accompanied by mild cognitive impairment (MCI). Traditional MCI criteria have focused on memory loss, overlooking other important elements of neurodegenerative illnesses, despite the fact that memory loss is just one of many complicated biochemical and functional signs of dementia. This means that there is currently no consensus on how to define MCI in a way that makes it easy to detect and understand even modest functional alterations. Early symptomatic stage of neurodegenerative illnesses is characterized by cognitive decline, and mild cognitive impairment (MCI) is one of them. This deterioration, if left untreated, may make even the most basic tasks difficult, and eventually lead to a dementia diagnosis. The degree of subjectivity, however, is substantial when determining if a person's functionality is compromised. This is because of the complex interplay between the patient's thoughts and feelings, the clinician's experience and standards, the patient's surroundings, and the patient's everyday functioning. It is impossible to objectively measure a notion as complicated as function, and there are no clear standards for what is considered to be an individual's anticipated level of performance in relation to their age, socioeconomic status, or cultural background. It can be more helpful to look at MCI in the bigger picture of a person's whole life. Recent large-scale disease modeling studies suggest that predicting progression to more severe stages of neurodegenerative diseases may be easier if MCI is seen as part of a spectrum that includes two main components: (1) cognition and its closely related function and (2) biological factors, rather than as a separate category. Incorporating two more elements—(3) changes over time and (4) fixed and adjustable risk factors—can further strengthen these models. The four-dimensional probability spectrum is formed by these elements taken together.43

➢ *Biomarker Testing to Improve Diagnostic Accuracy*

Cognitive complaints were the main means of diagnosing Mild Cognitive Impairment (MCI) for quite some time. People with mild cognitive problems caused by neurodegenerative diseases are more accurately identified and treated when MCI is seen as a continuum rather than a separate category. This is because these people are at a high risk of developing more severe stages of the disease, such as

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Alzheimer's disease (AD). A significant change in the categorization of MCI since the 2012 editorial by Ritchie and Ritchie has been the inclusion of biomarkers to help detect, but not yet predict, AD as the underlying source of symptoms. The National Institute on Aging-Alzheimer's Association (NIA-AA) updated their Alzheimer's disease (AD) criteria in 2011 to include a preclinical stage. In this stage, biological markers may be used to determine the presence of AD pathology in the brain, but there are no obvious clinical symptoms. Focusing on people who are exhibiting brain alterations associated with AD pathology but are cognitively normal and functionally unimpaired is made possible by this. The use of individual biomarkers, however, has not yet shown to be very reliable. When diagnosing or forecasting the course of a disorder, biomarkers should be used with caution, taking into account the available scientific data on their efficacy. Cognitive decline thought to be caused by neurodegenerative illnesses is being more and more assessed using magnetic resonance imaging (MRI) and positron emission tomography (PET) scans, although the best accurate method is still unclear. One research that focused on fluid biomarkers found that core neurodegenerative biomarkers are very sensitive to both Alzheimer's disease (AD) and moderate cognitive impairment (MCI) caused by AD. The specificity compared to sensitivity in predicting which individuals with mild cognitive impairment (MCI) will progress to Alzheimer's dementia is significantly lower when using amyloid-β levels or the cerebrospinal fluid (CSF) amyloid-β/tau ratio, according to four Cochrane Diagnostic Test Accuracy reviews. This holds true whether the assessment is done in CSF or through PET imaging. Although amyloid-β measures may help determine who is more likely to have Alzheimer's dementia, these tests are better at excluding AD as the reason for symptoms than they are at proving it. Upcoming research is expected to enhance specificity via the use of models that include genetic risk factors, short-term changes in conditions, and more sensitive cognitive assessments. By analyzing these studies, we were able to find clinically meaningful diagnostic improvements using likelihood ratios; for example, we learned that negative test findings significantly outperform positive ones when it comes to ruling out the chance of dementia development. Given the complexities this scenario brings to the table between patients and physicians, it is critical that patients be given accurate information on the benefits and drawbacks of the testing. It also highlights the need of scheduling follow-up sessions for further testing.

In addition, specialists with extensive training in neurodegenerative disease contexts provide the nuanced and intricate interpretation of these test findings. Patients may suffer emotional and mental trauma as a result of a lack of accurate information about their risk of developing dementia, which may worsen the neurodegenerative illness. Research into the patho-clinical relevance of the biomarkers is important, but so is the detrimental effect of insufficient communication of test findings.44

- *The Future of MCI Incorporates Biomarkers as well as Risk Factor Identification.*

It is believed that the onset of Alzheimer's disease (AD) occurs at a time when the affected individual does not exhibit any cognitive issues, long before the observable clinical symptoms of dementia become apparent. Thus, employing biomarker data and comprehensive cognitive evaluations, present research on neurodegenerative illnesses is focusing on at-risk younger adults who are asymptomatic. To combat the growing worldwide problem of dementia, a new assessment of dementia innovations (Dementia Innovation Readiness Index; Global Coalition on Aging and Alzheimer's Disease International, 2017) emphasised the need of preventing the disease and reducing its risk factors. If cases could be better identified, therapies could be evaluated in the right groups, and this may lead to substantial results in halting the transition of minimally impaired or healthy states to Alzheimer's dementia.45 Based on current knowledge of the biology of Alzheimer's disease, neurofibrillary tangles have likely already permeated the whole brain by the time cognitive symptoms manifest, maybe caused by the development of amyloid-β plaques. In addition to other important disease processes including inflammation and cerebrovascular illness, the substantial but achievable task of understanding the systems-level sequence and interplay of biological changes must be met. Although biomarker testing helps clinical trials weed out participants who do not have Alzheimer's disease pathology, many people who test positive may never have dementia. Therefore, to further refine diagnostic criteria, it is necessary to identify the various stages of neurodegeneration. This can be achieved by combining risk factors like age and APOE status with cognitive assessments that can detect early signs in specific brain areas, such as the entorhinal cortex, posterior hippocampus, and precuneus. More sensitive assessments of hippocampus function and tracking changes in people across two or three time periods are also required by this approach, which will ultimately lead to the development of the four-dimensional model discussed earlier. No pharmaceutical therapies have been shown to influence the course of Alzheimer's disease in clinical studies targeting younger, preclinical populations, despite intensive investigation over the years. Preventing dementia by targeting the prodromal period makes sense from a therapeutic perspective, but it's important to avoid testing medicines on inappropriate samples, which might lead to misleading results (e.g., false positives). To reduce this danger, recent research on Alzheimer's disease have focused on younger, healthier volunteers beginning in midlife, collecting data on risk variables throughout time and looking at very early pathology changes. A combination of nine risk factors, including poor education, hypertension and obesity in middle age, hearing loss, depression in late life, diabetes, lack of physical exercise, smoking, and social isolation, is thought to be related with about 35% of dementia cases. The most important thing is to find pathological alterations as soon as possible by using neuropsychological testing, comprehensive neuroimaging, and biomarker evaluations. Preliminary suggestions for altering risk variables may emerge from this, and pharmaceutical therapies or combinations of them might be offered if substantial progress is made in understanding the condition.46

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➢ *The Necessity for Advanced Statistical Methods to Advance Precision Medicine.*

Alterations in younger persons should be observed using sensitive techniques and in well-designed studies in order to discover early pathogenic changes. Frequent data collection is crucial to ensure these early alterations are not noticed, however additional research is required to establish the ideal study design for reliably recognizing the beginning of decline. However, in order to capture the complex, multidimensional dynamics of different underlying processes, which are not addressed by commonly used predictive models such as logistic regression or Cox proportional hazards models, innovative research programs that implement new data collection methods must also create and use appropriate analytical tools. There are better statistical models out there, but nobody is using them just yet. As an example, these novel risk prediction models may benefit greatly from multivariate joint longitudinal survival models, which are powerful tools that fulfill many of the necessary characteristics.47 Furthermore, models need to recognize that there are groups with distinct patterns of change and provide a better explanation for the observed heterogeneity across people in clinical settings. If this variation is not taken into account, we can miss particular groups' responses to risk factors or those who are more vulnerable.

Embracing this heterogeneity is crucial for achieving precision medicine approaches that focus on individualized disease drivers, patterns of decline, and consequently, tailored interventions for each person.48

VIII. DISCUSSION

Due to its strong correlations with Alzheimer's disease (AD) and other types of dementia, the detection and prediction of Mild Cognitive Impairment (MCI) have emerged as critical domains of study. Machine learning (ML) and artificial intelligence (AI) have become game-changers in this field, helping with pattern recognition, automating diagnosis, and enhancing clinical decision-making.This paper provides an overview of current developments, as well as future prospects, in the use of AI and ML for MCI identification.

➢ *Progress in Data-Driven Diagnosis*

AI and ML have demonstrated impressive abilities to analyze diverse datasets, including neuroimaging modalities (MRI, PET, fMRI), cognitive assessments, speech patterns, gait data, genetic biomarkers, and electronic health records (EHR). Traditional techniques of diagnosis often rely significantly on the subjective, changeable, and time-consuming clinical judgment of the treating physician. By contrast, ML algorithms like RNNs, SVMs, Random Forests, and CNNs can handle complicated, high-dimensional data and identify subtle indicators that would not be obvious from a clinical examination alone. For example, deep learning has shown superior performance in identifying structural brain changes and neurodegeneration patterns, facilitating earlier diagnosis compared to conventional methods. Likewise, natural language processing (NLP) models have demonstrated potential in analyzing speech coherence, vocabulary richness, and acoustic features, providing non-invasive and cost-effective options for MCI screening.49

➢ *Significance of Multimodal Integration*

Current research highlights that relying on a single type of data—such as only MRI scans or solely neuropsychological assessments—often does not yield the best accuracy. Mild Cognitive Impairment (MCI) is a complex and varied condition; thus, combining multiple sources of information greatly enhances the reliability of predictions. Models that integrate various data types, including imaging, clinical evaluations, genetic factors, and demographic information, generally perform better than those using just one data type. However, merging such diverse datasets requires advanced data fusion methods and poses challenges related to data alignment, missing information, and standardization across different sources. Despite these difficulties, multimodal approaches are the leading trend in cutting-edge MCI research.50

➢ *Model Generalizability and Practical Use*

While many studies report high accuracy under controlled conditions, applying AI and machine learning models broadly remains challenging. Models developed using uniform datasets—often from specific geographic regions, languages, or clinical groups—may not perform well in varied real-world settings. Common issues include overfitting, lack of validation across multiple sites, and small sample sizes. Many investigations depend on public datasets like ADNI, which, although valuable, lack wide demographic representation. For clinical use, models need validation across diverse populations, healthcare environments, and different imaging technologies.51

➢ *Ethical, Privacy, and Bias Issues*

Deploying AI in healthcare requires careful attention to ethical and privacy concerns. Neuroimaging and genetic information are highly sensitive, necessitating strong data protection measures, secure storage, and clear consent procedures. Moreover, algorithmic bias can occur if models are trained mainly on data from specific ethnic, social, or age groups, potentially resulting in inaccurate or unfair outcomes for underrepresented populations. The use of explainable AI (XAI) is increasingly important to help clinicians and patients understand how decisions are made. Transparent and interpretable models are crucial in medical settings, where unclear or incorrect recommendations can have serious consequences.52

➢ *Challenges in Clinical Integration and Adoption*

Despite promising research findings, the incorporation of AI and machine learning into clinical practice remains limited due to several obstacles:

- Lack of compatibility between AI systems and existing healthcare infrastructure.
- Clinicians' hesitation to trust automated decision-support tools.
- High computational demands of deep learning methods.

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- Regulatory and approval hurdles, as medical AI tools must satisfy rigorous validation criteria.

Successful implementation requires not only strong technical capabilities but also user-friendly interfaces and effective collaboration between clinicians and AI systems.53,54

➢ *Future Research Directions*

The future of AI and machine learning in detecting Mild Cognitive Impairment (MCI) looks promising, with several new trends emerging:

- Federated Learning: This approach enables training models on distributed datasets without transferring sensitive patient information, thereby enhancing privacy and model generalizability.
- Longitudinal Modeling: Monitoring patient data over time, rather than relying on a single point, can greatly improve prediction accuracy.55
- Wearable and Mobile-Based Screening: AI systems that analyze gait, sleep patterns, speech, and daily cognitive activities through smartphones or wearable devices will make early diagnosis more accessible.
- Integration with Personalized Medicine: Combining AI with genetic information and lifestyle data could allow for individualized risk assessments and early intervention plans.
- Explainable and Transparent AI: Improving the interpretability of AI models will increase clinician trust and help with regulatory approvals.56,57

➢ *Overall Impact on MCI Research and Healthcare*

AI and machine learning technologies are transforming cognitive healthcare. Their capacity for early, accurate, and non-invasive detection of MCI has the potential to significantly delay or even prevent progression to Alzheimer's disease.59 Although challenges such as ethical issues, data diversity, and clinical implementation remain, the rapid advancement of technology indicates that AI-driven tools will soon become essential in neurological evaluation and treatment.60

IX. CONCLUSION

The incorporation of Artificial Intelligence (AI) and Machine Learning (ML) into the early detection and prediction of Mild Cognitive Impairment (MCI) marks a significant breakthrough in healthcare, especially concerning neurodegenerative diseases. Utilizing advanced algorithms, pattern recognition, and data-driven models, AI/ML systems can detect subtle cognitive, behavioral, and biological changes much earlier than traditional clinical methods. Early detection is vital as it allows for timely interventions, personalized treatments, and the potential to slow or prevent progression to Alzheimer's disease and other dementias. Current studies show that ML models—particularly deep learning, ensemble techniques, and multimodal diagnostic frameworks—achieve high accuracy when applied to neuroimaging, genetic data, speech analysis, and digital biomarkers from wearable technology. These strengths not only improve diagnostic accuracy but also reduce subjectivity and enhance scalability for large populations. Nevertheless, challenges persist, including limited data availability, lack of standardized evaluation methods, privacy concerns, and the opaque nature of complex algorithms, which hinder widespread adoption. Future research should prioritize developing explainable, ethical, and clinically validated AI systems that integrate smoothly into healthcare practices. In conclusion, AI and ML have transformative potential in the early detection and prediction of MCI. Through continuous innovation, enhanced data integration, and responsible application, these technologies have the potential to enable earlier diagnoses, support clinicians in their decision-making processes, and ultimately result in better patient outcomes and a more profound understanding of cognitive decline.

REFERENCES

[1]. Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. Journal of Internal Medicine, 256(3), 183–194.
[2]. Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G., & Kokmen, E. (1999). Mild cognitive impairment: clinical characterization and outcome. Archives of Neurology, 56(3), 303–308.
[3]. Jack, C. R., Jr., Bennett, D. A., Blennow, K., Carrillo, M. C., Dunn, B., Haeberlein, S. B., ... & Sperling, R. (2018). NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimer's & Dementia, 14(4), 535–562.
[4]. Mueller, S. G., Weiner, M. W., Thal, L. J., Petersen, R. C., Jack, C., Jagust, W., ... & Beckett, L. (2005). The Alzheimer's Disease Neuroimaging Initiative. Neuroimaging Clinics of North America, 15(4), 869–877.
[5]. Venugopalan, J., Tong, L., Hassanzadeh, B., & Damaraju, E. (2021). Multimodal deep learning models for early detection of Alzheimer's disease using MRI and PET. Scientific Reports, 11, 1–14.
[6]. Weiner, M. W., Veitch, D. P., Aisen, P. S., Beckett, L. A., Cairns, N. J., Green, R. C., ... & Trojanowski, J. Q. (2013). The Alzheimer's Disease Neuroimaging Initiative: A review of papers published since its inception. Alzheimer's & Dementia, 9(5), e111–e194.
[7]. Sperling, R. A., Rentz, D. M., Johnson, K. A., Karlawish, J., Donohue, M., Salmon, D. P., & Aisen, P. S. (2014). The A4 study: Stopping AD before symptoms begin? Science Translational Medicine, 6(228), 228fs13.
[8]. Jack, C. R., Jr., Knopman, D. S., Jagust, W. J., Petersen, R. C., Weiner, M. W., Aisen, P. S., ... & Trojanowski, J. Q. (2013). Tracking pathophysiological processes in Alzheimer's disease: An updated hypothetical model of dynamic biomarkers. The Lancet Neurology, *12*(2), 207–216.
[9]. Blennow, K., Zetterberg, H., & Fagan, A. M. (2012). Fluid biomarkers in Alzheimer disease. Cold Spring Harbor Perspectives in Medicine, *2*(9), a006283.
[10]. Frisoni, G. B., Fox, N. C., Jack, C. R., Jr., Scheltens, P., & Thompson, P. M. (2010). The clinical use of

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25dec048

structural MRI in Alzheimer disease. Nature Reviews Neurology, *6*(2), 67–77.
[11]. Small, G. W., et al. (2006). PET of brain amyloid and tau in mild cognitive impairment. The New England Journal of Medicine, *354*(3), 250–260.
[12]. Bevilacqua, R., et al. (2023). Radiomics and artificial intelligence for the diagnosis and prognosis of Alzheimer's disease: A systematic review. Journal of Clinical Medicine, 12(16), 5432.
[13]. Singh, S. G., et al. (2024). Early Alzheimer's disease detection: a review of machine learning approaches. Diagnostics, 14(16), 1759.
[14]. Mohammed, E. M., et al. (2024). Detection of Alzheimer's disease using deep learning models — systematic review. Heliyon / Data Science Reviews
[15]. Odusami, M., et al. (2023). Explainable deep-learning-based diagnosis of Alzheimer's disease. Biomedical Engineering Letters, *13*(3), 463–480.
[16]. Jiao, F., et al. (2023). Tau PET radiomics analysis for predicting progression from MCI to AD. Journal of Nuclear Medicine / Radiology Research.
[17]. Zhang, Y., et al. (2025). Radiomics of PET using neural networks for prediction in Alzheimer's disease. Statistics in Medicine.
[18]. Venkatraman, V., et al. (2019). Deep learning in neuroimaging: A review of recent advances and future directions. Frontiers in Neuroscience, *13*, 1–19.
[19]. Huang, Y., Xu, J., Zhou, Y., & Zhuang, X. (2019). Diagnosis of Alzheimer's disease via multi-modality 3D convolutional neural network using ADNI. arXiv preprint arXiv:1902.09904.
[20]. Beare, R., et al. (2020). Graph neural networks for brain network classification in Alzheimer's disease. NeuroImage, *223*, 117352.
[21]. Li, Y., et al. (2025). A radiomics model predicts progression from MCI to AD: large-scale validation using ADNI. Scientific Reports.
[22]. Gao, H., et al. (2025). Comparison of radiomics and conventional SUVR methods for Aβ PET analysis. Frontiers in Neurology.
[23]. Kale, M., et al. (2024). AI-driven innovations in Alzheimer's disease: Integrating multi-modal biomarkers and clinical data. Artificial Intelligence in Medicine, *132*, 102--- (review).
[24]. AlHarkan, K., et al. (2024). Artificial intelligence approaches for early detection of mild cognitive impairment and dementia: A review. Journal of Clinical Neuroscience / PMC.
[25]. Rasi, R., et al. (2024). Predicting amyloid positivity from FDG-PET using radiomics and machine learning. *European Journal of Nuclear Medicine and Molecular Imaging.*
[26]. Hao, J., et al. (2024). Early detection of dementia through retinal imaging and deep learning (Eye-AD). *NPJ Digital Medicine.*
[27]. Lohner, V., et al. (2025). Machine learning approaches to vascular neuroimaging and cognitive impairment. Alzheimer's Research & Therapy.
[28]. Quek, L. J. V., et al. (2023). Use of artificial intelligence techniques for detection of mild cognitive impairment: A scoping review. Journal of Clinical Nursing.
[29]. Odusami, M., et al. (2021). Explainable deep-learning-based diagnosis: methods and clinical applicability for AD and MCI. IEEE Transactions on Medical Imaging.
[30]. Christodoulou, R., et al. (2025). AI-Based classification of MCI and cognitively normal individuals using ADNI data. Journal of Clinical Medicine.
[31]. Liu, H., et al. (2025). Machine learning applied to mild cognitive impairment: trends and bibliometric analysis. Frontiers in Neurology
[32]. Gaser, C., et al. (2013). BrainAGE in MCI and AD: accelerated brain aging as a biomarker. NeuroImage, *63*(3), 1363–1373.
[33]. Suk, H.-I., Lee, S.-W., & Shen, D. (2014). Hierarchical feature representation and multimodal fusion with deep learning for AD/MCI diagnosis. NeuroImage, *101*, 569–582.
[34]. Eskildsen, S. F., et al. (2013). Prediction of AD conversion in MCI patients using structural MRI and machine learning. NeuroImage: Clinical, *3*, 452–461.
[35]. Lebedev, A. V., et al. (2014). Random forest classification of AD and MCI from MRI features: what matters most? PLoS ONE.
[36]. Ding, Y., Sohn, J. H., Kawczynski, M. G., Trivedi, H., Harnish, R., Jenkins, N. W., ... & McCurtain, B. (2019). A deep learning model to predict a diagnosis of Alzheimer disease by using 18F-FDG PET of the brain. Radiology, *290*(2), 456–464.
[37]. Korolev, S., Safiullin, A., Belyaev, M., & Dodonova, Y. (2017). Residual and plain convolutional neural networks for 3D brain MRI classification. Proceedings of the International Conference on Information Technology and Data Science.
[38]. Sarraf, S., & Tofighi, G. (2016). DeepAD: Alzheimer's disease classification via deep convolutional neural networks using MRI and fMRI. *bioRxiv.*
[39]. Zhang, D., Shen, D., & the ADNI. (2012). Multi-modal classification of Alzheimer's disease and MCI. NeuroImage, *55*(3), 856–867.
[40]. Dukart, J., Mueller, K., & Barthel, H. (2013). The importance of partial-volume correction for PET-based quantification in Alzheimer's disease research. NeuroImage, *59*(1), 357–368.
[41]. Tong, T., et al. (2017). Prediction of conversion from MCI to AD with longitudinal and multimodal biomarkers. *Scientific Reports, 7*, 1–12.
[42]. Jo, T., Nho, K., Saykin, A. J., & the ADNI. (2019). Deep learning in Alzheimer's disease: Diagnostic classification and prognostic prediction using neuroimaging and clinical data. Alzheimer's Research & Therapy.
[43]. Basaia, S., et al. (2019). Automated classification of Alzheimer's disease and mild cognitive impairment using MRI: An ensemble deep learning framework. *NeuroImage: Clinical, 21*, 101602.
[44]. Noh, Y., et al. (2014). Using pattern recognition to detect early AD in MRI scans. Proceedings of MICCAI.

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[45]. Korolev, I., et al. (2016). Predicting progression from MCI to AD using machine learning on structural MRI: Comparison of classifiers and features. Neuroinformatics.
[46]. Hao, X., et al. (2020). EEG-based detection of MCI using deep learning: a systematic review and meta-analysis. Frontiers in Aging Neuroscience.
[47]. Knight, R. A., et al. (2021). Blood-based biomarkers and machine learning models for early detection of MCI and AD: A systematic review. Alzheimer's Research & Therapy.
[48]. O'Bryant, S. E., et al. (2017). A blood protein signature for early detection of Alzheimer disease. *Neurology.*
[49]. Raamana, P. R., et al. (2015). Machine learning models to predict cognitive decline: Methods, pitfalls, and opportunities. Frontiers in Neuroinformatics.
[50]. Bengio, Y., Courville, A., & Vincent, P. (2013). Representation learning: A review and new perspectives. IEEE Transactions on Pattern Analysis and Machine Intelligence. (Background on deep learning methods)
[51]. Lundervold, A., & Lundervold, A. (2019). An overview of deep learning in medical imaging focusing on MRI. *Z. Med* Phys. (methodological review)
[52]. Jack, C. R., Jr., et al. (2010). Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. The Lancet Neurology*, 9*(1), 119–128.
[53]. McKhann, G. M., et al. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups. Alzheimer's & Dementia*, 7*(3), 263–269.
[54]. Sperling, R. A., et al. (2011). Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association. Alzheimer's & Dementia*, 7*(3), 280–292.
[55]. Jack, C. R., Jr., et al. (2009). Serial MRI and CSF biomarkers in MCI to predict progression to AD. Neurology.
[56]. Kermany, D., et al. (2018). Identifying medical diagnoses and treatable diseases by image-based deep learning. Cell. (illustrative example of medical imaging DL success)
[57]. LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. Nature*, 521*, 436–444. (methodological foundation)
[58]. Beach, T. G., et al. (2012). Correlates of AD neuropathology in MCI patients: Clinicopathologic studies. *Journal of Alzheimer's Disease.*
[59]. Donohue, M. C., et al. (2014). The preclinical Alzheimer cognitive composite: Measuring subtle cognitive decline in preclinical AD. JAMA *Neurology.*
[60]. Frost, S., et al. (2020). Wearable sensors and digital biomarkers for early detection of cognitive impairment: opportunities and challenges for ML. Journal of Medical Internet Research.