EMERGING BIOMARKERS AND ARTIFICIAL INTELLIGENCE IN THE EARLY DIAGNOSIS AND MANAGEMENT OF NEURODEGENERATIVE DEMENTIA

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Abstract: Neurodegenerative dementia, particularly Alzheimer's disease (AD), represents a growing global health challenge due to progressive neuronal loss, cognitive decline, and the absence of curative therapies. Early diagnosis is difficult because pathological changes begin years before clinical symptoms and often overlap with normal ageing. This review examines the emerging role of biomarkers, non-invasive diagnostic technologies, nanomedicine, and artificial intelligence (AI) in the early detection and management of neurodegenerative dementia. Conventional cerebrospinal fluid biomarkers, including amyloid-beta (Aβ), phosphorylated tau, total tau, and neurofilament light chain, provide high diagnostic accuracy but are invasive. Consequently, blood-based biomarkers, MRI and PET neuroimaging, wearable devices, digital cognitive assessments, eye-tracking, speech analysis, motion sensors, and biosensors are being developed as safer, accessible, and patient-friendly alternatives. These technologies generate multimodal data that can reveal subtle preclinical changes in brain structure, metabolism, behaviour, movement, and language. AI, machine learning, and deep learning can integrate and analyse these complex datasets to identify hidden patterns, classify dementia subtypes, predict disease progression, and support personalised treatment decisions. Explainable AI further improves clinical transparency and trust by revealing the biomarkers driving model predictions. In AD, nanotechnology-based systems, including Aβ-targeted nanoparticles, ROS-sensitive and RAGE-targeted carriers, and targeted protein-degradation platforms, offer promising strategies for brain delivery, amyloid clearance, and disease modification. However, clinical translation remains limited by biological heterogeneity, blood–brain barrier complexity, cost, data privacy, and the need for validation. Integrating non-invasive biomarkers with AI-driven nanomedicine may enable earlier diagnosis, continuous monitoring, and more effective personalised care for dementia.

Keywords: Neurodegenerative dementia; Alzheimer's disease; Biomarkers; Artificial intelligence; Nanomedicine; Early diagnosis

1.0 Introduction

The role of emerging biomarkers and artificial intelligence (AI) in the early diagnosis and management of neurodegenerative dementia. Dementia is a progressive neurological condition that affects memory, thinking, behaviour, and the ability to perform daily activities. Diseases such as Alzheimer's disease, Parkinson's disease dementia, frontotemporal dementia, and Lewy body dementia are among the most common forms. Since these disorders develop slowly and their symptoms often overlap with normal ageing, early diagnosis remains a major challenge.

I learned that biomarkers are measurable biological indicators that help detect changes in the brain before noticeable symptoms appear. Recent advances in blood based biomarkers, cerebrospinal fluid (CSF)

biomarkers, and neuroimaging techniques have made early detection more accurate. Biomarkers such as amyloid beta, phosphorylated tau, total tau, and neurofilament light chain provide important information about disease progression and help clinicians identify the specific type of dementia at an early stage.

I also explored the growing role of artificial intelligence in dementia care. AI uses machine learning and deep learning algorithms to analyse large amounts of medical data, including brain imaging, laboratory results, genetic information, and cognitive assessments. These technologies can detect hidden patterns that may not be easily recognised by clinicians, improving diagnostic accuracy and supporting earlier intervention. Another important area I studied was the integration of biomarkers with AI-based models. Combining these technologies helps in predicting disease progression, classifying different types of dementia, and assisting healthcare professionals in making informed clinical decisions. AI can also support personalised treatment planning by identifying patients who are more likely to respond to specific therapies and by monitoring disease progression over time. Emerging biomarkers and artificial intelligence are transforming the diagnosis and management of neurodegenerative dementia. Their combined use has the potential to improve patient outcomes through earlier diagnosis, timely treatment, continuous monitoring, and personalised care. Although challenges such as data privacy, accessibility, cost, and the need for clinical validation still exist, these innovations represent an important step towards improving dementia care in the future.

1.1 Making the Early Detection of Alzheimer's Disease by using Non-Invasive Biomarkers

Currently, there is no permanent cure for Alzheimer's disease. Existing therapies can only help control symptoms and improve a patient's quality of life for a limited time. Today, Alzheimer's has become a major global health concern because the number of elderly people is increasing rapidly. As a result, the number of people living with Alzheimer's disease is also expected to rise significantly in the coming years. This growing trend has encouraged researchers and healthcare professionals to focus on finding better ways to detect and manage the disease. Alzheimer's disease (AD) is a progressive brain disorder that slowly destroys a person's memory, thinking and behavior. It is the most common cause of dementia and mainly affects people over 65.

The article explains that Alzheimer's disease does not develop because of a single cause. Instead, it is the result of several factors working together, including genetics, environmental conditions, metabolism, and lifestyle. This makes the disease difficult to diagnose and treat. Traditionally, doctors have used cerebrospinal fluid (CSF) tests to diagnose Alzheimer's disease. These tests measure important biomarkers such as amyloid-beta and tau proteins, which are strongly associated with the disease. Although these tests are highly accurate, they require a lumbar puncture, which is an invasive procedure and may cause discomfort to the patient. Because of these limitations, researchers are now focusing on developing non-invasive methods that are safer, easier, and more comfortable for patients. One of the main messages of the article is that early diagnosis is extremely important. Alzheimer's disease begins affecting the brain many years before visible symptoms such as memory loss or confusion appear. During this early stage, harmful changes are already taking place inside the brain, even though the patient may appear healthy. If the disease can be detected during this period, doctors can begin treatment earlier, recommend lifestyle changes, and help slow down the progression of the disease. Early diagnosis also gives patients and their families more time to prepare and plan for future care. This is why scientists are giving so much importance to developing non-invasive diagnostic techniques that are safe, affordable, and suitable for regular screening.

The article discusses several promising non-invasive diagnostic techniques. Medical imaging methods such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) allow doctors to observe structural and functional changes in the brain. MRI helps identify brain shrinkage and damage to brain tissues, while PET scans can detect abnormal glucose metabolism and the accumulation of amyloid plaques. Another important development is the use of blood-based biomarkers. By analysing blood samples, researchers can measure proteins such as amyloid-beta, tau, phosphorylated tau (p-tau181), and neurofilament light chain

(NFL), which provide valuable information about Alzheimer's disease. Blood tests are simple, less expensive, and much more comfortable for patients than traditional CSF testing, making them highly promising for future diagnosis. Devices such as smartwatches, fitness trackers, and smartphones can continuously monitor a person's daily activities, sleep quality, walking pattern, heart rate, and physical activity. Researchers have found that small changes in these daily behaviours often appear years before noticeable memory problems develop. Digital memory tests, navigation tasks, and smartphone-based cognitive assessments can also identify early signs of cognitive decline. Since these devices collect information continuously, doctors can monitor patients over a long period without requiring frequent hospital visits. This makes wearable technology an effective and convenient tool for early diagnosis and disease monitoring.

Another important area discussed in the article is the use of sensor-based technologies. Eye-tracking devices can monitor eye movements and pupil responses because people with Alzheimer's often show abnormalities in these functions during the early stages of the disease. Similarly, speech analysis software can detect changes in speaking patterns, pronunciation, vocabulary, and language ability. Motion sensors and wearable devices can evaluate walking speed, body balance, movement, and physical activity, while heart rate sensors monitor changes in the autonomic nervous system that may indicate early Alzheimer's disease. Together, these sensors provide valuable digital biomarkers that help doctors identify the disease before severe symptoms appear.

Biosensors are advanced devices designed to detect Alzheimer's-related biomarkers in blood and other body fluids with very high sensitivity. Different types of biosensors, including electrochemical sensors, fluorescent sensors, graphene-based sensors, and immunosensors, have shown excellent accuracy in identifying amyloid-beta proteins, tau proteins, and other disease-related molecules. These technologies are fast, cost effective, and less invasive, making them highly suitable for routine clinical testing in the future. As biosensor technology continues to improve, it is expected to become an important part of Alzheimer's screening and monitoring. Because all these technologies generate enormous amounts of data, analysing the information manually becomes extremely difficult. This is where Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL) play a vital role. These advanced computational techniques can analyse MRI scans, PET images, blood biomarkers, speech recordings, wearable device data, and sensor information much faster and more accurately than traditional methods. AI models are capable of identifying hidden patterns, distinguishing Alzheimer's patients from healthy individuals, and predicting the disease even during its earliest stages. Many studies have shown that combining medical data with AI significantly improves the accuracy and speed of Alzheimer's diagnosis, making it one of the most promising developments in modern healthcare.

While AI models are highly accurate, they often work like a "black box," meaning doctors cannot easily understand how a particular decision was made. Explainable AI solves this problem by showing which features or biomarkers influenced the AI's prediction. This improves transparency, helps doctors trust AI-generated results, and supports better clinical decision-making. It also allows researchers to better understand the biological mechanisms behind Alzheimer's disease and improve future diagnostic models. In conclusion, the article states that the future of Alzheimer's diagnosis lies in combining non-invasive diagnostic technologies with Artificial Intelligence and Deep Learning. MRI, PET scans, blood-based biomarkers, wearable devices, biosensors, and digital sensors all provide valuable information that AI can analyse quickly and accurately. This combined approach has the potential to detect Alzheimer's disease years before symptoms become noticeable, allowing earlier treatment, better patient monitoring, and improved quality of life. The authors conclude that as these technologies continue to develop, they will transform the diagnosis and management of Alzheimer's disease, making healthcare more effective, accessible, and patient-friendly.

1.2 NDDs

It involve the progressive loss of neurons and glial cells in specific regions of the CNS. Although AD, PD, ALS, and MS differ in molecular triggers and clinical presentation, they converge on shared pathological

features: misfolded protein accumulation, oxidative stress, neuroinflammation, mitochondrial dysfunction, and eventual neurodegeneration. These overlapping mechanisms offer opportunities for platform-based therapeutic strategies, yet also complicate diagnosis and intervention due to their biological complexity and patient heterogeneity. Nanomedicine is well-positioned to address these challenges through targeted drug delivery and biomarker detection, especially when paired with AI-driven models for patient stratification and treatment optimization. However, as the following disease-specific sections reveal, while numerous nanoparticle systems show promise in preclinical models, clinical translation remains rare highlighting a gap between scientific innovation and therapeutic reality.

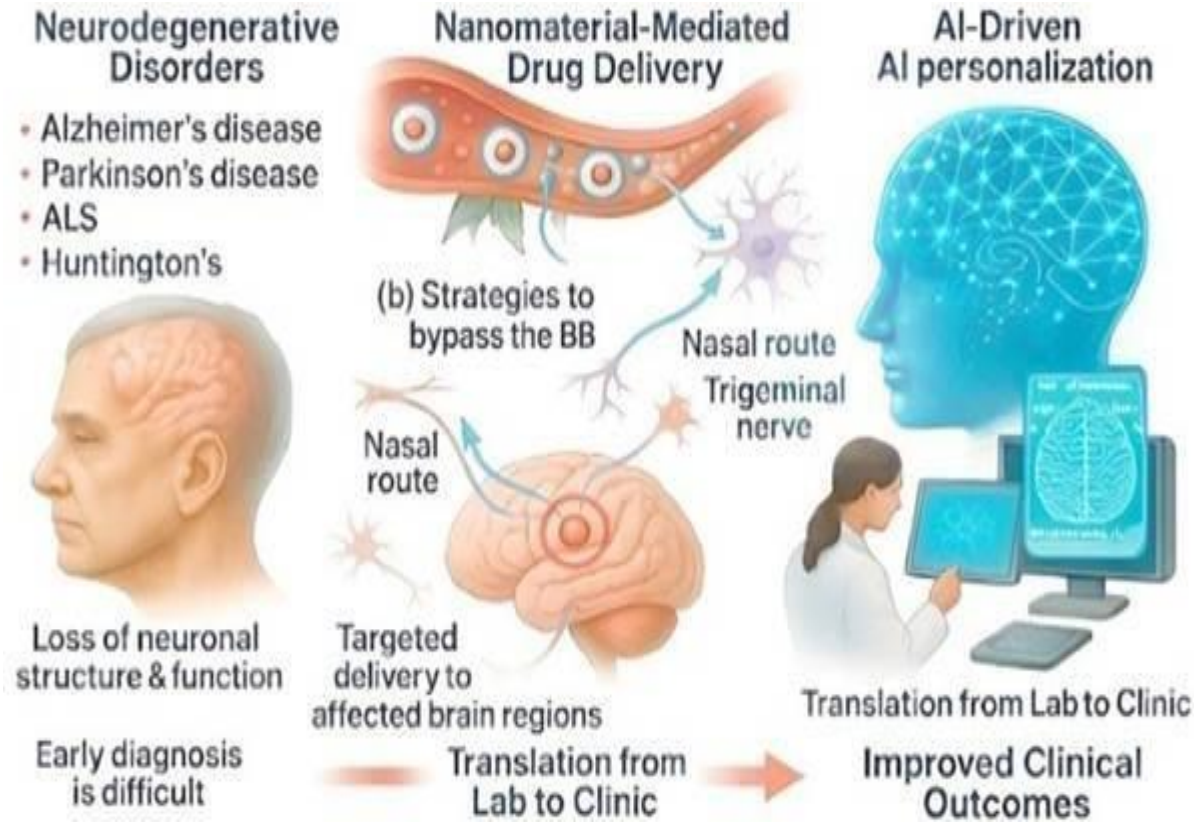


Figure: shows the ”AI-Driven Nano medicine for Neurodegenerative Disease Management”

1.3 AD:

AD is the most common neurodegenerative disorder, which is characterized by a progressive decline in memory, cognitive abilities, and intellect. The disease progresses because of the formation of amyloid-β (Aβ) plaques around neurons and neurofibrillary tangles of hyperphosphorylated tau protein inside the neurons. Aβ and neurofibrillary tangles are abnormal protein aggregates that disrupt normal neuron activity, cause oxidative stress and neuroinflammation, and lead to neuron death. In recent years, researchers have made considerable progress in identifying biomarkers that allow Alzheimer's disease to be detected before severe symptoms appear. Cerebrospinal fluid (CSF) biomarkers, including Aβ1–42, phosphorylated tau (p-tau181), and neurofilament light chain, have shown high diagnostic value. Blood-based biomarkers are also gaining attention because they provide a less invasive and more convenient alternative for screening. The formation of amyloid-β fibrils is widely recognized as one of the key pathological events in Alzheimer's disease. Because of this, preventing their formation or breaking down existing fibrils has become an important therapeutic objective. Although several Aβ-targeting compounds have been investigated, many have produced limited clinical benefits because they do not bind strongly enough to amyloid proteins. To address this limitation, researchers have developed sequence-matching strategies that improve the interaction between therapeutic agents and Aβ aggregates. One example is the B6-PNI nanoparticle system, which has demonstrated stronger binding to amyloid-β, promoting the breakdown of fibrils while also supporting the natural clearance of Aβ

from the brain. Nanotechnology has also opened new possibilities beyond simply blocking amyloid aggregation. Advanced nanoparticle-based targeted protein degradation systems are being designed to remove harmful extracellular proteins more efficiently. These platforms utilize the body's own proteolytic mechanisms to selectively degrade pathological amyloid and tau aggregates rather than merely preventing their formation. Such innovative approaches have the potential to overcome some of the limitations of conventional therapies and may contribute to more effective disease-modifying treatments for Alzheimer's disease in the future.

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1.4 Epidemiology of AD

It is the leading cause of dementia worldwide and is the reason for nearly two thirds of all dementia cases. It is a slowly progressive neurological disorder that predominantly affects older adults, although a small proportion of individuals develop symptoms before the age of 65, a condition referred to as early-onset Alzheimer's disease. As life expectancy continues to increase across the globe, the number of individuals with AD is rising steadily, presenting as one of the most significant public health challenges.

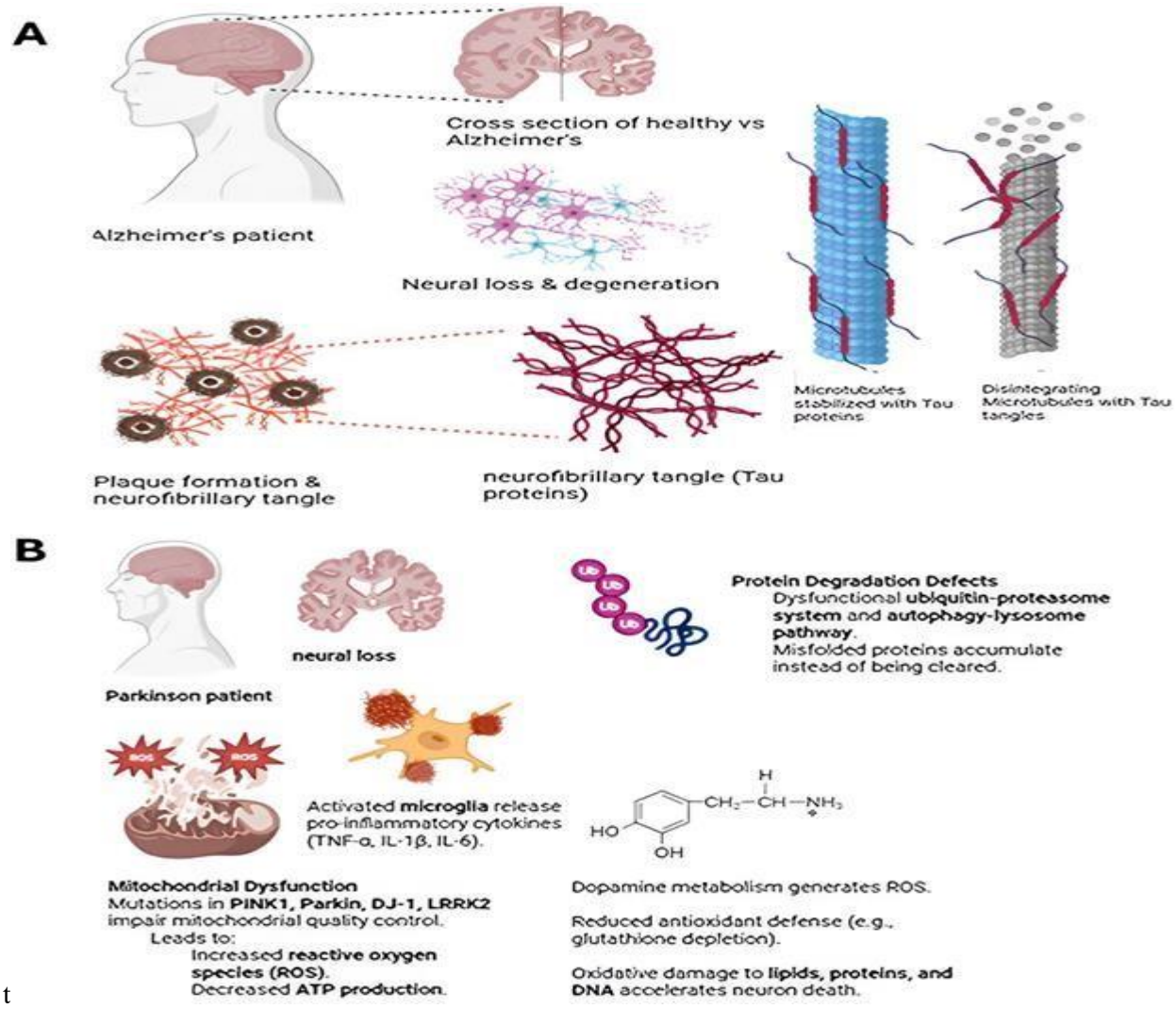


Figure 2. Schematic illustration of the preparation process and therapeutic mechanism of the nanoplatform.

Current estimates indicate that more than 55 million people worldwide are living with dementia, with Alzheimer's disease accounting for the majority of these cases. The number of affected individuals is projected to increase dramatically over the coming decades, reaching approximately 78 million by 2030 and more than 139 million by 2050. This rapid increase is largely driven by the growing elderly population. Beyond its impact on patients, Alzheimer's disease places a considerable emotional, social, and financial burden on families, caregivers, healthcare providers, and national healthcare systems.

The development of Alzheimer's disease is influenced by a combination of genetic, biological, and lifestyle-related factors. Increasing age remains the strongest and most consistent risk factor. Genetic susceptibility also contributes to disease development, particularly in individuals carrying the APOE ε4 allele or rare mutations in the APP, PSEN1, and PSEN2 genes. In addition, several modifiable risk factors—including hypertension, diabetes, obesity, cardiovascular disease, smoking, physical inactivity, limited education, and social isolation—have been associated with an increased likelihood of developing AD. Addressing these factors through healthy lifestyle choices and preventive healthcare may help lower the overall risk of the disease. Epidemiological studies have consistently shown that Alzheimer's disease is more common in women than in men. While this difference is partly explained by women's longer life expectancy, hormonal, genetic, and biological factors may also contribute to the increased prevalence. Given the continued rise in Alzheimer's disease worldwide, greater emphasis on early diagnosis, public awareness, preventive measures, and the development of effective therapies is essential. Strengthening healthcare systems and promoting healthy aging strategies will be crucial for reducing the future burden of this devastating disorder.

2.0 Dugs and Therapeutic Approaches for Alzheimer's Disease

Alzheimer's disease (AD) is a progressive neurological disease that destroys a person's memory capacity, cognitive abilities, behaviour, and capacity to perform daily activities. Despite the fact that there is currently no cure for Alzheimer's disease, there are several treatments that may assist patients with managing their symptoms as well as enhancing their quality of life. The drugs that are used in the treatment of AD fall into two categories: the acetylcholinesterase inhibitors, such as donepezil, rivastigmine, and galantamine, and memantine, which is a glutamate modulator. In recent years, new treatments have focused on the underlying cause of Alzheimer's rather than only controlling its symptoms. Drugs such as lecanemab and donanemab are monoclonal antibodies that target and help remove beta-amyloid, a protein that can build up in the brain in Alzheimer's disease. These treatments may slow disease progression in some people with early Alzheimer's disease, although they are suitable only for selected patients and require careful medical monitoring. Overall, treatment for Alzheimer's disease has moved from mainly managing symptoms toward also targeting the biological changes associated with the disease.

2.1 Cholinesterase Inhibitors

Acetylcholinesterase inhibitors are commonly used to manage the symptoms of Alzheimer's disease. The brain's cholinergic system is closely involved in memory, attention, and learning. In Alzheimer's disease, some of the nerve cells that produce acetylcholine, an important chemical messenger in the brain, become damaged or are lost. The three main medicines in this group are donepezil, rivastigmine, and galantamine. These medicines do not cure Alzheimer's disease or stop the damage occurring in the brain, but they may provide modest improvements or help maintain cognitive and daily functioning in some patients.

Donepezil is one of the most commonly prescribed medicines for Alzheimer's disease. It works by selectively and reversibly blocking the enzyme acetylcholinesterase, which normally breaks down acetylcholine. Because of this action, more acetylcholine remains available in the brain, which may help improve or maintain memory and thinking abilities. Donepezil can be used in mild, moderate, and severe stages of Alzheimer's disease. However, its benefits are usually limited and temporary because it does not prevent the ongoing loss of brain cells. Some people may experience side effects such as nausea, diarrhoea, vomiting, weight loss, difficulty sleeping, dizziness, or tiredness. Rivastigmine is another medicine used to control symptoms associated with Alzheimer's disease. Rivastigmine is available as a tablet or liquid taken by mouth and also as a skin patch. The patch may be a useful option for people who have difficulty swallowing medicines or who experience stomach-related problems with oral treatment. Like other drugs in this class, rivastigmine does not reverse Alzheimer's disease or stop its underlying progression. Possible side effects include nausea, vomiting, diarrhoea, loss of appetite, weight loss, and dizziness. Galantamine is mainly used for people with mild-to-moderate Alzheimer's disease. It increases the amount of acetylcholine available in the brain by inhibiting acetylcholinesterase. It also has an additional effect on certain nicotinic acetylcholine receptors, which may further support communication between nerve cells. However, some patients may develop nausea, vomiting, diarrhoea, or reduced appetite, particularly when treatment is started. For this reason, doctors usually begin treatment with a lower dose and increase it gradually so that the body has time to adjust. Overall, donepezil, rivastigmine, and galantamine can help some people with Alzheimer's disease manage symptoms and maintain their abilities for longer. Their effects vary from person to person, and they do not stop the underlying brain changes associated with the disease.

2.2 Memantine

Memantine is a medicine mainly used to manage the symptoms of moderate-tosevere Alzheimer's disease. It works differently from drugs such as donepezil, rivastigmine, and galantamine because it acts on the brain's glutamate system. This may help protect nerve cells from further stress and support brain function.Memantine may be prescribed on its own or together with a cholinesterase inhibitor, particularly donepezil, when

Alzheimer's disease becomes moderate or severe. Research suggests that memantine may provide modest benefits in areas such as memory, thinking, everyday activities, and some behavioural symptoms. However, the response varies from one person to another, and the medicine does not reverse the disease or stop the underlying changes occurring in the brain. Overall, memantine is an important option for people with moderate-to-severe Alzheimer's disease, especially when symptoms become more difficult to manage. It can be used alone or alongside a cholinesterase inhibitor such as donepezil. However, it is important to understand that memantine is a symptom-relieving treatment, not a cure. It does not remove the amyloid plaques or tau-related changes responsible for the underlying disease. Researchers are continuing to study whether combining medicines that manage symptoms with newer treatments that target Alzheimer's disease itself can provide better long-term outcomes.

2.3 Anti-Amyloid Disease-Modifying Therapies: -

One of the most important changes in Alzheimer's disease treatment in recent years has been the development of medicines that target amyloid-beta in the brain. According to the amyloid hypothesis, the abnormal accumulation of beta-amyloid may contribute to the series of changes that eventually damage nerve cells and affect brain function. Unlike traditional medicines, which mainly help control symptoms, anti-amyloid drugs are designed to remove amyloid deposits and slow the progression of the disease. These medicines are not intended for everyone with dementia. Careful monitoring is also necessary because these medicines can cause important side effects.

Lecanemab is an antibody that targets beta-amyloid and helps the body remove amyloid deposits from the brain. It is used for adults who are in the mild cognitive impairment or mild dementia stage of Alzheimer's disease and who have evidence of amyloid pathology. Clinical studies have shown that lecanemab can slow the rate of cognitive and functional decline compared with placebo. However, it is important to understand that the medicine does not restore memories that have already been lost or reverse Alzheimer's disease. Its main purpose is to slow further progression. Lecanemab is also available in a subcutaneous form, which means it can be administered under the skin. In 2026, the FDA approved a regimen that allows appropriately selected patients or their caregivers to give the initial subcutaneous dose at home. This may make treatment more convenient for some patients, although regular medical supervision and safety monitoring remain important. Donanemab is another antibody treatment that targets beta-amyloid. Donanemab binds to a particular form of beta-amyloid found in plaques and helps the body clear these deposits. Clinical research has shown that treatment can slow cognitive and functional decline compared with placebo. One notable feature of donanemab is that treatment may be stopped once a substantial reduction in amyloid plaque levels has been achieved, depending on the treatment plan and prescribing guidance.

2.4 Treatment of Behavioural and Psychological Symptoms

Alzheimer's disease does not affect memory and thinking alone. As the condition progresses, some people may develop changes in mood and behaviour, including agitation, aggression, anxiety, depression, hallucinations, sleep problems, or psychosis. These symptoms can be very difficult for both patients and caregivers and may have a major effect on quality of life. Before starting medication, doctors should first look for possible causes that can be treated. Pain, infections, constipation, dehydration, poor sleep, medication side effects, and changes in the surrounding environment can all make behavioural symptoms worse. Brexpiprazole is an atypical antipsychotic approved in the United States for treating agitation associated with dementia caused by Alzheimer's disease. It may be considered when agitation is severe or persistent and non-drug approaches have not been sufficient. However, antipsychotic medicines require caution in older adults with dementia because they carry important safety risks. The possible benefits should therefore be weighed carefully against the risks before treatment is started.

2.5 Non-Pharmacological Approaches

Medicines are only one part of Alzheimer's disease management. Non-drug approaches are also important because they can help patients remain active, independent, and socially connected. These approaches are often combined with medicines to provide more complete care. Cognitive stimulation therapy involves activities designed to keep the brain engaged. These may include conversations, reading, music, memory-based activities, puzzles, and simple problem-solving exercises. Such activities can encourage mental engagement and may support cognitive function and quality of life. However, they cannot stop the underlying progression of Alzheimer's disease. Regular physical activity is also helpful. Activities such as walking, aerobic exercise, light resistance training, stretching, and balance exercises can help maintain muscle strength, mobility, and physical independence. Exercise may also support better sleep and mood. The type and intensity of exercise should be adjusted according to the person's physical condition and abilities.

Occupational therapy focuses on helping people continue everyday activities as independently and safely as possible. An occupational therapist may help a patient manage tasks such as dressing, bathing, eating, cooking, or taking medicines. They can also assess the home and suggest changes that may reduce the risk of falls, wandering, accidents, and other safety problems.

3.0 Support for Caregivers

Caregiver support is another essential part of Alzheimer's disease management. Looking after someone with Alzheimer's can become physically, emotionally, and financially demanding, particularly as the person becomes more dependent on others. Caregivers can benefit from clear information about the disease, medication schedules, communication techniques, nutrition, safety, and ways to respond to difficult behaviours. Support groups, counselling, respite care, and community services can provide valuable assistance to families. Giving caregivers opportunities to rest and seek support may help reduce stress and make it easier for them to continue providing good-quality care.

Overall, the management of Alzheimer's disease is becoming broader than simply treating memory problems. Traditional medicines such as cholinesterase inhibitors and memantine continue to play an important role in symptom management, while newer treatments such as lecanemab and donanemab aim to slow disease progression in carefully selected patients. At the same time, behavioural management, physical activity, cognitive stimulation, rehabilitation, and caregiver support remain important parts of comprehensive Alzheimer's care. The pharmacological management of Alzheimer's disease has progressed from primarily symptomatic treatment toward therapies that may modify the underlying disease process. Donepezil, Rivastigmine, and Ralantamine remain important cholinesterase inhibitors for symptomatic treatment, while memantine provides an alternative mechanism through NMDA receptor antagonism and is particularly useful in moderate-to-severe disease. These conventional therapies generally provide modest symptomatic benefits and do not stop neurodegeneration. Nevertheless, their benefits must be weighed against treatment burden, cost and access, the requirement for biomarker confirmation and monitoring, and potentially serious adverse effects such as ARIA. Therefore, modern Alzheimer's treatment is best viewed as a comprehensive approach combining symptomatic medication, disease modifying therapy when appropriate, behavioral management, physical and cognitive interventions, safety planning, and caregiver support.

3.0 Biomarkers for Diagnosis and Management of Neurodegenerative Dementia

Neurodegenerative dementias are a group of brain disorders in which nerve cells gradually become damaged and lose their normal function. As the disease progresses, a person may develop problems with memory, thinking, behaviour, language, movement, and everyday activities. Alzheimer's disease (AD) is the most common cause of neurodegenerative dementia. Other important disorders. Diagnosing these diseases can sometimes be difficult because many of their symptoms are similar. For example, memory problems are common in Alzheimer's disease but can also occur in dementia with Lewy bodies. Similarly, changes in

behaviour or language may occur in frontotemporal dementia but can sometimes look like psychiatric disorders or other forms of dementia. In older people, more than one type of brain pathology may also be present at the same time. A biomarker is a measurable biological indicator that provides information about a disease or a biological process. In dementia, biomarkers can help identify abnormal proteins, neuronal damage, brain atrophy, or changes in brain function. They can support early diagnosis, differentiate between diseases, predict disease progression, and help doctors decide whether a patient may benefit from particular treatments. The development of biomarkers has also changed the way Alzheimer's disease is understood. It groups biomarkers according to amyloid-beta (A), pathological tau (T), and neurodegeneration or neuronal injury (N). The revised Alzheimer's Association criteria published in 2024 further developed the biological approach to Alzheimer's disease diagnosis. However, biomarkers should not completely replace clinical assessment. The patient's symptoms, medical history, cognitive examination, and other possible causes of dementia must still be considered.

3.1 Major Types of Biomarkers

Biomarkers used in neurodegenerative dementia can be divided into two major groups:

(1) Cerebrospinal fluid (CSF) biomarkers

(2) Blood-based biomarkers

3.1.1 Cerebrospinal Fluid Biomarkers

Cerebrospinal fluid, or CSF, surrounds the brain and spinal cord. Because it is in close contact with the central nervous system, changes in CSF can provide useful information about diseases affecting the brain. Amyloid-beta 42 is one of the main proteins involved in the formation of amyloid plaques in Alzheimer's disease. In Alzheimer's disease, amyloid-beta tends to accumulate in the brain. As a result, the amount of Abeta42 present in CSF decreases. Therefore, a low CSF Abeta42 level can indicate amyloid pathology. However, Abeta42 alone is not sufficient to make a complete diagnosis. It is usually interpreted together with other biomarkers, especially tau. The Abeta42/Abeta40 ratio is considered more useful than measuring Abeta42 alone in many situations. Abeta40 is another form of amyloid-beta and can be used as a reference. A reduced Abeta42/Abeta40 ratio is associated with amyloid deposition in the brain. Using the ratio can reduce the effect of differences in overall amyloid production between individuals and may improve the reliability of CSF amyloid testing. Total tau is a protein associated with nerve cells. When neurons are damaged, tau can be released into CSF. In Alzheimer's disease, CSF total tau is often increased. However, increased tau does not occur only in Alzheimer's disease. Other conditions that cause neuronal injury can also increase t-tau Therefore, total tau is mainly considered a marker of neuronal injury rather than a completely specific marker of Alzheimer's disease.

Phosphorylated tau, commonly called p-tau, is more closely associated with Alzheimer's disease pathology than total tau.

3.1.2 Blood-Based Biomarkers

Blood-based biomarkers have become one of the most rapidly developing areas of dementia research. Compared with CSF testing and PET scans, blood tests are easier to perform, less invasive, and potentially less expensive. This makes them particularly attractive for early screening and repeated monitoring.

Plasma p-tau217 is currently one of the most promising blood biomarkers for Alzheimer's disease. It is associated with both amyloid and tau pathology in the brain. Research has shown that p-tau217 can distinguish Alzheimer's disease from several other neurodegenerative conditions. Recent studies have reported very high

diagnostic performance for some commercially available p-tau217 tests. Because of this, blood-based biomarkers are gradually moving from research settings toward clinical practice. The 2025 Alzheimer's Association Clinical Practice Guideline stated that blood-based biomarker tests with sufficiently high sensitivity and specificity may be used in appropriate specialized memory-care settings. However, the test must meet the required performance standards, and clinical assessment remains necessary.

Plasma p-tau181 is another widely studied blood biomarker. Its concentration can increase during different stages of Alzheimer's disease, including mild cognitive impairment and dementia. Plasma p-tau181 has also shown a relationship with CSF p-tau181 and tau PET findings. It may therefore help identify Alzheimer's disease pathology without requiring an invasive CSF procedure.

The Abeta42/Abeta40 ratio can also be measured in blood. A lower ratio is associated with amyloid accumulation in the brain. Blood Abeta testing may help predict whether a person has abnormal amyloid PET findings. This could reduce the number of patients who need expensive PET imaging. However, the accuracy of this test depends greatly on the laboratory method and assay being used. Therefore, different blood tests should not automatically be considered equivalent.

3.2 Role of Biomarkers in Diagnosis and Management

Biomarkers can be useful at different stages of dementia care.

3.2.1 Detection Early

Some pathological changes can occur in the brain many years before severe symptoms appear. Biomarkers may help identify these changes earlier than clinical symptoms alone.

3.2.2 Differential Diagnosis

Biomarkers can help doctors distinguish between different types of dementia.

For example, they may help differentiate:

*Alzheimer's disease from FTD

*Alzheimer's disease from DLB

*Neurodegenerative disease from some psychiatric conditions

*Alzheimer's disease from mixed or alternative causes of cognitive impairment

3.2.3 Treatment Selection

Biomarkers have become increasingly important because disease-modifying treatments for Alzheimer's disease require evidence of amyloid pathology. Biomarker testing can therefore help identify patients who may be suitable for specific treatments or clinical trials.

3.2.4 Monitoring Treatment

Researchers are studying whether biomarkers can be measured repeatedly to determine whether a treatment is changing the underlying disease process. Plasma p-tau, amyloid PET, and tau PET are among the biomarkers being studied for this purpose.

3.2.5 Clinical Trials

Biomarkers allow researchers to select participants based on biological evidence of disease rather than symptoms alone. This can make clinical trials more focused and may help researchers detect treatment effects more efficiently.

3.3 Limitations of Biomarkers

Although biomarkers have many advantages, they also have certain limitations. First, the accuracy of a biomarker can depend on the testing method. This is particularly important for blood-based tests because different laboratory assays may produce different results. Second, many biomarkers are not specific to one disease. For example, NFL indicates neuronal injury but can be elevated in many neurological conditions. Third, a positive biomarker result does not always explain all of a patient's symptoms. Older individuals may have more than one type of brain pathology at the same time. Another important problem is accessibility. CSF testing and PET scans can be expensive and may not be available in all hospitals or regions. Bloodbased biomarkers could help overcome some of these problems because they are easier to collect and potentially less expensive. However, proper validation, standardization, and clinical interpretation are still required.

Future Perspectives

The future of dementia diagnosis will probably involve a combination of different types of information rather than relying on a single biomarker. A possible approach could be:

Clinical assessment → Cognitive testing → Blood biomarker screening → CSF or PET confirmation when needed → Biological classification → Individualized treatment Plasma ptau217 is expected to become increasingly important because it can provide useful information about Alzheimer's disease pathology through a relatively simple blood test. Other biomarkers such as plasma Aβ42/Aβ40 and GFAP may provide additional information, while NFL can help assess neuronal damage and disease progression. For dementia with Lewy bodies and Parkinson's disease dementia, alpha-synuclein seed amplification assays may become important diagnostic tools. For FTD, combining NFL with genetic testing and brain imaging may improve diagnosis and prediction of disease progression. In the long term, the combination of clinical symptoms, cognitive testing, blood biomarkers, CSF biomarkers, brain imaging, and genetic information may allow a more personalized approach to dementia diagnosis and treatment.

4.0 AI and Brain Imaging

One of the clearest applications of AI in neurodegenerative dementia is the analysis of brain images. MRI is particularly useful because it can show changes in brain structure, including shrinkage of the hippocampus, loss of cortical tissue, enlargement of the ventricles, and changes in different brain regions. PET scans provide additional information about brain metabolism and can also be used to examine pathological processes such as amyloid and tau accumulation. These images contain a large amount of information, making them suitable for machine-learning and deep-learning algorithms.

Borchert and colleagues carried out a systematic review of AI used for diagnostic and prognostic neuroimaging in dementia. They identified 255 studies and found that algorithmic classification was the most common approach. AI models generally performed well when distinguishing people with Alzheimer’s disease from healthy individuals. However, the study also identified a major weakness in the existing literature: around 71% of the studies relied on the ADNI dataset, while relatively few studies tested their models using an independent dataset. This is an important point because a computer model may perform extremely well when it is tested on data that are similar to the data on which it was developed. Its performance may be very different when it encounters patients from another hospital, a different ethnic group, a different age group, or images obtained using a different scanner. Deep learning has also become increasingly common in MRI-based Alzheimer’s research. Convolutional neural networks (CNNs) are particularly useful because they can learn spatial patterns directly from medical images. A recent review of deep-learning applications in Alzheimer’s disease found that researchers are using CNNs, transfer learning, hybrid models, attention mechanisms, and other approaches for automated disease classification. The review also emphasized that problems with dataset size, model interpretation, privacy, robustness, and real world validation remain important.

The usefulness of AI is not limited to identifying patients who already have Alzheimer's disease. Researchers are also investigating whether MRI can be used by AI to predict whether a patient is likely to have amyloid pathology. This is potentially valuable because amyloid PET and cerebrospinal fluid testing may not be available everywhere and may be more expensive or invasive than MRI. If an AI model can identify patients who are more likely to have amyloid accumulation using a routine MRI scan, it could potentially help doctors decide which patients should undergo further testing. At present, however, these systems should be considered supportive tools rather than replacements for established biomarkers.

4.1 AI for Early Detection of Alzheimer's Disease

Early detection is probably one of the most important goals of AI research in dementia. Alzheimer's disease does not suddenly appear when a person receives a diagnosis. Biological changes usually develop gradually, and cognitive decline may occur over a long period. Mild cognitive impairment (MCI) is particularly important because some people with MCI remain stable, while others eventually develop Alzheimer's disease.

AI can potentially combine information from several sources to estimate a person's risk of progression. For example, a model might consider age, cognitive test scores, MRI findings, PET information, APOE genotype, and CSF biomarkers at the same time. This is difficult for a human to calculate because the number of possible relationships between these variables is very large. Kaur et al. reviewed 100 studies investigating machine learning and deep learning for Alzheimer's prediction. Their review found that MRI and PET were commonly used and that researchers were increasingly incorporating other information such as APOE genotype, diffusion tensor imaging, and CSF biomarkers. The important message from this research is that AI is moving away from using only one source of information. Instead, researchers are trying to develop models that consider the disease from several biological and clinical perspectives. A recent systematic review of AI research in Alzheimer's disease also placed considerable emphasis on multimodal approaches. The review analyzed 156 peer-reviewed studies and reported increasing interest in combining neuroimaging, genetics, biomarkers, and clinical information. According to the review, multimodal approaches may provide better diagnostic and predictive information than relying on a single type of data. At the same time, the authors noted that generalizability and clinical implementation remain significant problems.

It is important, however, to distinguish between detecting existing disease and predicting future disease. A model may be very good at recognizing patients who already have clear Alzheimer's related changes but may be less reliable when asked to predict whether a person with mild cognitive symptoms will develop dementia several years later. Long-term studies following patients over time are therefore particularly important.

4.2 AI for Speech and Language Analysis

Another interesting area of dementia research is the use of speech as a digital biomarker. Speech may change as cognitive abilities decline. A person with Alzheimer's disease may have difficulty finding words, use less specific vocabulary, pause more frequently, repeat information, or have difficulty organizing a story. These changes can be difficult to measure consistently during an ordinary clinical conversation, but AI can analyze speech recordings and identify measurable acoustic and linguistic patterns.

Research on spontaneous speech has shown that machine-learning methods can extract physical and acoustic characteristics from relatively short speech samples and relate these characteristics to cognitive status. This is attractive because speech collection is inexpensive, non-invasive, and potentially possible using a smartphone or computer. Unlike MRI or PET, speech recording does not require a hospital visit or specialized equipment.

Speech analysis may also be useful for distinguishing different forms of neurodegenerative disease. In research involving frontotemporal dementia, automated speech classification was used to distinguish Alzheimer's-related neuropathology from frontotemporal lobar degeneration. This is significant because FTD and Alzheimer's disease can sometimes produce overlapping clinical symptoms, particularly in the early stages. AI-based analysis could therefore potentially provide additional information when the clinical diagnosis is uncertain. The broader research literature also suggests that speech and gait can be useful non-invasive sources of information for dementia screening. A systematic review of machine-learning approaches using these digital features concluded that they have potential as relatively inexpensive screening tools. This could be especially useful in areas where access to neurologists, advanced imaging, or specialist dementia clinics is limited.

However, speech-based AI also has an obvious problem: people do not all speak in the same way. Accent, language, education, age, hearing ability, culture, and even the recording environment can affect the results. A model trained mainly on English-speaking participants may not work equally well for Hindi, Bengali, Tamil, or other languages. For this reason, future research needs more linguistically and culturally diverse datasets.

4.3 AI and Multimodal Diagnosis

One of the most promising developments in this field is the combination of different types of information. Alzheimer's disease is biologically complex, so it is unlikely that a single measurement will provide a complete picture of every patient. MRI can show structural changes, PET can provide information about metabolism or molecular pathology, blood and CSF biomarkers can provide biochemical information, genetics can indicate susceptibility, and cognitive tests show how the disease is affecting the individual. AI is well suited to combining these different forms of information. Instead of asking whether one MRI image indicates Alzheimer's disease, a multimodal system can consider the MRI together with the patient's cognitive score, age, genetic information, biomarkers, and other relevant information.

The recent systematic review by Mou and colleagues analyzed 156 studies and specifically examined multimodal AI approaches. Their findings suggest that multimodal approaches are becoming an important direction for future research. This approach could eventually support personalized medicine. Two people may receive the same clinical diagnosis but have different underlying biological processes. One person may have a strong amyloid and tau profile, another may have significant vascular disease, and another may have mixed pathology. An AI system capable of considering multiple biomarkers could potentially produce a more individualized risk profile.

Nevertheless, multimodal AI is more complicated than simply combining datasets. Different tests may be performed at different times, use different measurement scales, or contain missing information. Researchers therefore need carefully designed datasets and methods that can deal with incomplete or inconsistent information.

4.4 AI in Electronic Health Records and Clinical Decision-Making

Another application of AI is the analysis of electronic health records (EHRs). Medical records contain information collected over many years, including diagnoses, medications, laboratory results, cognitive assessments, hospital admissions, and clinical notes. Much of this information is difficult to analyze manually because it may be spread across numerous consultations. Natural language processing can be used to examine unstructured clinical notes and identify information related to cognitive decline. For example, an AI system

might identify repeated reports of memory problems, changes in daily functioning, falls, medication changes, or other symptoms that could indicate increasing dementia risk.

This does not mean that AI would diagnose dementia independently. Instead, it could act as an additional warning system. If the computer identifies a pattern that suggests cognitive decline, it could prompt a doctor to perform a more detailed assessment. Machine learning is also being studied in dementia care more broadly. A systematic review published in 2025 examined machine-learning methods used for dementia assessment, management, and treatment and concluded that the field is promising but still faces substantial challenges related to data quality and clinical implementation. One difficulty with EHR-based AI is that medical records are not created primarily for research. They may contain missing information, inconsistent terminology, differences between doctors, and differences between hospitals. A computer model could accidentally learn the way one hospital records information rather than learning the actual biological characteristics of dementia. For this reason, EHR-based AI systems need testing across multiple healthcare settings.

4.5 AI for Biomarker Discovery and Precision Medicine

AI is also being investigated as a tool for discovering new biomarkers. Traditional research may examine one biomarker at a time, whereas machine learning can analyze many variables simultaneously. This makes it possible to search for combinations of genetic, biochemical, imaging, and clinical characteristics that are associated with disease. This is particularly relevant because Alzheimer's disease is not a completely uniform condition. Different patients can have different combinations of amyloid pathology, tau pathology, vascular changes, inflammation, genetic risk, and other biological abnormalities. A deep-learning review published in 2025 highlighted applications of AI not only in disease detection but also in areas such as drug repurposing and natural language processing. It also emphasized the increasing importance of multimodal data and explainable AI. This suggests that the role of AI is expanding from simply identifying whether someone has Alzheimer's disease toward understanding the disease and potentially supporting treatment development.

It could also help identify new therapeutic targets by examining relationships among genes, proteins, disease pathways, and existing drugs. These applications are still developing, but they represent an important part of the broader movement toward precision medicine.

4.6 AI for Monitoring Disease Progression

AI may also be useful after a person has already been diagnosed. Dementia changes over time, and regular monitoring is necessary to understand how quickly a person's abilities are changing. Traditional assessments usually take place during periodic clinic visits. These assessments are valuable, but they only provide a snapshot of the person's condition at a particular time. Digital technologies may provide additional information between clinical appointments. Smartphones, smartwatches, wearable sensors, and home-monitoring systems can potentially record movement, sleep, physical activity, speech, and aspects of everyday behaviour. Machinelearning algorithms can then compare new measurements with the person's previous pattern. Gait is one example. Changes in walking speed, stride length, balance, turning, and variability may provide information about neurological function. Speech can similarly provide information about changes in language and cognition. These digital measures could potentially help clinicians identify gradual changes that might not be obvious during a short clinical assessment.

The major advantage of this approach is that it can provide longitudinal information. Instead of asking how a patient is doing once every six months, clinicians could eventually have a broader picture of changes occurring between appointments. However, this should complement rather than replace face-to-face clinical assessment.

4.7 AI for Differential Diagnosis

Another important application is distinguishing between different forms of dementia. Alzheimer's disease, frontotemporal dementia, dementia with Lewy bodies, Parkinson's disease dementia, and vascular cognitive impairment can sometimes produce similar symptoms. This makes diagnosis difficult, particularly when symptoms are mild or atypical. AI may help by learning disease-specific patterns from brain imaging, speech, gait, cognitive testing, biomarkers, and clinical records. For example, speech patterns may provide clues about whether a person's cognitive problems are more consistent with Alzheimer's pathology or frontotemporal degeneration. This could be clinically useful because the different forms of dementia may have different prognoses and management requirements. An AI system could potentially provide clinicians with a probability for several possible diagnoses and thereby act as a second opinion.

However, it would be dangerous to assume that a computer can always determine the correct diagnosis. Many older patients have mixed pathologies, and symptoms do not always follow textbook patterns. AI should therefore support clinical reasoning rather than replace it.

5.0 Limitations, Ethical Issues, and Future Research

Although AI has produced impressive results in dementia research, several problems prevent immediate widespread clinical use. One of the most important problems is the size and diversity of datasets. Deep-learning systems generally perform better when trained on large datasets, but many dementia studies involve relatively small and carefully selected research populations. Another major concern is the heavy dependence on ADNI. Borchert and colleagues found that 71% of the neuroimaging studies they reviewed relied on ADNI. ADNI has made an enormous contribution to Alzheimer's research, but it cannot represent every patient seen in everyday clinical practice. Real-world patients may have different ages, ethnic backgrounds, levels of education, coexisting diseases, medications, imaging protocols, and combinations of pathology. External validation is therefore essential. An AI model should be tested using information from hospitals and populations that were not involved in developing the model. Without this step, a model may appear highly accurate while actually being too specialized to one dataset. Another concern is explainability. Some deep-learning systems can make highly accurate predictions without clearly explaining why they reached a particular conclusion. In medicine, this is a serious issue because clinicians need to understand the reasoning behind an important diagnostic recommendation. Explainable AI methods may help by showing which regions of an MRI or which features of speech contributed to a prediction, but these explanations themselves need careful evaluation.

Privacy is another major concern. Brain scans, genetic information, speech recordings, facial images, and wearable-device data are highly personal. Patients should understand how their information will be collected, stored, and used. Strong security and appropriate consent procedures are therefore necessary.

Recent systematic research continues to emphasize the same problem: the field is developing rapidly, but clinical translation is slower. Reviews published in 2025 and 2026 have highlighted generalizability, interpretability, privacy, robustness, external validation, and real-world implementation as major research gaps.

6.0 Conclusion

Overall, the research reviewed here shows that artificial intelligence has considerable potential in the field of neurodegenerative dementia. Its applications are no longer limited to analyzing brain scans. Researchers are using AI to examine MRI and PET images, predict Alzheimer's disease progression, analyze speech and language, interpret electronic health records, identify biomarkers, monitor patients remotely, and distinguish between different forms of dementia. Among these applications, early detection and multimodal analysis appear particularly promising. AI can bring together information from several sources and identify patterns that may be difficult to recognize through conventional approaches. At the same time, the current evidence should be viewed realistically. High accuracy in a research study does not necessarily mean that an AI system is ready to be used independently in a hospital. Many studies use selected populations, relatively small datasets, or the same major research databases. External validation is still limited, and questions remain about fairness, explainability, privacy, and clinical usefulness. These limitations are especially important when AI is used to make predictions about a person's future health. The future of AI in dementia research will probably depend on combining several types of information rather than relying on one test. MRI, PET, blood biomarkers, genetics, cognitive assessments, speech, gait, electronic health records, and wearable data could eventually be analyzed together. This could lead to more personalized approaches in which clinicians receive an individual's estimated disease risk, likely progression, and relevant biological characteristics rather than simply a yes-or-no diagnosis. Recent research also points toward increasing use of transformer models, generative AI, and other advanced architectures, although technological sophistication alone should not be considered evidence of clinical value.

In conclusion, AI should currently be viewed as a tool that assists healthcare professionals rather than replaces them. Its greatest value may come from helping doctors recognize disease earlier, bringing together complex information, monitoring changes over time, and supporting more individualized decisions. If future studies use larger and more diverse populations, conduct independent external validation, improve transparency, and address ethical and privacy concerns, AI could become an important part of dementia research and clinical care. The goal should not simply be to create a computer that produces a high diagnostic accuracy, but to develop reliable and understandable systems that genuinely improve the lives of people living with neurodegenerative dementia and their caregivers.

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