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Exploring Alzheimer's Disease: A Comprehensive Analysis of Brain Impairment and Earlier Diagnostic Methods

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The type of dementia that affects people most often is Alzheimer's disease (AD) affecting brain functions, especially memory loss. Alzheimer's disease, an incurable disease that causes memory loss and cognitive impairment in the elderly. As a degenerative disease, it causes progressive irreversible cognitive decline, Alzheimer's disease is one of the severe form of the dementia affecting the elder people. Early diagnosis is essential for improving patient care and treatment outcomes. The early diagnose of AD can slow the progress of the disease. Early, accurate detection is essential for treatment. It is difficult to classify the similar brain patterns in AD classification due to the minor variations in biomarkers that can be detected in various neuro-imaging modes and image projections. In the last several years, the use of deep learning approaches has proven to really be very successful in the diagnosis of Alzheimer's. A variety of pre-processing methods and tools, datasets, and brain subregions most impacted by AD have all been examined. Additional in-depth examination of different biomarkers and feature extraction approaches, deep learning architectures and classification techniques have been completed for the survey.

Keywords: Alzheimer's disease; Deep Learning; Early diagnosis; Multiclassification; Neuro-Imaging.

1. Introduction

The neurobiological type of dementia referred as Alzheimer's disease (AD) tends to start with moderate cognitive impairment (MCI) and progressively worsens. Determining if the patient has MCI and estimating the likelihood that the MCI patient would acquire AD is the most difficult and crucial choice in the diagnosis of AD. It is symbolized via behavioral irregularities, memory depreciation, and neurological decline. It records for 60 to 80% of the

dementia cases and is the fourth most common cause of mortality worldwide [1, 5, 7]. Worldwide, currently there are 50 million sufferers of dementia sufferers; by 2050, the figure is expected to increase to 152 million [1, 7]. The main cause of AD is an increased rate of brain cell death induced by excessive levels of amyloid β protein buildup, which obstructs signal transmission in brain cells. It is discovered that aberrant changes in the volume and the loss of Gray Matter (GM) are frequently seen during the progression from MCI to AD and the structures of the temporal medial lobe. The Tissue loss begins in GM and progresses to the (HC) hippocampus, (WM) white matter, and (CC) corpus callosum. The cerebral cortex and the hippocampal regions shrink while there is expansion in AD sufferers' ventricles. In addition to memory loss, patients with this condition have mood swings, trouble making decisions, uncertainty while speaking, and a variety of behavioral issues in its early stages. AD sufferers gradually begin to lose their physical abilities, Patients with AD gradually lose their ability to operate their bodies, which ultimately results in death.

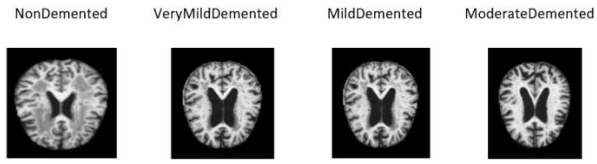

Fig. 1. Alzheimer disease various stages

The disorder gradually worsens everyday functioning and quality of life as it progress from moderate cognitive impairment (MCI) to severe dementia [5, 6, 20, 27]. Neurofibrillary tangles and Amyloid plaques that causes neurodegeneration and brain shrinkage, are Alzheimer's disease (AD) characteristics [5, 8, 12, 30]. Short-term loss of memory, language barriers, mood swings, and poor judgment are some of the early signs that lead to severe mental and physical abnormalities [5, 8, 30]. Even though AD not able to stopped, there are steps that may be used to decelerate its advancement if caught early on. These include taking part in physical activity, retaining a healthy diet, getting adequate sleep, and interacting with others. The diagnosis of AD has grown more difficult despite recent improvements in clinical trials because of the large rise in patients and potential errors in neuroimaging analysis. Thus, it is often chosen to combine neuroimaging data with clinical data such as MMSE (Mini-Mental State Examination) & CDR (Clinical Dementia Rating) scores for diagnosis.

Effective intervention involves early diagnosis, but this can be challenging since symptoms might appear gradually and individuals may not be aware of them [2, 9, 16]. Neuropsychological tests and neuroimaging method such as MRI, PET, and CT scans being the most common that usually involves in the diagnosis [2, 10, 14]. To enhance early detection and precisely identify AD phases, cutting-edge techniques like deep learning and computer-aided diagnostics are being evolved [7, 11, 12, 20, 30]. The treatment goal for AD, regardless of the fact that research is still continuing, is to manage symptoms and postpone the disease's development by lifestyle changes and perhaps disease-modifying medications [5, 7, 17, 18, 30]. The increasing incidence rate of AD highlights the need for better disease diagnosis along with more public awareness to enable prompt patient and caregiver assistance and intervention [1, 7, 20, 27].

There are limitations with conventional diagnostic techniques which rely on MRI, PET, and

CT scans that often result in a delayed diagnosis [2, 5]. It is beneficial to incorporate neuroimaging data with AI, especially machine learning (ML) and deep learning (DL) methods. By integrating genetic and cerebrospinal fluid (CSF) biomarkers and employing alternative modalities like EEG, these techniques aid in addressing issues such data scarcity and noise in medical pictures [14, 15, 17, 20]. CNNs can reduce inaccuracies associated with conventional approaches by dynamically learning features from images [1, 8]. Recent developments include lightweight networks like Mobile Net and Shuffle Net, which can be helpful in limited-resource settings, and hybrid CNN-LSTM designs [2, 3]. [31] Recommends the FEESCTL model to control computational costs and overfitting, attaining high accuracy in early AD identification. Convolutional Neural Networks (CNNs)—greatly enhance the capability to diagnose AD early and accurately using structural MRI (sMRI) analysis [8].

A comprehensive view of brain disease is provided by multi-modal techniques that integrate sMRI and functional MRI (fMRI) data, improving diagnostic accuracy [9]. Alzheimer's disease (AD) phases may be categorized more accurately with standard models because of the use of multi-task learning in models like AlzheimerNet [4]. Consolidating data from many neuroimaging modalities (MRI, PET, DTI) enhances diagnostic precision and offers unique perspectives on AD [13, 23]. Data from many modalities can be integrated using methods like wavelet transform and machine learning [13, 23]. Since MRI is non-invasive and generate high-resolution images of brain tissue, it is the recommended method [18] and differentiate between moderate cognitive impairment (MCI), stages of AD dementia, and healthy controls with good accuracy [15, 20, 25, 27, 29].

Efficiency and performance may be improved by using transfer learning with pre-trained models like ResNet-50 and VGG16 [16, 18]. Resolving class imbalance in datasets, creating techniques for AD diagnosis utilizes additional modalities like EEG, integrating genetic and CSF biomarkers, and enhanced model interpretability [14, 15, 17, 20, 28]. Techniques for ensemble learning may increase persistence and accuracy [29, 32]. Deep learning methods for voice analysis have the ability to detect language impairments and early indicators of AD [17, 24]. AI-driven techniques possess the capability to significantly improve patient care and AD diagnosis by offering earlier, more precise, and more effective diagnostic tools.

2. Biomarkers and Neuro Anatomy of Brain

Alzheimer's disease is a complicated degenerative brain illness which affects structure and function of the brain. Detecting AD involves a combination of clinical assessments, cognitive testing, and neuroimaging approaches. Medical experts may utilize numerous neuroimaging approaches to analyses the particular parts of the brain for functional and structural abnormalities while detecting Alzheimer's disease. Understanding the brain structure and how it changes in Alzheimer's disease can aid in early diagnosis and analyze. The rostral hippocampus, medial amygdala, globuspallidus, lateral amygdala, area 28/34 (entorhinal cortex), and caudal area 35/36 (Para hippocampal gyrus) are the most distinguishable areas for the categorization of AD vs. healthy controls. These regions are crucial in case of binary classification task.These were some of the important brain regions and structures that are quite often examined in the detection of Alzheimer's:

2.1 Neuro Anatomy of the Brain

Hippocampus: In the brain's medial temporal lobe, the hippocampus is tiny curving structure that is vital for memory formation and spatial orientation [20]. In individuals with Alzheimer's, the hippocampal regions are typically the earliest to be affected, resulting in challenges with memory and the ability to create new memories, and has been considered to be an effective biomarker for AD detection [11]. Neuroimaging approaches such as Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scans can detect hippocampal atrophy. MRI can detect the shrinkage of the hippocampus, confirming structural brain changes associated with Alzheimer's disease [22].Noticeably hippocampal, subcortical, and cortical subfields can be used as discriminating areas to categorize patients into cognitively normal (CN) and those who have early mild cognitive impairment (EMCI) [9].

Brain's Cortex: The Brain cortex incorporates the outer layer of the brain, is accountable for advanced cognitive activities such as thinking, reasoning, and problem solving. Alzheimer's disease also tends to affect the cerebral cortex, a pivotal brain region that controls cognition, perception, and voluntary movement [18, 24]. Neuroimaging can reveal cortical atrophy and thinning in Alzheimer's patients. Due to cerebral cortex damage, Alzheimer's patients have depleted function in the limbic region. [19], cortical regions begin to atrophy, leading to cognitive decline.

Amygdala: The amygdala, which is associated with emotional processing and is linked with the hippocampus, undergoes observable changes in Alzheimer's patients, frequently affecting mood and emotional regulation [29].

Basal Forebrain: The basal forebrain, responsible for acetylcholine production, a neurotransmitter crucial for memory as well as cognitive states may degenerate in Alzheimer's disease, resulting in lower acetylcholine levels. Changes in the structure or volume of the basal forebrain can be identified through neuroimaging.

Posterior Cingulate Cortex: The posterior cingulate cortex, integral to memory and attention processes, is frequently impacted in Alzheimer's disease. Imaging studies reveal diminished activity or atrophy in this brain region.

Entorhinal Cortex: The entorhinal cortex, crucial for memory and spatial navigation, is another brain region where alterations associated with Alzheimer's can be identified through neuroimaging.

White Matter Tracts: The brain's white matter comprises axons responsible for carry signals between various regions of the brain. In AD, changes in white matter can be captured through Diffusion Tensor Imaging (DTI), which assesses the validity of axonal pathways [21]. This allows for the visualization nerve conduction bundles walking direction in white matter. In AD, white matter may deteriorate due to the loss of myelin, the fatty substance that insulates axons, consequently impacting communication among brain regions.

Cerebrospinal Fluid (CSF) Analysis: Examining CSF can reveal information about the levels of biomarkers linked to AD, including tau proteins and beta-amyloid. Alzheimer's may be indicated by elevated tau and decreased beta-amyloid levels in CSF[15].

Functional Connectivity: Functional magnetic resonance imaging (fMRI) helps in the process

to gauge functional connectivity among distinct brain regions. With the context of Alzheimer's disease, observable disruptions in functional connectivity become apparent, signifying alterations in the communication patterns between various parts of the brain. This technique allows researchers and clinicians to discern changes in the dynamic interactions of brain regions, providing valuable insights into the functional aspects affected by Alzheimer's pathology.

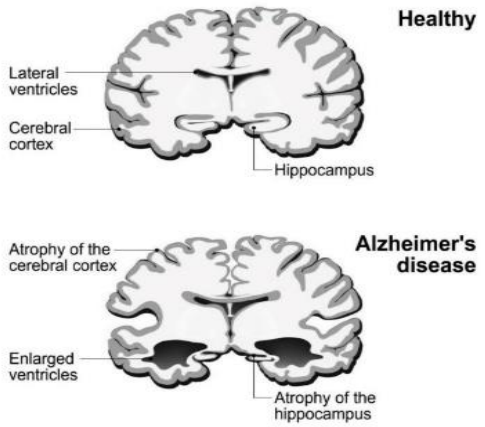

Fig. 2. Healthy brain and Alzheimer affected brain

Neurofibrillary Tangles: Within nerve cells, known as neurons, the presence of neurofibrillary tangles constitutes a prominent feature, particularly in the context of Alzheimer's disease. These tangles are characterized by abnormal protein deposits, primarily composed of tau proteins. In the Alzheimer's disease pathological progression, tau protein aggregates form intricate structures that are referred to as neurofibrillary tangles. Unfortunately, the existence of these tangles disrupts normal cellular function and, over time, contributes to the demise of the affected cells. The development of neurofibrillary tangles is a distinctive feature of Alzheimer's pathology,playing a crucial role in the neurodegenerative processes associated with the disease.

Amyloid Plaques: Abnormal clusters of beta-amyloid proteins that accumulate in between neurons are referred as amyloid plaques. These plaques are another defining characteristic of Alzheimer's that can interfere with cell-to-cell communication.

Ventricles: The brain's ventricles are areas that are filled with fluid. Brain imaging scans can show the enlargement of the ventricles due to atrophied brain tissue in Alzheimer's disease.

Shrinkage of Brain Tissue: Brain atrophy is the term for the shrinkage of brain tissue that occurs as Alzheimer's disease worsens. This is especially evident in areas such as the cerebral cortex and the hippocampus.

2.2 Biomarkers

A multimodal approach is used to detect Alzheimer's disease, and imaging methods including MRIs, PET scans, and cerebrospinal fluid studies are important in revealing relevant brain abnormalities. In order to exclude other possible causes of cognitive decline and to obtain a

definitive diagnosis, a thorough evaluation involving clinical exams and cognitive tests is required. Timely identification and management of the condition is facilitated by regular cognitive evaluations in at-risk persons. Early detection is critical since it enables more effective intervention.

Scientifically speaking, developments in imaging modalities like positron emission tomography (PET) and magnetic resonance imaging (MRI) have shown the temporal and geographical evolution of Alzheimer's disease, leading to a greater knowledge of the condition. These diagnostic tools, which include cerebral metabolism and amyloid deposits assessed by PET scans and structural and functional MRI, offer a complete picture of the disease's effects. Through the identification of distinctive patterns of structural and functional cerebral abnormalities, imaging, which was previously utilized to rule out surgically curable causes, is now actively supporting Alzheimer's disease clinical diagnosis. Furthermore, a major development is the capacity to see molecular disease, like amyloid deposits. Looking ahead, imaging is beginning to provide prognostic insights at this early stage, in addition to verifying a lengthy preclinical and presymptomatic time for identifiable harmful impacts.

MRI: An MRI, or magnetic resonance imaging, is a painless and safe test that creates detailed images of structural components of brain with radio waves and magnetic fields to acquire high resolution two-dimensional and three dimensional brain images with high quality. Radioactive tracers or X-ray radiation is not used in an MRI. In Alzheimer's disease detection, MRI scans play a crucial role by providing detailed images of key brain structures, such as the cerebral cortex, hippocampus, and ventricles [1]. Researchers extract features like voxel intensity and tissue density from MR images, employing various anatomical regions and mapping grey matter density to a high-dimensional space [10].

[11] Highlights the use of high-resolution T1-weighted sMRI scans at 1.5 T or 3.0 T, along with other modalities like FDG-PET, AV45-PET, Tau-PET scans, and rs-fMRI scans in Alzheimer's disease studies. These modalities offer insights into altered morphological patterns and functional connectivity associated with the disease. The benefits of MRI includes remarkable tissue contrast and enhanced imaging flexibility, the absence of ionizing radiation, and the capacity to provide valuable data on anatomy of the human brain [20]. MRI images can be widely classified into two types: structural MRI (sMRI) and functional MRI (fMRI).

sMRI: For the diagnosis of AD, it is the most often utilized MRI. The brain's morphological changes can be recorded and seen using sMRI. The primary structural alterations in Alzheimer's disease are typified by gray matter (GM) atrophy. The atrophy of gray matter linked to Alzheimer's disease can be seen and detected with high sensitivity using sMRI. Gray matter analysis, which uses sMRI to focus on the dense region of neuronal cell bodies that is essential for information processing, is used [3]. Three general types of sMRI are available: T1 weighted, T2 weighted, and FLAIR. [14] These scans provide detailed structural information about the brain, enabling the measurement of regional volumes, cortical thickness, and other morphological features that can be indicative of Alzheimer's-related pathologies.

T1 weighted:The longitudinal relaxation of a tissue's net magnetization vector (NMV) is required for a T1-weighted image. A gadolinium-infused T1-weighted MRI scan supplies information about state of the diseases by highlighting regions of the blood-brain barrier breakdown that symbolize inflammation. Tissues with a high fat content, like white matter,

appear bright on a T1-weighted scan, whereas regions filled with water (CSF) appear dark. [29] tested the performance of the final classifier ensemble based on three-axis slices. [27] Used T1-weighted MRI m VCC modality for imaging from the ADNI dataset. [16] Used MPRAGE baseline 1.5T T1-weighted MRI images in the axial plane, resized to 64 × 64 in the experiments. [5] Collected T1-weighted structural MR images for 379 subjects with Alzheimer's disease, mild cognitive impairment, and normal cognition from the ADNI dataset.

T2 weighted:Tissues that are high in fat content, like white matter, gives off a shadow appearance on a T2-weighted scan, while compartments filled with water, like CSF compartments, appear bright. Even though most, although not all, lesions (damaged tissue) have a tendency to develop edema and are linked to an increase in water content, this is a good way to demonstrate pathology [4, 16]. Using T1- and dual-echo T2-weighted sequences, the MRI images was centered on reliable longitudinal structural imaging with 1.5T scanners [8].

FLAIR: A sequence referred as fluid-attenuated inversion recovery (FLAIR) in magnetic resonance imaging (MRI) minimizes contrast between grey and white matter, suppresses the CSF signal, and generates strong T2 weighting. [8] The amalgamation of 2D FLAIR and T2-weighted imaging signifies focus on obtaining detailed data regarding tissue properties and pathologies.

fMRI: Functional Magnetic Resonance Imaging (fMRI) is a non-invasive imaging technique that successfully records both conscious and unconscious neural activity in the brain by utilizing a powerful magnetic field to yield detailed 3D images of the brain [5,15]. Changes in blood oxygen levels are used by the scan to measure neuronal activity because active neurons use more oxygen than do resting ones. Detailed visualization of brain activity throughout the entire organ is feasible with this indirect measure, which is called the magnetic resonance signal that is dependent on blood oxygen level-dependent (BOLD). Such extensive insights into the functioning of the entire brain cannot be obtained through any other technique. fMRI is used in the framework of Alzheimer's disease (AD) to look into functional alterations in the brain linked to the illness. [28, 9] However, when using functional mri (fMRI) to clearly differentiate between EMCI and NC, certain regions of the brain—like the occipital-mid-region, precentral-left, caudate-region, postcentral-left, and temporal-pole-mid-left—are more predominant. The following is how AD is identified using fMRI:

Resting State fMRI (rs-fMRI): [8] a common technique is to take a peek at impulsive blood oxygen level-dependent (BOLD) signals fluctuations, when an individual is at rest using resting state functional magnetic resonance imaging (fMRI). Resting state networks (RSNs) are identified, and variations in these networks can be symbolic changes in functional connectivity, which might be changed in individuals with AD.

Task-based fMRI: Task-based fMRI is another approach where participants carry out particular cognitive tasks while having their brain activity observed. This can assist identifying brain regions during specific cognitive tasks, are overactive or underactive. Task-based fMRI in AD reveal changes in brain activation patterns associated with language, memory, or other cognitive functions impacted by the illness. In AD, memory is especially affected. fMRI is frequently used by researchers to investigate memory-related tasks, including retrieval and encoding processes.

DTI: Diffusion tensor imaging tractography, or DTI tractography, is an MRI (magnetic resonance imaging) method that represents the internal structures of the body by measuring the rate at which water diffuses between cells. Diminishes in directional diffusion (fractional anisotropy, or FA) and incline in translational diffusion (mean diffusivity, or MD) can be used to assess white matter damage. Clinical medicine theory states that DTI illustrates the brain's fiber bundles' continuity of tissue structure [21]. In diffusion tensor imaging (DTI) studies, particular matter regions Lower fractional anisotropy (FA) values of Alzheimer's disease (AD) indicate compromised integrity connected to neuronal degeneration, beta-amyloid plaques, and tau tangles. Increased extracellular space and alterations in cellular architecture are reflected in elevated mean diffusivity (MD), which denotes neurodegeneration. Changes in radial diffusivity (RD) and axial diffusivity (AD) shed light on white matter pathology, such as demyelination or axonal degeneration. Regional differences in regions such as the hippocampus, cingulum bundle, and fornix underscore the diversity of DTI metrics, which are essential to understanding the course of AD [19].

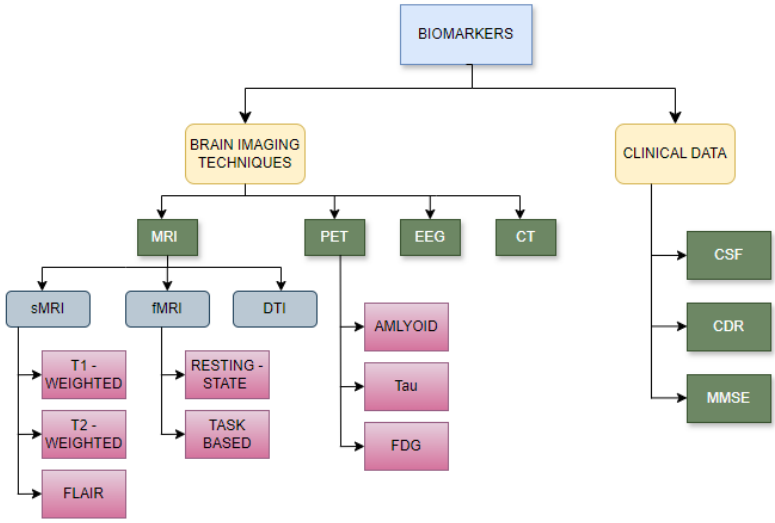

Fig. 3. Biomarkers to detect AD

PET:In Positron Emission Tomography imaging, a small quantity of a radioactive material, known as a radiotracer, is induced into the body. [4] The radiotracer emits positrons, which are positively charged particles. Gamma rays are generated when a positron and an electron in the body annihilate one another. A PET scanner detects these gamma rays, and the information it gathers is used to generate intricate three-dimensional images of the interior organs and structures [13, 23]. Here's how AD is identified using PET imaging.

Amyloid-PET (AV-45 PET): Amyloid-PET scans are a popular way for observing accumulation of beta-amyloid plaques in brain [11]. The protein beta-amyloid is responsible for the formation of plaques in the AD patients suffers brain. These plaques bind to the radiotracer used in amyloid-PET, making it possible to detect and quantify them. AD is symbolized by increased amyloid plaque deposition.

Tau-PET: Tau is a protein that causes tangles in the brains of AD patients [24]. With tau-PET,

misfolded tau pathology can be visualized and evaluated, offering insights into the development of the disease.

Fluorodeoxyglucose PET: [9] FDG-PET is used to assess brain glucose metabolism. Reduced glucose metabolism is a defining feature of Alzheimer's disease (AD), especially in areas related to memory and cognition. FDG-PET can highlight those areas of the brain which do not exhibit optimal neuro function, indicating neurodegeneration.

EEG: EEG, a non-invasive neuroimaging tool, diagnoses Alzheimer's disease (AD) by analyzing brain wave patterns (alpha, beta, delta, and theta). EEG detects AD-associated patterns like lowered alpha and elevated theta waves. ERPs reveal memory and attentional deficiencies in the brain. EEG measure impaired connectivity, indicating neural network issues in AD. Over an extended period of time tracks cognitive decline. [17] EEG technology is to describe abnormal neuronal activity related to different stages of AD. It involves changes in signal complexity in the parietal and occipital region along with changes in the power spectrum of low-frequency oscillations in the occipital area as neural biomarkers for diagnosis and forecasting AD.The occipital and parietal regions, responsible for visual processing and sensory information, respectively, are emphasized as key areas where EEG technology can detect Alzheimer's disease-related abnormalities in neural activity. It is illustrated that the occipital and parietal areas handle visual processing and sensory information, respectively—are important locations where EEG technology can identify abnormalities in neural activity linked to Alzheimer's disease.

CT: Computed tomography (CT) scans are not considered as the main imaging modality for AD detection. The primary feature of AD, which is a neurodegenerative condition, is the development of abnormal protein aggregates in the brain, such as tau tangles and beta-amyloid plaques. Although CT scans can provide precise images of the structure of the brain, they might not be sensitive enough or specific enough to identify these particular pathological alterations linked to AD.

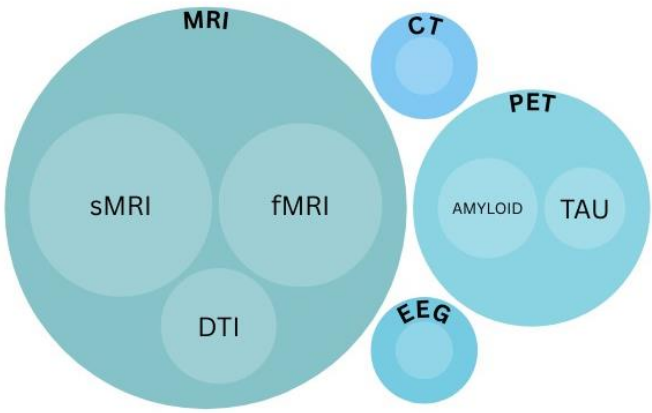

Fig. 4. Representing utilization ration of imaging techniques

CINICAL DATA: In Alzheimer's Disease (AD) detection, vital imaging data biomarkers include magnetic resonance imaging (MRI), positron emission tomography (PET), and

diffusion tensor imaging (DTI). The necessity of clinical validation by integrating imaging data with cognitive tests, especially Mini-Mental State Examination (MMSE) and Clinical Dementia Rating (CDR) scores enhance the accuracy of AD categorization.

CSF: Cerebrospinal fluid (CSF) analysis plays an important role in Alzheimer's disease (AD) diagnosis by assessing biomarkers associated with its underlying pathological processes. Key CSF /APOE ε4 biomarkers include Aβ(1–42), indicating beta-amyloid plaque deposition; phosphorylated Tau (p-tau), a marker for neurofibrillary tangles; and total Tau (t-tau), associated with neurodegeneration [5]. Low levels of Aβ(1–42) and elevated p-tau and t-tau in CSF are indicative of AD pathology [14] . The combination of these biomarkers aids in identifying peoples with an increased risk of AD, especially in early stages with subtle symptoms. [17] While CSF analysis provides valuable insights, AD diagnosis involves a comprehensive evaluation, including clinical assessments, cognitive tests, and imaging studies, with the use of CSF biomarkers more common in research and specialized clinical settings.

CDR: The Clinical Dementia Rating (CDR) is a employed to determine the progresses from normal to mild to moderate to severe stages of the disease [19]. The clinical dementia rating (CDR), which is a way of measuring the classes together for reviewing the occurrence and frequency of cognitive issues in Alzheimer's disease and related symptoms, can be utilized to differentiate these stages. This measure is utilized in both long-term research works and clinical testing. Six distinct neuro behavioral domains are evaluated by the CDR: memory, orientation, performance in the home and passions, judgment and problem-solving, community affairs, and personal care. The CDR scale has scores varies from 0 to 3, that correlate to different degrees of dementia. A CDR value of 0 indicates no dementia, 0.5 suggests questionable dementia, 1 signifies mild cognitive impairment (MCI), 2 denotes moderate cognitive impairment, and 3 reflects severe cognitive impairment.

MMSE: The Mini-Mental State Examination (MMSE) stands as a widely utilized cognitive screening tool crucial in the detection of Alzheimer's Disease (AD) [10]. It evaluates diverse cognitive domains, including memory, orientation, attention, language, and visuospatial abilities. With scores ranging from 0 to 30 points, lower MMSE scores signify more pronounced cognitive impairment [31]. Tracking changes in scores over time becomes instrumental in monitoring the progression of cognitive decline [32]. Hence, the MMSE, in conjunction with additional clinical and neuroimaging data sourced from the NACC dataset, contributes significantly to the identification, evaluation, and comprehension of Alzheimer's disease.

3. Datasets

Millions of people worldwide have been affected by Alzheimer's disease, which is a degenerative progressive neurological disorder that is characterized mainly by memory loss, cognitive decline, and behavioral issues. Researchers, data scientists, and healthcare experts utilize Alzheimer's datasets to better diagnose and come up with cures for this devastating disorder. All of these data types are required for investigating the progress of the disease, locating potential biomarkers, and creating deep learning models for early detection and

monitoring. These datasets, which include a broad range of data types, which includes clinical and demographic data, neuroimaging scans, genetic data, cognitive assessments, etc., are discussed here and are available publicly online.

3.1 ADNI Dataset

ADNI stands for "Alzheimer's disease neuroimaging initiative". ADNI is an latest research endeavor and collaborative effort which was initiated in the year 2004 to enhance our knowledge of AD and associated illness. This multi-centre project aims to just provide biological, imaging, and clinical measures for analysing the disease's progress and early detection. [12]. The ADNI database data repository contains information on roughly 2220 participants from four trials (ADNI1, ADNI2, ADNI GO, and ADNI3), including imaging, clinical, and genetic data.

The main goal of ADNI was to establish MRI imaging as well as other biomarkers for clinical trials or cognitive assessments along with the advanced understanding of AD [31]. To help develop and test new treatments for Alzheimer's ADNI collaborates with a wide range of organizations, including National Institute on Aging (NIA), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), the Food and Drug Administration (FDA), pharmaceutical companies and academic institutions.

Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, which is a large, publicly available dataset that includes MRI scans, PET and CSF analysis, from individuals with Alzheimer's disease, mild cognitive impairment, and normal cognition. The dataset includes both structural and functional MRI scans, as well as other clinical and demographic information [4]. Most of the research focuses mostly on ADNI, ADNI GO, ADNI 2 [1, 3, 9, 27].

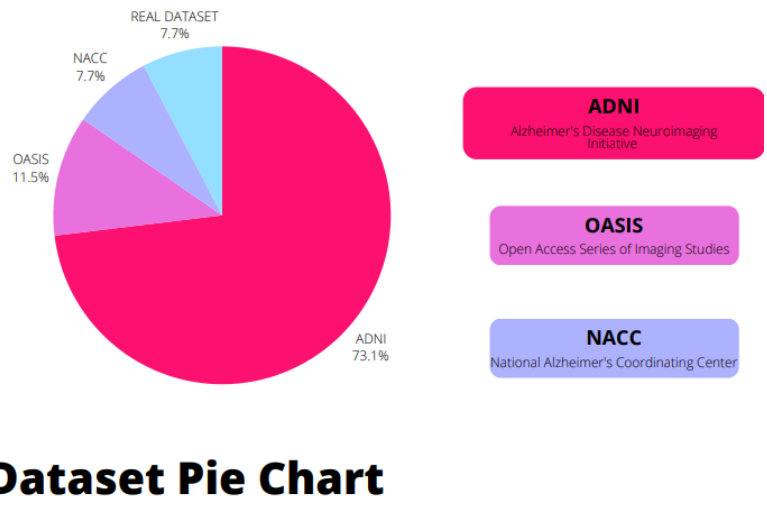

Fig. 5. Pie chart representing the different dataset utilization

3.2 OASIS Dataset

The "Open Access Series of Imaging Studies" (OASIS) collection is a set of neuro-imaging

datasets that are availble for research study and analysis at no cost, and includes cross-sectional and longitudinal MRI and PET data [12]. With the use of the open-access dataset, major advancements in neuroscience have been made in understanding neurodegenerative disorders and how they affect the structure and function of the brain. The dataset provides a flexible resource for clinical and cognitive study which is neuroimaging-based, spanning a variety of genetic, cognitive, and demographic variables. The Clinical Dementia Rating (CDR) classifies it into many categories, ranging from healthy aging to psychological determination. The OASIS provides the base for a wide range of study initiatives in this field [6, 16].

3.3 NACC Dataset

The National Alzheimer's Coordinating Center, or NACC, was founded by the National Institute on Aging (NIA) in 1999. Various Alzheimer's Disease Centers (ADCs) in different parts of the US are coordinated by NACC to gather, preserve, and evaluate data from numerous ADCs engaged in Alzheimer's research. Information about patients with Alzheimer's disease and other dementias is included in this data. Several researchers have adopted this repository for their model [32].

3.4 Real Dataset

[17] Bin Jiao, et. al., used real dataset from Xiangya Health Management Center and were approved by the Institutional Review Board of Xiangya Hospital, Central South University, China. 890 individuals were used for the research. The patients were enrolled between March 2017 and January 2022 in the Department of Neurology, Xiangya Hospital, Central South University.

Other Dataset

[24] The other datasets used for detection used for Alzheimer disease detection includes Hungarian MCI-mAD Database, the Wallet Story database, and the DementiaBank, Pitt corpus, ADReSS database, ADReSSo database subsets of the ADReSS database and Max Planck Institute Leipzig Mind-Brain-Body dataset. [28]

4. Preprocessing

Raw data must be preprocessed in order to be cleaned, transformed, and refined. To train machine learning models, it entails performing activities like noise reduction, addressing missing values, guaranteeing consistent scales, and generally improving data quality. In the end, this procedure helps to enhance the generalization and performance of the model. Preprocessing serves various essential purposes:

4.1 Intensity Normalization

[13] In the domain of deep learning, intensity normalization is an essential pre-processing phase that attempts to improve model performance and training by normalizing pixel intensities among input pictures [4, 7, 12, 30, 31]. Normalizing the input data helps the neural net to converge during training and guarantees that it can learn from a variety of data sources [3, 23, 26, 27, 10, 15]. Various types of intensity normalization methods for deep learning are as follows:

With Z-Score Normalization, pixel intensities are scaled to have a mean of 0 and a standard deviation of 1, and it is commonly used in medical imaging datasets.[10] With the simple technique of min-max scaling, pixel intensities are scaled to a range [0, 1]. Histogram equalization is very useful for bringing out fine features in medical pictures since it distributes pixel intensities over the whole dynamic range, improving contrast in images. To lessen the effect of outliers, percentile normalization modifies pixel intensities according to percentiles.

Moreover, there are MRI-specific normalization methods developed to rectify intensity fluctuations in MRI data brought on by non-uniform magnetic fields, such as N4ITK Bias Field Correction. [11, 14, 20, 29] Spatial normalization are often used on T1-weighted MRI data for brain imaging analysis. [24] The training process and model performance can be enhanced by scaling the extracted features to a standard range to guarantee that their magnitudes are comparable. All these methods work together to optimize deep learning models for medical image processing tasks, such as Alzheimer's disease diagnosis and other neuroimaging research.

4.2 DeNoising Filter

Noise reduction describes the process of reducing unwanted or irrelevant changes, interruptions, or abnormalities in the data when it comes to preprocessing for Alzheimer's Disease (AD) diagnosis [5, 9, 17]. The objective is to reduce or remove extraneous background noise while enhancing the signal or key AD-related properties. [2, 24] To remove MRI film artifacts, labels and X-ray markers, elevated-frequency components are targeted for elimination based on pheromone content and heuristics in MRI images using the Ant-Colony Optimization (ACO) technique. This method improves precision and lowers noise in delicate medical imaging data. [12, 27] noise reduction techniques, such as median and Gaussian filters, highlighting their value in improving neuroimaging quality and aiding in the training of classification models. Overall, by addressing issues linked to noise, these preprocessing methods help to increase the accuracy and dependability of medical imaging data [7].

4.3 Data Augmentation

Data augmentation methods like image flipping, random cropping and rotating can improve model resilience in deep learning to diagnose Alzheimer's disease by artificially varying the training dataset to handle issues with class imbalance and inadequate training data in the regard of image processing, especially MRI scans. [1, 4, 11, 18]. [5, 24] highlights transforming raw MRI pictures into 1-channel images of various sizes, cropping and resizing images to remove white areas and improve image quality, retrieving the region of interest (ROI) to concentrate on certain brain regions, and using data augmentation methods including rotation, zooming in and out, horizontal and vertical flipping, and lighting modifications. These methods are intended to improve MRI scan quality and deep learning model performance. [30] Transforming the original voice samples—for example, by introducing background noise, adjusting pitch, or changing speed is to provide more training data. Thus the robustness and generalization of the deep learning models are enhanced by data augmentation.

4.4 Registration

[9, 29 - 31, 20, 25, 26] Co-registration of PET and MRI images is crucial for the best possible fusion since MRI and PET include various types of information. Aligning the structural

information from MRI with the functional information from PET is possible through image registration. Procrustes analysis, a statistical technique, is applied in this work to match PET and MRI. The pictures are aligned as best they can be by scaling, rotating, and translating them [8]. Finding the matching sites in the two images is the first step in doing the Procrustes analysis on MRI and PET. The points that have been found may be landmarks or characteristics that appear in both PET and MRI scans. [15] Brain images can be registered to the Montreal Neurological Institute (MNI) T1 template. For this, the Linear Image Registration Tool (FLIRT) from FMRIB is frequently utilized. In order to match the input pictures with a reference template—such as the MNI T1 template [10]. FLIRT uses linear registration. This allows for uniform spatial normalization across patients enabling analysis in a standardized coordinate space later on.

4.5 Brain Extraction and Skull Stripping

Skull stripping and brain extraction are essential preprocessing techniques used on medical pictures, especially MRI scans. [10] Brain extraction is the process of separating brain tissue from non-brain components, such the scalp and skull. A variety of approaches, from deep learning models like convolutional neural networks (CNNs) and U-Net topologies to conventional thresholding, are used in this process. [20, 26,29] Skull stripping improves the procedure after brain extraction by removing any remaining non-brain material. This solves issues like as unpredictability in image quality and guarantees a more accurate portrayal of the anatomy of the brain. Skull stripping can be performed using methods like Otsu thresholding to extract the weak boundaries between brain and non-brain tissues. [4,11, 30]

4.6 Resampling

Resampling is the process which converts input data, usually images, to a standard format or resolution by changing its size or resolution [7, 8, 18]. The technique of upsampling, in which the labels with fewer images are enlarged or unsampled, is used to balance the data. The total size of the dataset is 2900 when all the classes are resampled to create 580 MRI pictures. The data are suitably structured, denoised, scaled, standardized, and improved. The technique of downsampling is to decrease the supplied data's resolution, this is usually accomplished by using methods like pooling layers [11, 27]. Preprocessing methods like oversampling minority classes or undersampling majority classes can assist build a more balanced training set in circumstances when classes are uneven, improving the model's ability to digest from all classes [10].

4.7 Other Preprocessing Tools

[12, 31] The neuroimaging framework FreeSurfer is utilized for preprocessing and feature extraction. The setup not only performs normalization but also volumetric analysis of brain structures from MRI data, cortical parcellation, subcortical and automated white matter segmentation, and skull stripping. The Alzheimer's disease diagnosis is influenced by these actions. [4, 13] CNN's ability to analyze T1-weighted MRI data is intended to be improved through the integration of FreeSurfer.[8] The ADNI dataset was preprocessed and divided into planes of cerebrospinal fluid, white, and grey by the authors using SPM 12. The VBM-DARTEL method is used for detailed preprocessing of sMRI images. This includes segmentation, template creation, flow field generation, and normalization. [10] Using the

FMRIB's Linear Image Registration Tool, all the images of brain are registered to Montreal Neurological Institute (MNI) T1 template (FLIRT).

[29] The CAT12 toolbox is emphasized since it is widely used for structural brain MRI preprocessing and provides features including image smoothing, spatial normalization, and skull stripping. The additional preprocessing tools include SPM (Statistical Parametric Mapping), ANTs (Advanced Normalization Tools), FSL (FMRIB Software Library) for the examination of brain extraction metrics in 3D-CNN, and DPABI [25,30], [21,28]. Brain extraction, white matter and gray matter segmentation, cerebrospinal fluid extraction, skull stripping, and normalization are among the preprocessing procedures. While some studies list the tools used specifically, others just describe typical tools without going into depth.

Research emphasize the need of quality control and standardization in preprocessing, such as t-distributed stochastic neighbor embedding (tSNE) algorithms, manual inspection, and harmonization to guarantee data consistency and reduce biases [15] . Preprocessing methods and tools are generally chosen based on particular research goals, data properties, and the requirement for uniform and standardized processing throughout various studies.

5. Feature Extraction

Feature extraction is crucial for several of reasons in the AD detection. Identifying or converting features that capture important brain structure or function characteristics associated with AD, it helps to minimize the dimension of the data of complicated brain images, such as Neuroimaging or PET scans which in turn improves data representation and computing performance. Feature extraction enhances classification performance by giving machine learning algorithms access to more pertinent data. This leads to improved differentiation between various cognitive states and higher model preciseness, specificity, and sensitivity. Furthermore, these methods frequently find underlying patterns or biomarkers linked to the pathology of AD, providing insights into the disease's causes, pinpointing intervention targets, and assisting in the creation of individualized treatment plans. All things considered, feature extraction improves classification, helps with early detection and prognosis, finds pertinent biomarkers, streamlines data, improves comprehension of the disease's causes, and extends our knowledge of AD.

5.1 Patch- Based

Feature extraction from input photos using patch-based techniques, which entails extracting features from specific areas of the data. [4] Understanding underlying structures in image analysis jobs requires the ability to capture precise information and patterns existing in specific sections of the pictures, which is made possible by this technique. [3, 11, 5, 7] The usage of architectures or techniques that operate on patches of image data, such as InceptionV3, PartialNet, and pre-trained CNN architectures. [11, 16, 18] are likewise classified as patch-based; they discuss the usage of architectures such as VGG16, InceptionV3, ResNet, and DEMNET. In [20, 29] features are extracted from brain MRI data using a DenseNet model. DenseNet is suited for patch-based feature extraction, particularly in situations where local spatial information is crucial, because of its dense connection structure, which enables features to spread across the network.

5.2 Voxel- Based

In neuroimaging, voxel-based methods take each voxel as a data point and extract characteristics directly from the data's voxel intensities. They also capture the spatial distribution of voxel values in brain pictures. This technique works especially well for deciphering 3D volumetric data, such as MRI or fMRI images, because the spatial arrangement of voxels provides important details on the composition and operations of the brain. [8, 10] focus on directly extracting features from the voxel intensities of the neuroimaging data, they are classified as voxel-based approaches because they use techniques that function either explicitly or implicitly at the voxel level. [30] Covers voxel-based features and other feature extraction.

5.3 Slice – Based

With slice-based methods, specific characteristics from individual thin strips of brain images, such MRI scans, are extracted to provide comprehensive details on the patterns and architecture of the brain in each slice. This approach is useful for situations where knowledge from particular slices is relevant to comprehending the fundamental properties of the data since it evaluates features at the slice level. [6] Incorporates feature extraction and pre-processes 2D MRI images, concentrating on intra- and inter-slice information. [23] Also uses wavelet transform fusion and ResNet-50; the first fusion stage probably includes processing whole image data slices, suggesting a slice-based method. In addition to voxel-based features, Slice-based characteristics [30] which enables in-depth examination of brain patterns and structures associated with Alzheimer's disease. [31] Uses the entropy image slicing approach, which falls within the slice-based category and focuses on extracting features from individual MRI data slices according to their information content.

5.4 ROI - Based

In order to precisely characterize various classes or circumstances, ROI-based techniques include extracting characteristics from preset areas of interest in neuroimaging data, such as certain brain regions. By focusing on specific brain areas that are known to be impacted by Alzheimer's disease, these techniques make it possible to extract distinguishing characteristics for accurate disease categorization. In addition to voxel- and slice-based characteristics, [30] addresses ROI-based features, providing insights into brain areas associated to the pathways of Alzheimer's disease. Furthermore, [13,14] specifically discuss the use of methods such as radiomic analysis and Freesurfer to extract features from segmented brain regions or particular areas of interest in MRI images, improving our knowledge of alterations associated with Alzheimer's disease in these regions.

6. Deep Learning Techniques

Deep learning is a sub-set of machine learning has become increasingly popular, especially with the addition of Convolutional Neural Networks (CNNs), which are quite good at retrieving characteristic features from input data. CNNs impressive performance in detecting, classifying, and segmenting pictures has given rise to its proposal in a variety of fields, which includes medical imaging. Convolutional, pooling, activation, and fully connected layers render up a common CNN architecture, which eventually results in a SoftMax activation

function for probability based classification. In extracting features, the convolutional layer utilizes filters with shared weights, and padding diminishes information loss at image borders. Max- pooling and average pooling are typical tasks in pooling layers, which reduce dimension of the data and optimize training efficiency. The non-linearity which activation layers introduce is vital for improving the network's reasoning capacity; common functions are ReLU, Sigmoid, and Tanh. Finally, for accurate label prediction, fully connected layers make use of the information extracted. All things considered, CNNs are an efficient approach for feature extraction and classification applications, especially in the study of medical images. Using pre-trained convolutional layers from a model obtained on a large dataset, transfer learning with CNN involves extracting attributes from input images. The complete model is then fine-tuned on the objective dataset when further layers are added or modified for the particular task. This method is very helpful in areas with little labelled data, such medical image analysis, as it expedites training and enhances generalization.

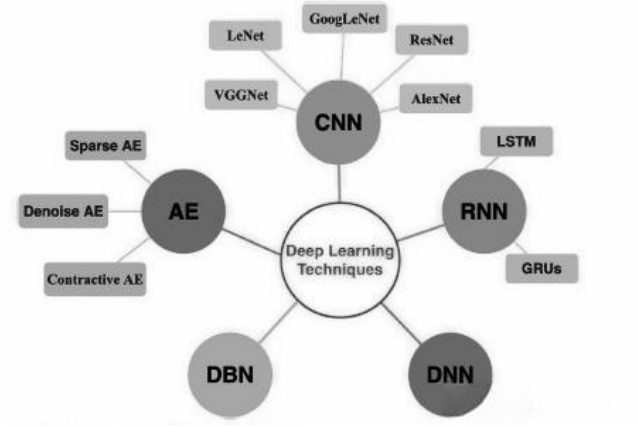

Fig. 6. Deep Learning Techniques

CNN: [1] Introduces a shallow CNN architecture with transfer learning and hybrid classification techniques, aiming for accurate AD diagnosis and staging from brain MRI images. [11] Explores transfer learning by adapting pre-trained 2D CNN models to the AD classification task, highlighting reduced training time and improved performance. The utilization of deep learning techniques, including CNNs and deep neural networks, along with image pre-processing and hybrid approaches to enhance AD detection and classification accuracy while mitigating overfitting challenges [12]. Fusion model combining CNN processing of MRI scans with traditional machine learning classifiers to improve dementia assessment and AD diagnosis accuracy, leveraging both imaging and non-imaging data [15]. [16] Introduces a Siamese CNN architecture for 4-way AD classification, utilizing both pre-trained and non-pretrained CNNs to address data scarcity issues. [25] Focuses on 3D CNNs for automatic brain segmentation and classification to differentiate AD dementia from mild cognitive impairment and normal cognition. [26] Employs CNNs for high-accuracy early detection and prediction of AD using MRI images. [29] Introduces a novel approach combining CNNs with Ensemble Learning for accurate classification of subjects with MCI or AD, aiming to distinguish between different cognitive states.

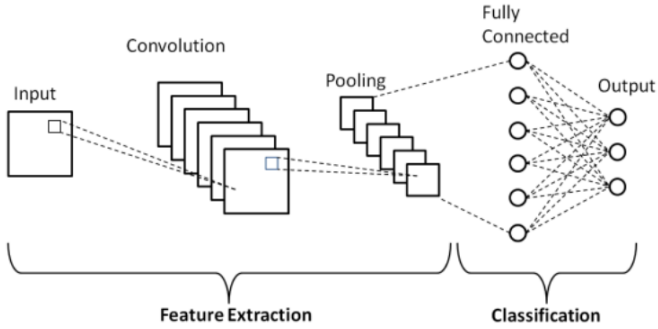

Fig. 7. CNN Architecture

[2] Introduces a Hybridized Deep Learning Approach to detect Alzheimer's Disease using MRI data which enhances the neural network performance through simultaneous channel usage, Ant-Colony Optimization for pre-processing, and Modified Fuzzy C-means for clustering. The goal is to enhance AD detection by extracting common characteristics across multiple MRI slices. [8] Presents a Neuro-Dynamic Functional Network for the detection of Alzheimer's Disease using rs-fMRI images. It employs customized deep learning models to leverage higher-order functional connections throughout the frequency bands in the brain. The approach includes an ensemble process and utilizes the Inception V2 architecture to improve AD and MCI detection accuracy. [24] Aims on analyzing voice data for Alzheimer's disease detection in various health situations. It utilizes techniques such as Deep Neural Networks (DNNs), pre-trained models like BERT, Machine Learning Classifiers, Data Augmentation, and fine-tuning pre-trained models on dementia-related databases. [32] Aims to improve deep ensemble learning based classification. It employs Sparse Autoencoder (SAE), Base Classifiers, Deep Belief Network (DBN), Neural Networks (NNs), and Ensemble of Probabilistic Predictions.

[23] Proposes a unique approach to diagnose the Alzheimer's disease earlier by integrating PET and MRI scans. It uses multimodality fusion based on wavelet transform for comprehensive data analysis, ResNet-50 for feature extraction, and a Random Vector Functional Link (RVFL) classifier for classification. An evolutionary algorithm optimizes the process, leveraging complementary information from both modalities to enhance diagnostic accuracy and effectiveness. [31] Proposes an approach for early Alzheimer's Disease diagnosis using structural MRI data, employing techniques such as Entropy Image Slicing, Transfer Learning with VGG-16, and a Three-Way Classification Model. [27] Focuses on early detection and classification of Alzheimer's disease stages through an end-to-end framework incorporating simple CNN architectures, VGG19 transfer learning, and data augmentation.

[7] Presents an ensemble of CNN models, notably featuring the MobileNet model, for Alzheimer's disease diagnosis and progression prediction by combining neuroimaging data with clinical evaluations. [3] Introduces a multimodal diagnosis method for Alzheimer's Disease using 3DShuffleNet, PCANet fusion, and SVM classification, enhancing accuracy with both structural and functional MRI data. [5] Leverages a multi-resolution ensemble PartialNet architecture for Alzheimer's Disease detection, emphasizing feature reuse and ensemble learning for improved performance. [10] Develops a modified 3D EfficientNet and CNN-based classifier for Alzheimer's Disease and high-risk MCI detection, achieving high

accuracies with architecture selection using the AutoML NAS framework.

[6] Presents Biceph-Net, a simple framework for Alzheimer's disease diagnosis using 2D MRI scans. It employs both intra-slice and inter-slice information using the deep similarity learning techniques and the Biceph-module. In order to achieve high classification accuracy and computational efficiency, the technique focuses on feature embedding and similarity learning to ensure accurate AD diagnosis. [4] Presents AlzheimerNet, a deep learning network which utilizes brain MRI images to classify AD stages. It also enhances hyperparameters through the use of an ablation study and fine-tunes the InceptionV3 architecture. The model's 98.67% classification accuracy for AD shows how well deep learning works for AD diagnosis.

Table 1. Deep Learning Architectures for the diagnosis of Alzheimer's Disease

Reference	Input Modality	Type of Input Data	Architecture	Methodology	Strengths	Limitations
1, 4, 26	MRI	T1-Weighted/T2-Weighted MRI	CNN	Varied (Preprocessing, Data Augmentation, Fine-tuning)	Non-invasive, Early Diagnosis, High Accuracy	Validation on specific dataset, Needs further testing
2, 23, 30	MRI+PET	T1-Weighted MRI & PET Scans	CNN+LSTM, Wavelet transform, ResNet-50, RVFL	Varied (ACO noise reduction, MCFM segmentation, Wavelet fusion)	Improved accuracy with multi-modal data	Limited by data size, ROI-based limitations, data fusion challenges
3	Multimodal	Gray matter (sMRI), PCA kernels (fMRI)	3DShuffleNet, PCANet, SVM	Preprocessing, Fusion (KCCA), Classification (SVM)	Comprehensive feature fusion, lightweight networks	Performance variability, Dataset size limitation
5, 7	MRI	T1-Weighted/T2-Weighted MRI	PartialNet, CNN+MobileNet	Cascaded multi-resolution ensemble, Data augmentation	State-of-the-art performance, efficient feature extraction	Interpretability issues, limited to single dataset
6, 31	sMRI	T1 MR Images	Biceph-Net (VGG-16), VGG-16 (Transfer Learning)	Deep similarity learning, Entropy slicing	High accuracy, computational efficiency	Lack of preprocessing details, limited dataset comparison
8	rs-fMRI	T1, dual-echo T2	InceptionV2	Resting-state fMRI analysis	Novel approach, promising results	Small sample size, single modality limitation
9	Multimodal	T1, 18F-FDG-PET	Fusion (DWT, VGG16, ViT)	Pixel-level fusion	Comprehensive data integration, high accuracy	Limited dataset, fusion optimization
10	MRI	T1-Weighted MR	3D EfficientNet (MBConv)	Modified EfficientNet	Competitive classification results	Sample size limitation
13	Multimodal	Subcortical and Cortical Regions	Freesurfer + Machine Learning + Multimodal Fusion	Feature extraction, Multimodal Fusion Framework	Captures Intra/Inter-Relations, Improved Accuracy	Freesurfer preprocessing details missing
14	CSF Biomarkers & MRI	T1-weighted MRI	ApV Biomarker Derived from LASSO	Train model to compute biomarker	Highly Accurate	Requires further validation

15	Multimodal	Demographics, MRI, fMRI	Deep learning framework (PyTorch)	Analysing MRI with CNN, others with traditional classifiers	High accuracy, competitive with specialists	Needs further development for specific dementia types
16	MRI	T1-Weighted MRI	Siamese CNN	Triplet-loss function	Robust feature learning, efficient with limited samples	Limited performance due to training sample size
20	MRI	Hippocampus	CNN+VGG16	Feature extraction	High accuracy	Class imbalance in data
21	DTI	Not specified	Encoder, WCU (Wavelet Convolution Unit), Decoder, FC layers, Softmax activation	Network uses WCU for feature extraction	Improved classification performance	Lacks discussion on computational efficiency and scalability
27	MRI	2D/3D T1w structural brain MRI	CNN+VGG19	Resampled imbalanced data, data normalization, feature extraction	High accuracy	Sample size limitation
32	MRI	Not specified	Deep Ensemble Learning (DBN, Neural Networks)	Sparse autoencoders for feature learning, ensemble classification	Improved accuracy	Needs further validation on diverse cohorts

[9] Introduces a method for Alzheimer's Disease (AD) detection which combines the Vision Transformer (ViT) model with wavelet transform. The ViT model fine-tuned on natural images, is adapted for feature extraction from medical data, while the wavelet transform reduces noise in MRI and PET images. An MLP classifier is then used for classification. [13] Utilizes methods like train-test-split and cross-validation to analyze illness categorization frameworks based on MRI and PET data. These methodologies help to assess model performance parameters including as accuracy, precision, specificity, recall, F1-score, and AUC, as well as prediction stability.

[14] Introduces the "Alzheimer's Predictive Vector" (ApV), a predictive model on inter statistical morpho-functional characeristics from T1-weighted MRI scans which uses a two-stage LASSO. It is instructed on the ADNI dataset and evaluated on several cohorts to enhance the Alzheimer's disease diagnosis accuracy by integrating cognitive scores with CSF-based biomarkers. [17] Focuses on the study of EEG signals to identify biomarkers of Alzheimer's disease in its initial stages. preprocessing EEG signals with filtering and re-referencing, feature extraction using absolute power, relative power, and Hjorth metrics, classifying groups with AD, MCI, and healthy controls utilizing LDA and SVM, statistical analysis to find relevant EEG features and perform ANCOVA tests, and using EEG features combined with CSF biomarkers and APOE measurements to predict and assess the course of the illness. For the purpose of early Alzheimer's disease diagnosis and surveillance, it offers an integrated strategy that combines statistical analysis, feature extraction, classification algorithms, and EEG signal processing.

[18] Using methodologies for transfer learning, data augmentation, and feature extraction, this activity presents a strong deep learning solution for Alzheimer's disease identification. It

utilizes CNN models like Inception V4 in conjunction with cutting-edge techniques like capsule networks, VBM-DARTL, and GANs to enhance the classification accuracy. Besides that, SMOTE and cognitive assessment scores help to improve the overall approach's performance.

[20] Proposes DEMNET "a deep learning model specifically designed for early detection of dementia and Alzheimer's disease. In elaborating on DEMNET's design, the study highlights the early detection emphasis and its unique ability to identify specific situations at an early stage. In [21] a novel deep learning technique for Alzheimer disease diagnosis called WCU-Net is proposed. To extract cross-modal characteristics from data, WCU-Net blends CNN-based network topology with single-scale and multi-scale wavelet decomposition. It offers a distinct way of data analysis by combining wavelet decomposition with CNNs, which may enhance the precision of Alzheimer's disease detection techniques and progress the field by fusing deep learning, novel neural network designs, and EEG signal analysis.

7. Classification

[3] and [12] utilize Support Vector Machine (SVM) classifiers to diagnose Alzheimer's disease via the use of SVM's ability to handle high-dimensional data and binary classification problems well. Paper [18] focuses on the classifying MRI pictures into three groups: Normal Control (NC), Mild Cognitive Impairment (MCI), and Alzheimer's Disease (AD). [2] CNNs combined with Long Short-Term Memory (LSTM) networks extract features from MRI and PET images for early Alzheimer's detection, capturing temporal dependencies.

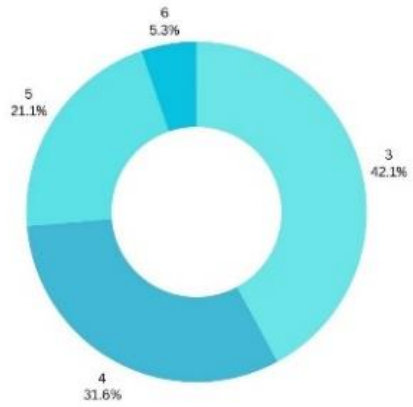

Fig. 8. Number of stages classified

CNN-based models like AlzheimerNet, DEMNET [20], SCNN [17], and others classify Alzheimer's disease stages using MRI images, with approaches including fine-tuning InceptionV3 [4], transfer learning [7], and triplet-loss functions. [5] Deep learning models, including 3D CNNs [25], distinguish cognitive states from MRI features, with approaches like transfer learning and multi-class support [27] for accurate Alzheimer's disease detection [26]. [9] Multilayer Perceptron (MLP) classification technique used with features from the vision transformer (ViT) model and wavelet transform for Alzheimer's disease detection. [29] CNN-

EL approach, combining CNN with Ensemble Learning for accurate classification of MCI or AD subjects using MRI data.

[31] Utilization of the VGG-16 network-based F E ES C T L model for sMRI image classification into AD, MCI, and CN categories. [32] Implementation of a deep ensemble learning framework for Alzheimer's disease classification, leveraging diverse base classifiers.

Table 2. Representing classification done in various studies

Dataset	Participants	No. of Stages	References used	Accuracy
ADNI	379 subjects (197 male and 182 female) with Alzheimer's disease, mild cognitive impairment, and normal cognition	3(AD, MCI, NC)	5	98.46%
ADNI	total of 153 baseline subjects(AD, MCI, and NC)	3(AD, MCI, NL)	8	98.10%
ADNI2	EMCI - 50 and LMCI - 50 participants were selected	3(AD, EMCI, LMCI)	9	MRI data: 81.25% PET data: 93.75%
Xiangya Health Management Center,	890 participants (MCI, AD, FTD, VCI, DLB, and HC)	3(HC, MCI, and AD.)	17	70%
ADNI	210 CN subjects, 210 MCI subjects, and 210 AD	3(NC,MCI, AD)	23	96%
ADNI	7635(1290 MRI images of ADNI1 Annual 2 Yr 3T and ADNI1 Baseline 3T, in nii extension format.)	3(NC,MCI,AD)	26	99%
ADNI	1,500 subjects, encompassing individuals with AD, MCI, and CN classifications	3(AD, MCI, NC)	31	93.05%, 86.39%, and 92.00%
OASIS	6400 3200, 64, 896, and 2240 for ND, MoD, MD, and VMD, respectively	ND, VMD,MD, and MoD	1	99.68%
OASIS - 3	512 MRI images from Kaggle and 112 PET images from Munich database	MCI people to stable people	2	98.50%
ADNI	34 cases of AD, 18 cases of early MCI, 18 cases of late MCI, and 50 cases of NC	4(AD, LMCI, EMCI,NC)	3	The accuracy is mentioned using Global Brain model and Cerebrum model: 1. For AD versus NC 88.0 % and 84.0 %. 2. For AD versus MCI 80.0 % and 85.0 %. 3. MCI versus NC, 68.0 % and 76.0 %. 4. EMCI versus LMCI, 90.0 % and 100.0 %.
ADNI, NACC, NIFD, PPMI, AIBL,	8916 participants with different cognitive statuses, including NC, MCI, AD, and dementia	4(NC, MCI, AD, and non-AD dementias)	15	95%

OASIS -3, FHS, LBDSU				
ADNI	162 participants: 37 are AD patients, 12 are CN, 53 are MCI, and 60 are in the EMCI.	4(CN and EMCI, AD and MCI)	16	ADNI and OASIS - 91.83% and 93.85%
ADNI	6400 MR Images of four classes with MID, MOD, ND, and VMD.	4(ND,VMD,MD,MODERATE DEMANTED)	20	95.23%
ADNI	902 - 153 AD patients, 167 LMCI, 363 EMCI, and 219 NC	4(AD vs. LMCI vs. EMCI and NC vs. LMCI vs. EMCI)	21	95%
ADNI	300 patient divided into four classes AD, EMCI, LMCI, and NC.	4(NC,EMCI,LMCI,AD)	27	93.61% and 95.17% for 2D and 3D
ADNI	1101 participants with 145 images in the AD class, 204 images in the EMCI class, 61 images in the LMCI class, 198 images in the MCI class, and 493 images in the NC class.	5(AD, LMCI, EMCI, MCI, CN)	7	96.22%
ADNI	579	5(AD, NC, MCI, pMCI, sMCI)	10	95.00%, 86.67%, and 83.33% for NC versus AD, NC versus pMCI, and sMCI versus pMCI, respectively
ADNI-2/ADNI-GO	183 ADNI subjects (69 in the AD group and 114 in the CN group),	5	13	98.94% from ADNI & 98.75% from ADNI2/GO
ADNI	783 different subjects (NC, MCI, and AD.)	5(HC, stable MCI, progressive MCI, MCI, AD)	14	HC / AD patients: 93% HC /progressive MCI: 90% HC / MCI: 80% stable /progressive MCI patients: 79%
ADNI	2456 different subjects (NC, MCI, EMCI, LMCI, SMC, and AD.)	6(AD, CN, EMCI, LMCI, MCI, SMC)	4	98.68%

8. Conclusion

Due to the significant increase in the number of diagnosed patients worldwide, Alzheimer's disease is a serious chronic issue. It has also one of the major reasons for elder people die from neurological impairment. Since it is harder to diagnose this disease in its early stages using traditional approaches, the results of computer-based system applications and medical healthcare experts are incorporated to detect different stages of AD. In order to successfully achieve this goal, deep learning techniques have become more important. We have analyzed the state of art in the AD detection over the several years in this report. In the introductory part, we covered the symptoms of AD and the numerous factors that is responsible to its progression. Additionally, we have compiled the several brain subregions that are primarily impacted by Alzheimer's disease. In the next part, a comprehensive analysis of different neuroimaging and clinical evidence utilized for diagnosis is presented. Combining several

neuroimaging modalities with clinical data has been shown to produce diagnostic results that are more accurate. The brain's complicated structure prompts the use of several pre-processing methods and techniques for effective neuroimage augmentation and extraction. Additional feature extraction techniques and their benefits and drawbacks have been enclosed. Better classification is achieved by the exact information it provides concerning the boundaries and textures of different brain subregions. In this survey, several Deep Learning models have been examined, with CNN being utilized most commonly in conjunction with other methods such as mobilenet, transfer learning etc., giving superior accuracies when compared with other models. The survey also covered the benefits and drawbacks of each approach. A few tables summarizes the AD stage categorization along with their accuracy and a comparative assessment of various literatures. The categorization and pervasiveness of various methodologies, imaging modalities, and datasets have been showcased using a variety of charts and pictures. Research is continuously being conducted to enhance the accuracy of AD stage detection and address the problems associated with early diagnosis. Researchers working in this field can get assistance from this survey on AD detection.

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